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Comparative evaluation of postoperative pain, periapical damage and bacterial disinfection after using endodontic needle and Eddy tips during root canal irrigation

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RESUMO

Introdução:

Um dos fundamentais objetivos do tratamento endodôntico é o controlo da dor, nomeadamente a eliminação da dor após o tratamento. A lesão química dos tecidos peri-radiculares após a extrusão, para além da constrição apical, dos irrigantes canalares, é um dos principais fatores que contribuem para a dor pós-operatória. Têm sido propostas técnicas e dispositivos para potenciar o efeito da desinfeção química no sistema de canais radiculares durante a preparação biomecânica, dada a dificuldade das soluções irrigantes atingirem toda a extensão do sistema de canais devido às suas complexidades anatómicas, permitindo que os biofilmes bacterianos persistam após os procedimentos de limpeza e instrumentação. Os detritos residuais e a *smear layer* podem promover a invasão bacteriana dos túbulos dentinários e diminuir a eficácia antimicrobiana dos medicamentos intra-canalares. O extravasamento de irrigantes durante o tratamento pode gerar sequelas, como dor, edema, equimose e dormência. Devido à pressão apical positiva gerada durante a irrigação, os irrigantes podem extruir para os tecidos periapicais, induzindo uma resposta inflamatória e dor pós-operatória. Sendo assim, são necessários sistemas/técnicas de irrigação seguros e efectivos, que previnam a inflamação periapical associada à extrusão de irrigantes.

Esta investigação avaliou o nível de desinfeção bacteriana, dano periapical e dor proporcionados pelo uso do sistema sónico EDDY®, um sistema recente de ativação do irrigante.

Objetivos: (1) Elaborar uma revisão sistemática da literatura, comparando os sistemas sónicos e ultrasónicos de ativação de irrigantes durante o tratamento endodôntico. (2) Realizar um estudo *ex vivo* para uma análise integrada dos sistemas sónico e ultrasónico durante a irrigação endodôntica, usando diferentes calibres apicais em termos de risco de extrusão, limpeza canalar e remoção de biofilme; (3) Conduzir um estudo clínico, para avaliar a dor pós-operatória subsequente à ativação do irrigante com o sistema sónico EDDY®.

Métodos:

A revisão sistemática da literatura baseou-se na pesquisa em 12 bases de dados. Foram incluídos todos os estudos *in vitro* que compararam a eficácia da ativação sónica e ultrassónica, abrangendo pelo menos um resultado de interesse (quantidade total de detritos removidos, quantidade de detritos remanescentes, profundidade de penetração dos irrigantes, quantidade total de *smear layer*, valores de força de *push-out*, percentagem de limpeza do canal).

O estudo *ex vivo* incluiu dentes anteriores e pré-molares, que foram instrumentados até um tamanho apical de 35/.06 (WaveOne® Gold) e 50/.06 (Protaper® Next). Os dentes de cada grupo de instrumentação foram atribuídos a um dos três grupos finais de irrigação; irrigação sónica com EDDY® (ED), irrigação ultrassónica (UAI) e irrigação manual sem ativação (MI). Após a irrigação, a extrusão apical do irrigante e dos detritos foi detetada usando M-cresol roxo e o modelo experimental de Myers e Montgomery (1991), respetivamente. A remoção de detritos e *smear layer* foi observada por microscopia eletrónica de varrimento (SEM), e a eliminação de um biofilme maduro de *Enterococcus faecalis* com 21 dias foi avaliada pelo ensaio de resazurina e por SEM.

O estudo clínico foi realizado em pacientes com indicação de tratamento endodôntico não cirúrgico. Foram selecionados 80 dentes, incisivos, caninos e pré-molares, com diagnóstico de pulpite irreversível ou de necrose pulpar. Foram divididos em 2 grupos: Grupo 1- (grupo controle) irrigação com NaOCl 5,25% com seringa e agulha endodôntica, sem ativação; Grupo 2- irrigação com NaOCl 5,25%, com seringa e agulha endodôntica, ativado com o sistema EDDY® (VDW, Munich, Germany).

Resultados:

A revisão sistemática comprovou que nenhuma das técnicas de irrigação avaliadas (sónica e ultrasónica) é superior à outra em termos de remoção de detritos, percentagem de limpeza canalar e profundidade de penetração do irrigante. Por sua vez, o estudo *ex vivo*, comprovou que a ativação mecânica dos irrigantes é vantajosa relativamente à ativação manual do irrigante no canal radicular. Também revelou que calibres apicais maiores, tornam mais eficaz a ativação com UAI e EDDY®. O estudo clínico mostrou que a introdução do sistema EDDY® durante o tratamento endodôntico inicial teve maior incidência de dor pós-operatória nas primeiras 8 horas, mas após esse período a dor pós tratamento endodôntico foi semelhante entre os grupos.

Conclusão:

Os resultados deste estudo não mostraram vantagem de uma técnica (ativação sónica/ativação ultrasónica) em relação à outra, segundo os parâmetros avaliados. Porém, tanto a ativação sónica como a ultrasónica, podem estar associadas a um maior risco de extrusão, em canais com calibres apicais aumentados, relativamente à irrigação manual. Foi também verificada uma maior eficiência de remoção de detritos, smear layer e biofilme, tanto com a ativação com EDDY® como pela ativação ultrasónica, em ambos os calibres apicais, relativamente à irrigação manual. Já em termos de dor pós-operatória, após as 8h, não existiu diferença de resultados entre técnicas. No entanto, pesquisas futuras com anatomias canalares mais complexas, poderão dar resultados efetivos que serão úteis para a prática clínica na Medicina Dentária.

ABSTRACT

Introduction:

A key goal in endodontic treatment is pain management, notably, eliminating pain after treatment. One of the main factors contributing to postoperative pain is the chemical injury to periradicular tissues by irrigating solutions, when extrusion occurs beyond the apical constriction. Various techniques and devices have been proposed to enhance the effect of chemical disinfection on the root canal system during biomechanical preparation, since it is difficult for irrigating solutions to reach the full extent of the canal system due to their anatomical complexities, allowing biofilms to persist after cleaning and shaping procedures. Residual debris and a smear layer can promote bacterial invasion of the dentinal tubules and, therefore, decrease the antimicrobial action of intracanal medicaments. The leakage of irrigants during treatment can cause sequelae, such as pain, swelling, ecchymosis and numbness. Due to positive apical pressure caused by irrigation, irrigants may extrude to periapical tissues, inducing an inflammatory response and postoperative pain. Therefore, there is a need of effective/safe irrigation systems/ techniques that prevent periapical inflammation associated with extrusion. This investigation studied the level of bacterial disinfection, periapical damage and pain provided by the use of EDDY®, a sonic powered irrigation activation system.

Objectives:

(1) Conduct a systematic review of the literature comparing sonic and ultrasonic activation systems for root canal treatment; (2) Conduct an integrated analysis of sonic and ultrasonic systems for endodontic irrigation within distinct apical dimensions through an *ex vivo* study; (3) Conduct a clinical study to evaluate the postoperative pain after using endodontic needle irrigation with 5,25% NaOCl activated with EDDY® during root canal irrigation.

Methods:

A systematic literature review was implemented, using 12 databases. All *in vitro* studies comparing the efficacy of sonic and ultrasonic activation and reporting at least one outcome of interest were included *i.e.*, total amount of debris removed, remaining debris scores, penetration depths of irrigants, total smear layer score, push-out bond strength values, percentage of canal cleanliness. The *ex vivo* study included anterior and premolar teeth, that were instrumented to an apical size of 35/.06 (WaveOne® Gold) and 50/.06 (Protaper® Next). Teeth from each group of instrumentation were assigned to one of the three final irrigation groups: sonically activated irrigation with EDDY® (ED), ultrasonically activated irrigation (UAI) and manual irrigation without activation (MI). After irrigation, apical extrusion of irrigant and debris were detected using M-cresol purple and the experimental model of Myers and Montgomery (1991), respectively. The removal of debris and smear layer were observed by scanning electron microscopy (SEM), and the elimination of a mature 21-days biofilm of *Enterococcus faecalis* was assessed by resazurin assay and SEM. The clinical study was carried out in patients with indication of initial nonsurgical root canal treatments. 80 incisors, canines and premolar teeth diagnosed with irreversible pulpitis or pulp necrosis were selected. Those patients were divided in 2 groups: Group 1: (control group) irrigation with 5,25% NaOCl with syringe needle irrigation alone; and Group 2: irrigation with 5,25% NaOCl with syringe needle irrigation, activated with sonic system EDDY® (VDW, Munich, Germany).

Results:

The systematic review proved that none of the evaluated irrigation techniques (sonic and ultrasonic) is superior to the other concerning the amount of debris removal, percentage of canal cleanliness, and irrigant penetration depth. The *ex vivo* study proved that mechanical activation of irrigants is advantageous, as compared to manual irrigation, concerning root canal debridement and disinfection. It also revealed that larger apical sizes make it more effective for UAI and EDDY® activation and the clinical study showed that the introduction of EDDY® during initial root canal treatment had higher incidences of postoperative pain, in the first 8 hours, but after that period post endodontic pain was similar between the groups.

Conclusion:

The results of this study showed no advantage of one technique (sonic activation/ultrasonic activation) over the other, according to the parameters evaluated. However, both sonic and ultrasonic activation may be associated with a greater risk of extrusion, in canals with increased apical calibers, compared to manual irrigation. A higher efficiency of debris, smear layer and biofilm removal were also verified, both with activation with EDDY® and by ultrasonic activation, in both apical calibers, compared to manual irrigation. In terms of postoperative pain, after 8 h, there was no difference between techniques. However, future research with more complex canal anatomies may yield results that will be useful for clinical practice in Dentistry.

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Research papers that resulted from this doctoral thesis:

1. Efficacy of sonic and ultrasonic activation during endodontic treatment: A meta-analysis of *in vitro* studies

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2. Effectiveness of ultrasonic and sonic irrigation systems on extrusion risk, canal debridement and biofilm removal within distinct apical dimensions – an *ex vivo* study in human teeth - Under review in "Clinical Oral Investigations"

3. Comparative Evaluation of Postoperative Pain After Using Endodontic Needle and Eddy® Tips During Root Canal Irrigation: a randomized clinical trial

   - Under review in "Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial"

Abbreviations

ANOVA	One-way analysis of variance
ANP	Apical negative pressure
BHI	Brain heart infusion
CBCT	Cone-beam computed tomography
CEJ	Cementoenamel junction
CHX	Clorhexidine
CI	Confidence Interval
CNI	Conventional needle irrigation
CRIS Guidelines	Checklist for Reporting *In Vitro* Studies
CT	Computed tomography
EA	EndoActivator
EDTA	Ethylenediamine tetraacetic acid
Er: YAG	Ytrrium aluminium garnet
LAI	Laser activated irrigation
MAF	Master apical file
MD	Mean Difference
MDA	Manual dynamic agitation
MDT	Master delivery tip
MI	Manual irrigation
NaOCl	Sodium hypochlorite
Nd: YAG	Neodymium: ytrrium aluminium garnet
NR	Non-reported
NSAIDS	Non-steroidal anti-inflammatory drugs
PBS	Phosphate buffered saline
PEP	Post-endodontic pain
PIPS	Photon-induced photoacoustic streaming)
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
RCT	Root canal treatment

RFU	Relative fluorescence units
SD	Standard deviation
SEM	Scanning electron microscopy
SI	Sonic irrigation
SMD	Standard mean difference
UIA	Ultrasonic irrigant activation
VAS	Visual analogue scale
WL	Working length
WMD	Weighted mean difference

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CHAPTER I

INTRODUCTION

1. DENTIN-PULP COMPLEX

The dentin-pulp complex is formed by the dental pulp and the dentin (Fig. 1.1). Both dentin and pulp are embryologically, histologically and functionally similar. (1-3) The odontoblast cells are an essential element of this complex. They are localized in the dental pulp periphery extending to the dentin inner part. (4)

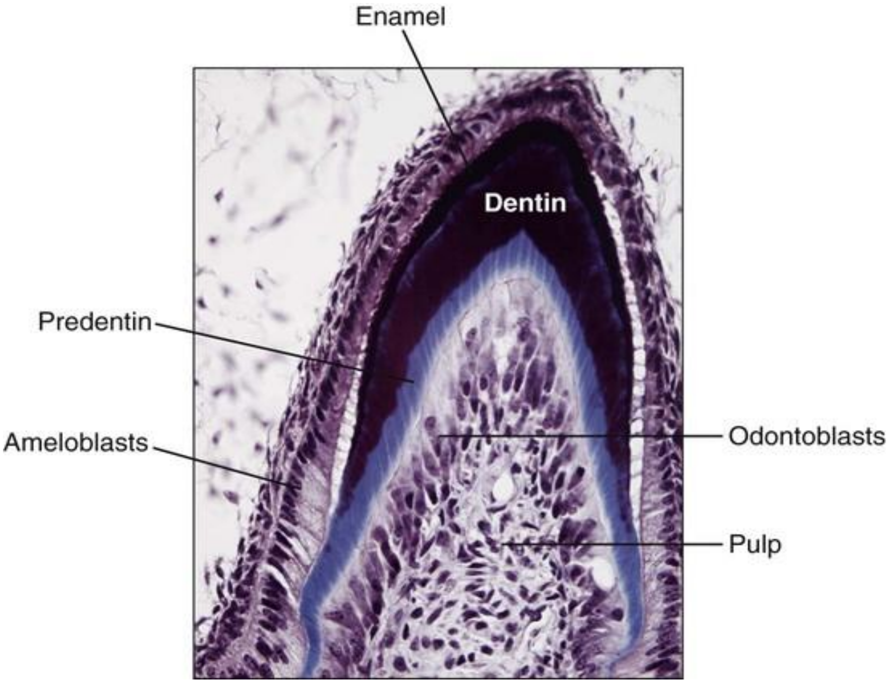

Figure 1.1: Dentin-pulp complex (5)

The dentin-pulp complex vitality allows teeth to maintain their function. The odontoblasts have a homeostatic function after teeth development. They secrete dentin, which works as a protector element, in case of offending stimuli. The restorative process (that happens after the aggression) is mediated by both pulp cells and dentin matrix, forming reparative dentine, which implies the importance of this complex in the maintenance of pulp vitality. However, damage to the dentin might affect the underlying pulp, thus altering the normal pattern of dentin production, both in terms of quality and quantity. The dentin-pulp complex also has a function to dissipate masticatory forces, hence protecting tooth enamel. (1, 3, 6)

Pulp space primarily comprises two parts: pulp chamber, which refers to the portion inside of the crown, containing the coronal part of the dental pulp, while the pulp canal is the one which lies within the roots, containing the radicular part of the pulp. (7)

When dental pulp undergoes pathological changes resulting from trauma or caries, microorganisms are able to enter the pulp chamber and invade the anatomic irregularities present in the root canal system, (8) which might lead to pulpal and periapical pathosis. When only the pulp is inflamed or damaged, it’s classified as a pulpal pathosis (reversible pulpitis, symptomatic irreversible pulpitis, asymptomatic irreversible pulpitis and pulp necrosis), but when the disease spreads through the apical foramen, the periapical tissues start to be affected and periapical pathosis starts (symptomatic apical periodontitis, asymptomatic apical periodontitis, chronic apical abscess, acute apical abscess and condensing osteitis). (9) Microorganisms can take different routes to enter the root canal system. They can enter due to caries or a dental procedure, through an open cavity with exposure of the dental pulp; through the gingival sulcus and they also enter through the bloodstream, as the bacteria present in it are attracted to the dental pulp after trauma or a procedure that has caused pulp inflammation, without pulp exposure. (10) Microorganisms can also enter due to a deficient restoration, as it’s known that bacteria can penetrate at the occlusal level and reach the root canals of filled teeth in less than 6 weeks. It is also described that bacteria from a contaminated tooth can migrate to the neighboring tooth and initiate an infection in the tooth. (10)

2. EPIDEMIOLOGICAL DATA

Epidemiological studies have shown that dental caries is the most common cause of pulp disease (90%), followed by crown fracture (9%) and occlusal trauma (1%). (11) For instance, Albuquerque *et al.*,2010, (11) found that 81% of patients were diagnosed with pulp pathologies, and among these, pulp necrosis (69%) is the most frequent. Periapical pathologies were diagnosed in 19%, and apical periodontitis (30%) was the most frequent. However, Özbas 2011 (12), determined that only 36% of teeth with periapical lesions had endodontic treatment and 64% of teeth with periapical lesions had no treatment. Additionally, this study, determined that the frequency of periapical lesions was highly significant among the endodontically treated teeth. (12)

Jakovljevic A. 2020, (13) published an updated systematic review of cross-sectional studies published between 2012 and 2020, revealed a worrying increase in the worldwide prevalence of apical periodontitis among endodontically treated teeth (from 36% to 41%). In accordance, El Ouarti 2021, (14) found that 72% of the root filled teeth had apical periodontitis. Chala *et al.*, 2011, (15) found the same condition in 64% of the root filled teeth and Jimenéz-Pinzón *et al.*, found it in 64% of root filled teeth. (14) Among the possible influencing factors, the quality of coronal restorations and root filling are the most consistently reported risk factors for apical periodontitis. (16)

3. MICROORGANISMS IN ENDODONTIC INFECTIONS

Endodontic infections have a polimycrobial nature. The bacterial communities in primary endodontic infections have been reported to be more diverse than those in persistent infections. (17) The infected canals offers a particular habitat to the microorganisms. They are able to grow in sessile biofilms, aggregates, coaggregates, and also as planktonic cells suspended in the fluid phase of the canal. (18) Biofilms are sessile multicellular microbial communities where microbes are entangled in a self-made extracellular polymeric substances, and firmly attached to surfaces. When microorganisms are protected in biofilms, they are much more resistant to biocides as the same organisms in planktonic form (18, 19) The polysaccharide matrix in biofilms slows antibiotic transport, allowing inactivating extracellular enzymes like β-lactamase to concentrate. Quorum sensing is used by microbial cells to support the growth of species that are helpful to biofilm structure. (20) To stay protected, subpopulations inside a biofilm might change gene expression. Cells remain inside the biofilm, where they are shielded from medications that only affect the microbes on the periphery. Bacterial cells in biofilms develop more slowly and have less metabolism than planktonic bacteria, allowing them to evade antimicrobial agents. Antibiotics may be harmed even more by biofilms' changing pH and oxygen levels. (19) In table 1.1, is presented the most commonly found species in every phase of disease: primary infections, extra radicular infections (which may or may not be dependent on an intraradicular infection), and secondary infections.

Table 1.1 – Endodontic Pathogens		
Primary infections		
Pathogens	**Species**	**References**
Black pigmented anaerobic Gram-negative	*Prevotella intermedia* *Prevotella nigrescens* *Prevotella tannerae* *Prevotella multissacharivorax* *Prevotella baroniae* *Prevotella denticola* *Porphyromonas endodontalis* *Porphyromonas gingivalis*	(10)
Periodontal pathogen	*Tannerella forsythia*	(10)
Obligately anaerobic Gram-negative *Dialister* spp.	*Dialister pneumosintes* *Dialister invisus*	(10)
Fusobacterium spp.	*Fusobacterium nucleatum* *Fusobacterium periodonticum*	(10)
Spirochetes Gram-negative	*Treponema denticola* *Treponema sacranskii* *Treponema parvum* *Treponema maltophilum* *Treponema lecithinolyticum*	(10)
Anaerobic Gram-positive rods	*Olsenella* spp. *Slackia exigua* *Mogibacterium timidum* *Eubacterium* spp.	(10)
Gram-positive cocci	*Parvimonas micra* *Streptococcus anginosus* *Streptococcus mitis* *Streptococcus sanguinis* *Enterococcus faecalis*	(10)

Table 1.1 – Endodontic Pathogens (continuation)

Primary infections

Pathogens	Species	References
Other bacterial spp. (Less frequent)	*Campylobacter rectus* *Campylobacter gracilis.* *Catonella morbic* *Veillonella párvula* *Eikenella corrodens* *Granulicatella adiacens* *Neisseria mucosa* *Centipeda periodontii* *Gemella morbillorum* *Capnocytophaga gingivalis* *Corynebacterium matruchotii* *Bifidobacterium dentium* Anaerobic lactobacilli	(10)
Fungi	*Candida albicans*	(10)
Archaea and Viruses		(10)

Secondary infections

Pathogens	Species	References
Gram negative anaerobic rods	*Fusobacterium nucleatum* *Prevotella* spp. *Campylobacter rectus*	(10)
Gram positive bacteria	*Streptococcus mitis* *Streptococcus gordonii* *Streptococcus anginosus* *Streptococcus oralis*	(10, 18)

Table 1.1 – Endodontic Pathogens (continuation)

Secondary infections		
Pathogens	**Species**	**References**
Gram positive bacteria	*Lactobacillus paracasei* *Lactobacillus acidophilus* *Staphylococcus* spp. *Enterococcus faecalis* *Olsenella uli* *Parvimonas micra* *Pseudoramibacter alactolyticus* *Propionibacterium* spp. *Actinomyces* spp. *Bifidobacterium* spp. *Eubacterium* spp.	(10, 18)
Yeasts	*Candida albicans*	(10, 18)
Extraradicular infections		
Pathogens	**Species**	**References**
Anaerobic bacteria	*Actinomyces* spp. *Propionibacterium propionicum* *Treponema* spp. *Porphyromonas endodontalis* *Porphyromonas gingivalis* *Treponema forsythia* *Prevotella* spp. *Fusobacterium nucleatum*	(10, 18)
Extraradicular Viruses		(18)

Enterococcus faecalis

Enterococcus faecalis is the most common specie found in obturated root canals and in persistent infections. The prevalence of *E. faecalis* in failed root canal treatments can range from 24% to 77% (21-25) and in primary endodontic infections, Roças *et al.,* 2004 (26), reported that *E. faecalis* was present in 18% of cases. It is a Gram-positive facultative anaerobic bacterium, capable to survive in the root canals as a single microorganism, or within a microbial community (*i.e.*, biofilm). It is a commensal microorganism of the human gastrointestinal tract and may inhabit the oral cavity and gingival sulcus. *E. faecalis* has many unique characteristics, making it a survivor in the root canal. It can live and survive in a poor nutritional environment; even in the presence of disinfectants. It invades and metabolize the fluid in the tubules and it adheres to the collagen; transforms into a viable but non-cultivable state; acquires antibiotic resistance; survives in extreme environments of low pH, high salinity, and high temperature; endures long-term starvation; and is able to use the periodontal ligament fluid as a nutrient. (10)

4. ENDODONTIC TREATMENT

The best way to prevent the evolution of an infection is through endodontic treatment, as soon as a tooth with irreversible pulpitis is diagnosticated. At this stage, the infection is fairly superficial and the dental pulp is vital. (27) However, if the infection extends to the entire root canal system, it will elicit the inflammation of periradicular tissues. (28) The endodontic treatment will prevent the spread of infection to the root canal spaces, avoiding periradicular tissues infection. (27)

Endodontic treatment follows a sequential set of steps namely, (29) pulpal tissue removal, (30) cleaning and shaping the root canal, and (31) root canal obturation. The endodontic treatment is considered complete after the definitive restauration of the tooth. The main goal of this treatment is to eliminate bacteria from the radicular canals and fill the entire space, to prevent the entry of new bacterial and entomb the remaining bacteria, and this way heal or prevent apical periodontitis. (30, 31) If all of these succeed, the treatment should be also able to heal existing periapical lesions. (32)

In order to obtain endodontic success, it is necessary to achieve bacterial elimination or at least bacterial reduction, compatible to levels of periapical tissues healing, in order to prevent the reinfection. (28, 33-35)

Despite the high success of endodontic treatment (85-98%), there are always cases of failure after treatment, mainly due to the presence of microorganisms intra or extra canal. In these situations, the first option is non-surgical endodontic retreatment. However, this latest treatment is associated with a lower success rate (62-91%). (36)

The retreatment success rate is also influenced by several factors including the number of canals, preoperative symptoms, apical extrusion of filling materials, quality of the final restoration, intraoperative complications and presence of periapical lesion. (18, 37) In cases where non-surgical endodontic retreatment is not possible, (*e.g.*, obliterated root canals, teeth with full coverage restorations where conventional access may jeopardise the underlying core, the presence of a post whose removal may carry a high risk of root fracture), one can opt for surgical endodontic retreatment. (36)

5. ENDODONTIC PROGNOSIS

The outcome of endodontic treatment is usually assessed using radiographic and clinical examination. (38) One of the most important factors prompting the prognosis of the treatment is the preoperative status of the teeth, with most of the studies establishing that the success is heavily dependent on the presence or absence of pre-therapeutic apical pathosis. (39-43) To better understand the influencing factors of endodontic treatment success, many studies evaluated numerous predictors of outcome. (40, 44-50) Scientific evidences have confirmed that apical periodontitis can be radiographically undetectable, and likewise, the quality of root filling (as determined by periapical radiographs) might be doubtful. (40) Therefore, cone-beam computed tomography (CBCT) has been recently used as a more accurate and reliable method to analyse risk variables associated with the prognosis of root canal treatment. (30, 51-53) Today, it's known that endodontic prognosis has a multifactorial nature including preoperative factors, intraoperative factors and postoperative factors, (38) as schematized in Fig. 1.2.

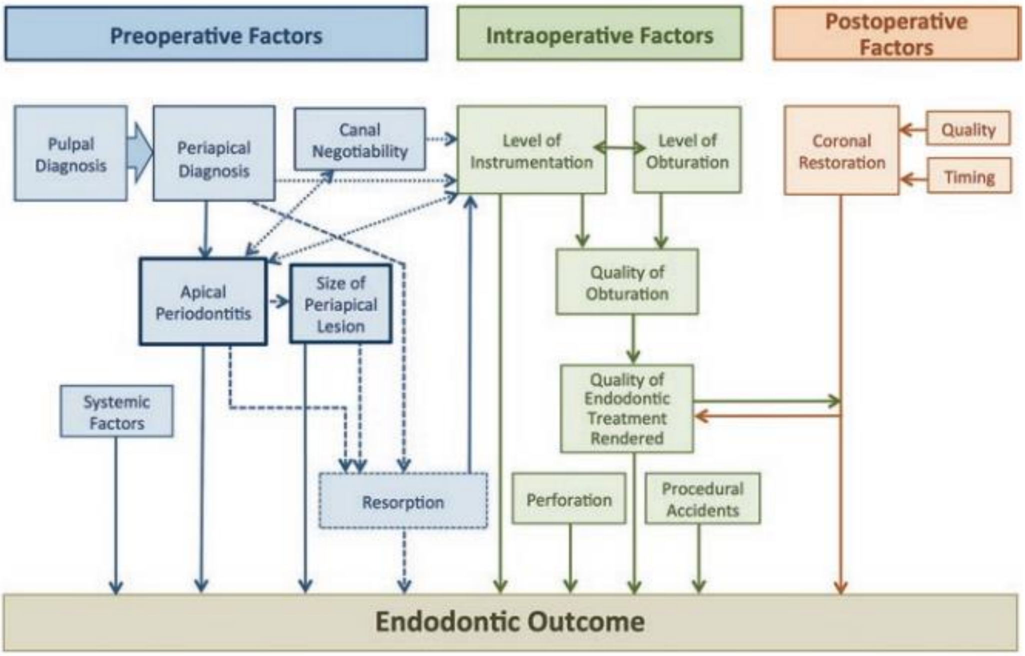

Figure 1.2- Relationship between prognostic factors that can affect endodontic treatment outcomes. (38)

6. ROOT CANAL ANATOMIES AND ITS DIFFICULTIES

Understanding the structures of the root canal is fundamental for a fruitful endodontic treatment. Complexity of root canals depends on reasons such as ethnicity, gender, age, the presence of lateral/accessory canals, isthmuses, the area of the teeth at the jaws and inconsistencies of the teeth (*dens invaginatus*, *dens evaginatus*, *fusion, gemination*, *dens in dente*). Other than all of these, a few physiological changes happen in enamel and dentin with age. Mineralization of dentin provoke calcification of dentinal tubules; hence, dentin gets sclerotic. (54) Different difficulties during the treatment are normally dependent on the type of tooth. Generally anterior and premolar teeth have straight roots/canals, but molars generally have curved roots and narrower canals, mainly in mesial roots of mandibular molars and vestibular roots of maxillary molars, but this does not exclude the existence of an anterior tooth with a more complex anatomy.

7. CHEMO-MECHANICAL PREPARATION OF THE ROOT CANAL

The root canal shaping is done with hand and rotary instruments, under constant irrigation, to remove the inflamed and necrotic tissue, microorganisms/biofilms and other debris that might be in the root canal space. However, many studies, through the use of advanced techniques as microcomputer tomography (CT) scanning, have demonstrated that some areas of the main root canal wall would remain untouched by the instruments. (55-59) This emphasizes the importance of using chemical agents to aid the cleaning and disinfection of the entire root canal area. (60-62)

Foreseeable eradication of bacterial infection requires physical disruption and removal of microorganisms. So, mechanical instrumentation can provide the removal of pulp tissue from root canal spaces and create enough space to root canal irrigation, inter-appointment medication and to an adequate root canal filling. (28)

To achieve a proper disinfection of the apical third of the canal, some studies have recommended apical preparation sizes of more than 30. (63) For NaOCl, it was found that 30 or 35 sizes were required for it to be effective. (64) But bearing in mind that there are different types of root canals, this might influence the endodontic treatment result and a vast arsenal of endodontic files has been developed, with different alloys, designs, tapers, motions surface treatments and tip sizes. (65)

Additionally, the obturation material should correctly seal the apical zone preventing the entrance of fluids/nutrients, that would keep bacteria inside the canal active. Also, the coronal seal of teeth is of extreme importance, preventing coronal bacteria from entering the root canal spaces. (32)

8. ROOT CANAL IRRIGATION

Irrigation is known to have a central role when it comes to endodontic treatment. It is a complementary step to instrumentation and assists in the proper disinfection and debridement of the root canal, through a flushing mechanism. The root canal irrigant should fulfil numerous requirements namely (35):

- ✓ Facilitate the removal of dentin;
- ✓ Washing action that helps the removal of debris;
- ✓ Penetrate the canal periphery;
- ✓ Reduce the instrument friction during the preparation;
- ✓ Dissolve the inorganic tissue;
- ✓ Dissolve the organic matter;
- ✓ Kill bacteria and yeasts; and
- ✓ No cytotoxic or caustic effects to vital periapical tissue.

However, there is no single irrigating solution that would alone be sufficient to cover all the functions required from an irrigant. The irrigating solution that is used in endodontics could be classified as antimicrobial solutions, chelating solutions, solutions with detergent or a combination of both antibacterial and chelating solutions. (66-68)

Overall, irrigation aims to introduce a flow of irrigants to(69):

✓ Cover the entire root canal system to ensure it makes close contact with the substrate and would carry away the debris and provides the required lubrication for the instruments.

✓ Ensure proper distribution of the irrigant throughout the root canal system, mixing the irrigant and the refreshment, to maintain the effective concentration of active chemical components and to tackle rapid inactivation.

Irrigants are also known to prevent the packing of hard and soft tissues in the apical region, due to the flushing out action of debris, which prevents the extrusion of infected material into the periapical area.

Several solutions are known to have cytotoxic potential, which could cause severe pain if they gain access to the periapical tissues.

The agents that are currently used for irrigation can be grouped mainly as decalcifying or anti-microbial agents. In certain situations, the mixture of both is used. Table 1.2 summarizes the most used irrigants for root canal irrigation. (70)

Table 1.2 – Endodontic Irrigants

Irrigant	Advantages	References
Sodium Hypochlorite (NaOCl)	Tissue dissolving capacity Antimicrobial agent Lubricant Short action time	(34, 71-73)
Clorhexidine (CHX)	Antimicrobial agent	(34, 71-73)
Ethylenediaminetetraacetic Acid (EDTA)	Decalcifying agent	(34, 71-73)
Quaternary ammonium compounds (EDTAC)	Decalcifying agent	(71, 72)
Citric Acid	Decalcifying agent	(34, 71-73)
Etidronic acid (HEBP)	Decalcifying agent	(71-73)
Maleic Acid	Decalcifying agent	(73)
MTAD (3% doxycycline hyclate, 4.25% citric acid, and 0.5% polysorbate (Tween) 80 detergent)	Antimicrobial agent Decalcifying agent	(34, 71, 72)
Tetraclean (doxycycline hyclate (at a lower concentration than in MTAD), an acid, and a detergent)	Antimicrobial agent Decalcifying agent	(34, 71)
SmearClear (water-soluble solution containing water, 17% EDTA salts, a cationic surfactant) (cetrimide), and anionic surfactants	Decalcifying agent	(34, 71)
QMix (Solution of EDTA, CHX, detergent)	Antimicrobial agent Decalcifying agent	(34, 71)

Table 1.2 – Endodontic Irrigants (continuation)

Irrigant	Advantages	References
Chlor-XTRA (sodium hypochlorite mixed with a surfactant)	Antimicrobial agent	(34)
CHX-Plus (2% Chlorhexidine Gluconate solution with powerful wetting agents and proprietary surface modifiers)	Antimicrobial agent	(71)
Hydrogen Peroxide	Antimicrobial agent	(71, 72)
Iodine potassium iodide	Antimicrobial agent	(71, 72)
Saline Solutions	Rinsing solution between irrigants	(34, 71)
Distilled Water	Rinsing solution between irrigants	(34, 71)
Green Tea	Natural product with antibacterial activity (No evidence)	(71, 73)
Triphala	Natural product with antibacterial activity (No evidence)	(71, 73)
Silver diamine fluoride	Antimicrobial agent	(73)
Triclosan and Gantrez	Antimicrobial agent	(73)

Among all the irrigants mentioned, ***sodium hypochlorite (NaOCl)*** has a central position, as being the most used in endodontics. It is known to have excellent antimicrobial activity and better tissue solubility in the range of 1-15% concentration, and has an alkaline pH of 11. (74) NaOCl is cheap and easy to store, which has helped in its increased use. (74)

Sodium and hypochlorite ions, provided by NaOCl in combination with water, help to balance the hypochlorous acid responsible for the antibacterial activity. The solution is able to dissolve organic components like collagen and pulpal remnants, however it is not capable of removing all the smear layer that is formed during the instrumentation stage. When in contact with the organic tissue, it acts as a solvent and releases chlorine which combines with the protein amino group and leads to the formation of chloramines. Hypochlorous acid and ions lead to degradation of the amino acids and hydrolysis. (61, 75, 76) Some disadvantages of using NaOCl include (77):

- ✓ Risk of damaging the permanent tooth follicles;
- ✓ Unpleasant odour and taste;
- ✓ Reactivity with other solutions; and
- ✓ Toxicity to periradicular tissues.

Additionally to the choice of irrigant, other parameters must have been taken into account during the irrigation process, namely:

Duration of Irrigation: According to the type of irrigant used, the time of exposure may have to be different. Literature mentions that NaOCl could kill the target microorganisms in merely seconds, even at lower concentrations. (71) Nevertheless, there is an adequate working time required to reach NaOCl potential. (78) A previous study has demonstrated that for NaOCl at 5.25%, 40 minutes of irrigation is effective while lower concentrations and the same time-frame proved to be ineffective. Accordingly, higher concentrations and longer exposure times could lead to better outcomes. (79)

Concentration: NaOCl solution is available in different concentrations between 0,5% and 6%. It has been found to be effective in removing the pulpal remnants and predentin from the uninstrumented surfaces. Hereupon, the 0.5% concentration was not able to be completely effective, and it did leave fibrils on the surface. (80) Based on the preference of dentists, it was found that the most used NaOCl concentrations range between 2.5 to 5%. Research also found that endodontists used the higher concentrations and the longer duration, as well as activated irrigant more than the general practitioners. (81) In studies that evaluate the effectiveness of NaOCl to eliminate *E. faecalis*, it was found that NaOCl, in its different concentrations of 0.5, 1, 2.5, 4 and 5.25% was highly effective. (74) Based on dentists' preference, NaOCl is often used at concentrations of 2.5 to 5%. (81)

Irrigation Sequence: Over the years, many protocols have been created for irrigation during root canal treatment. The currently recommend protocol is provided in Fig. 1.3. The protocol advises the use of NaOCl as irrigant with concentrations between 2.5 - 6%, followed by the use of a master apical file (MAF) that has been selected. The next step aims the removal of the smear layer, that could be achieved using MTAD, Tetraclean or 17% EDTA for 1 min. In the cases where saline solution is used, the QMiX should be used to finish the protocol whereas if EDTA and Smear Clear are used, a final rinse with 2.5% NaOCl for 30 seconds or with saline solution should be performed. If saline solution is used for rinse, then CHX should be used in the end as the final step.

Saline solution is known to be isotonic to the body fluids. It is universally accepted as one of the most common solutions used in irrigation in all endodontic procedures. It has no side effects even in case of extrusion to the periapical tissues. (82) It can be used between irrigation solutions like chlorhexidine and sodium hypochlorite in order to prevent reactions between them. That said, saline should not be used as the only solution. (35)

Chlorhexidine digluconate is used for the disinfection process as it is known to have very good antimicrobial activity, but there is a lack of tissue dissolving capability. (83-85) It is known to absorb onto the cell wall of the microorganism and would lead to a leakage of the intracellular components. At low concentrations, the small molecular weight substances leak out, which would include potassium and phosphorus. This would lead to a bacteriostatic effect. At higher concentrations, the solution has bactericidal effect due to the precipitation and the coagulation of the cellular cytoplasm, which is often a result of the cross-linking of the proteins. (86)

CHX is considered an alternative to the NaOCl due to its broad antimicrobial activity spectrum and its lower toxicity. The most common used concentrations range between 0.2 % and 2% and it comes in two forms, either as gel or as a liquid. (83)

Hydrogen peroxide is considered to be used in sterilization and disinfection and the used concentrations vary from 1-30%. Peroxide helps creating an effervescence, which helps removing the debris, also acting as an oxidizing agent capable of denaturing the proteins from the bacteria and DNA, but when used in higher concentrations, it loses tolerance, and there is a potential for causing cervical resorptions.(66)

The ***mixture of Tetracycline isomer, detergent, and acid (MTAD)*** is developed as an irrigant that combines the antimicrobial and chelating properties. MTAD is a mixture made of 3% doxycycline, detergent and 4.25% citric acid. It is recommended to be used as the final rinse, after the root canal preparation. It is capable of eliminating bacteria and the smear layer from the root canal when used as the final rinse solution. (87)

Citric acid is also used in irrigation in concentration between 1-10%. The use of 10% citric acid is known to be used in final irrigation as it is highly effective in removing the smear layer. (34)

Ethylenediaminetetraacetic acid (EDTA) a chelating agent capable of removing the smear layer, specifically the inorganic portion. NaOCl is an adjunct solution when it comes to the removal of the remaining organic components. The commonly used form is 17% or 15% concentration. (34)

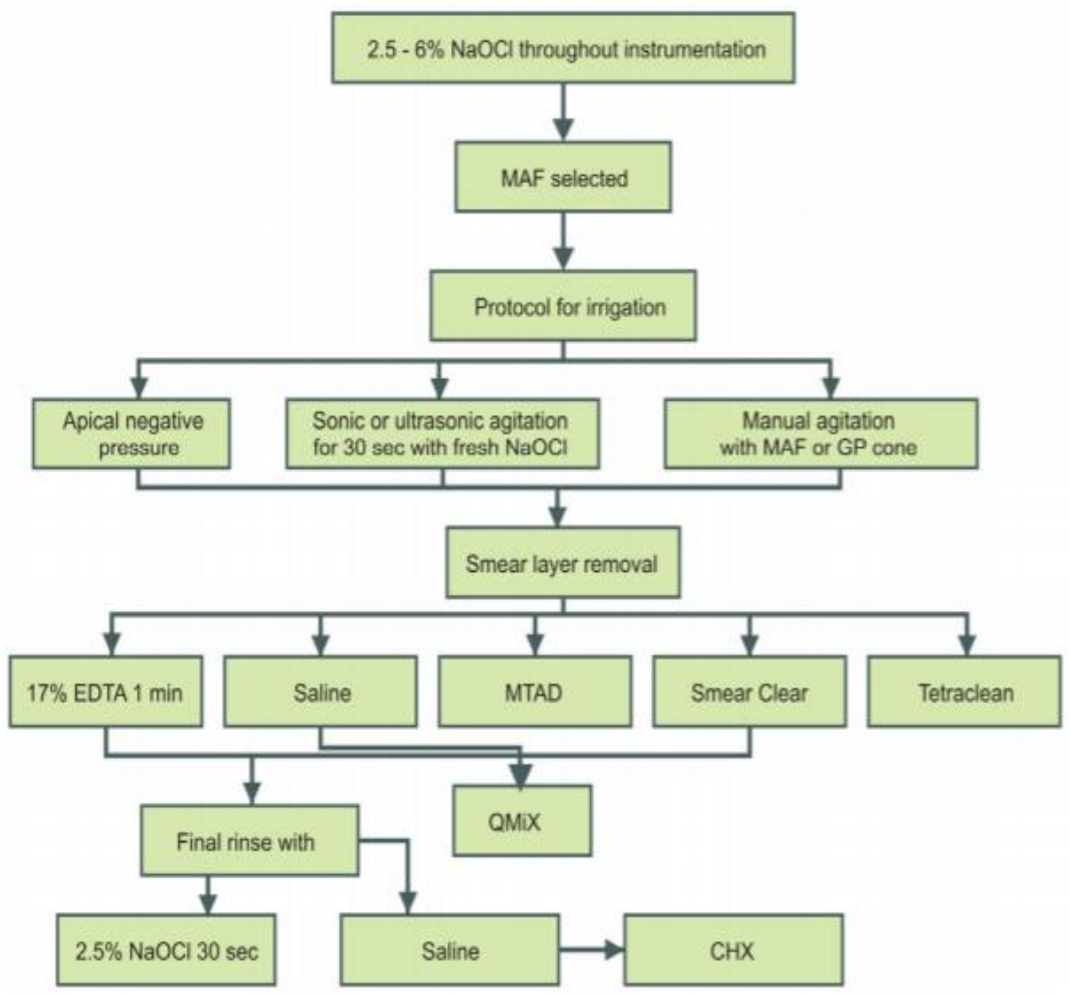

Figure 1.3- Recommended Irrigation protocol. (71)

9. ACTIVATION OF THE IRRIGANT

The root canal systems have a complex anatomy, and root canal instrumentation, leaves approximately 60% of the root canal wall surface undisturbed. Despite comprehensive chemomechanical disinfection, uninstrumented sections of the root canal system and anatomical complications such as accessory canals, apical ramifications, fins and isthmus areas can contain tissue debris as well as microbes and their harmful by-products. To improve the removal of endodontic biofilms, additional irrigation methods like as irrigant activation techniques are required.(88) Normally, the delivery of the irrigant to the root canal spaces is carried out by syringes. These syringes are coupled to metal needles of different sizes and different tip designs. (89-92) Conventional needle irrigation (CNI) fails to deliver the irrigant solution 0 to 2 mm past the top of the needle, to the intricate areas of the root canal and air vapour is also known to become entrapped, producing a vapour lock effect. (93-95) In order to counter the limitations of CNI, different manual or machine-assisted irrigation activation techniques have been developed to improve the disinfection of the root canal system , namely, manual dynamic activation (MDA), brushes, continuous irrigation, sonic irrigation (SI), apical negative pressure (ANP) and ultrasonic irrigant activation (UIA). (96)

The root canal irrigant agitation and delivery systems can be divided in 2 groups: manual-assisted agitation techniques and machine-assisted devices, which will be explained below.

9.1 MANUAL-ASSISTED AGITATION TECHNIQUES

Different methods have been used under manual-assisted agitation techniques. Syringe irrigation with needles/cannulas is the most conventional, and it has been often advocated as an effective and efficient method for irrigant delivery. Agitation is achieved by moving the needle vertically in the canal space. The irrigation tip gauge design is known to have a significant influence on the irrigation flow pattern. It also impact the irrigant velocity, pressure on the walls and the depth of penetration. (96) The 27-gauge needles are considered the preferred needle tip size. Different studies over the years have shown a limited effect beyond the tip of the needle, as a dead-water zone is created or air bubbles are formed in the apical root canal, hampering the penetration of the solution as it is intended. (97)

The design of the needles, as mentioned, plays a critical role and smaller needles allow the delivery of the irrigant close to the apex. Over the years, many modifications have been made to the needles tip, and these are presented in Fig. 1.4.

Open-ended needles let the irrigant flow out the end towards the apex, while the close-ended tips have side vents, creating more pressure on the walls of the root canal. This allows to create a higher reflux, causing the coronally displacement of debris, and minimize any inadvertent extrusion of the irrigant towards the periapical tissues. (98) The main advantage of syringe irrigation is the easier penetration, achieving better depths within the canal. (97, 99) Syringes can come in different sizes with varying capacities from 1 to 20 mL. Large-volume syringes are known to be timesaving, however, they are extremely difficult when it comes to controlling the pressure, which could lead to accidents. These syringes should follow the Luer-Lok design (Fig. 1.5) (the hub of the female fitting (dispensing needle) has tabs or threads which screw into threads in a sleeve on the male part (dispensing syringe)), ensuring that the needle that is attached to the syringe, will remain secure throughout the irrigation procedure. Considering possible chemical reactions between solutions, each irrigant should have their own individual syringe. (100)

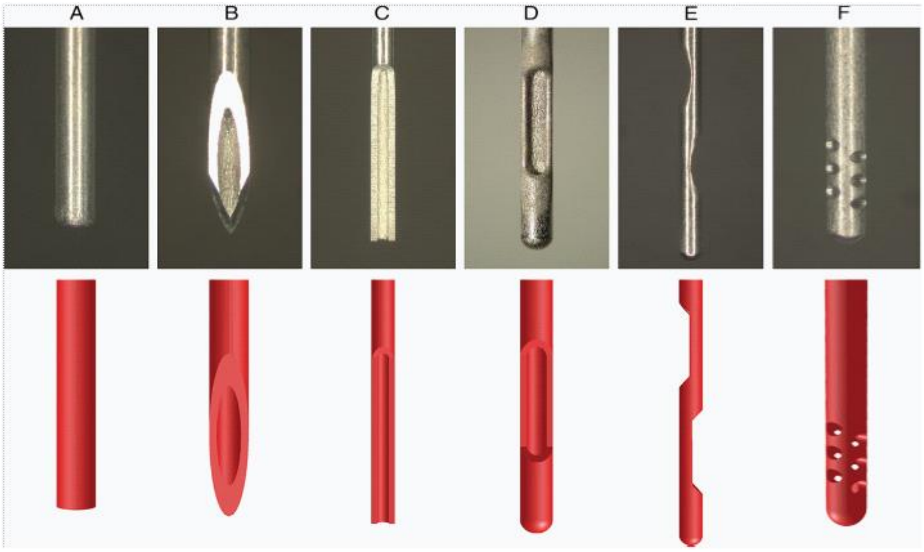

Figure 1.4 – Several examples of needle tip design for endodontic manual-assisted agitation: (101) (A-C) Open-ended needles: (A) flat, (B) beveled and (C) notched. (D-F) Closed-ended needles: (D) side vented, (E) double side vented and (F) multivented.

Figure 1.5- Syringes Luer-Lock design.

Brushes are used as adjuncts to debridement of the canal walls, but they can also be useful as an agitation technique. Recently, 30-gauge irrigation needles covered with a brush have been introduced. Recent studies reported that the cleaning of the coronal third of instrumented root canal walls that were irrigated and agitated with the aid of these needles (*i.e.,* NaviTip FX) was improved, as compared to brushless needles. However, the friction created between the bristles of the brush and the canal irregularities, results in the dislodgement of the radiolucent bristles, which are often not identified by the clinicians even when a microscope is used, which is a major disadvantage of this technique. (102) The size of the brush limits its ability to clean properly, as some of the debris might be packed into the apical part of the canal after the brush is used.

Manual-dynamic irrigation is a simple technique to agitate irrigants inside the root canal system that consists in a 2 mm in-and-out movement in the irrigating solution using the master cone 1 mm set from the working length. (103) The irrigant needs to be in direct contact with the canal walls to be effective, which is difficult, especially due to the inability of the irrigant to reach the apical part of the canal, as a result of the vapour lock effect. The studies carried out in the past mention that the gentle movement of the well-fitting gutta-percha master cone in the vertical path in short 2-3 mm strokes within the canal could lead to the production of a hydrodynamic effect that is effective and would significantly improve exchange and displacement of any reagent that is given. (104-109)There are various factors that impact and contribute to the positive results attained with manual-dynamic irrigation. (110-112) Firstly, the push-pull motion of the gutta-percha point in the canal will be able to generate higher intra-canal pressure changes during these movements, leading to a more effective form of delivery of the irrigant to the canal surfaces that have been untouched. Secondly, the frequency of the motion of the gutta-percha, which is at 3.3 Hz, 100 strokes every 30 seconds, is higher than the hydrodynamic pressures that are generated by the RinsEndo (an automated irrigation technique using combined irrigation and suction under hydrodynamic pressure. The irrigant is agitated to an oscillation of approximately 1.6Hz), and it helps to generate more turbulence. (113)

9.2 MECHANICAL-ASSISTED AGITATION TECHNIQUES

Several studies have mentioned that machine-assisted agitation promotes a better root canal disinfection and debris removal, allied to a lower prevalence of postoperative pain, which arise as a result of root canal treatment. (114, 115) Over the years, many types of mechanical-assisted agitation devices have been introduced.

Rotary Brushes

The rotary brush is a rotary handpiece that Ruddle (116) used for removal of debris and smear layer from the root canals that have been instrumented. The brush is composed by a shaft and a tapered section that holds the brush. It has multiple bristles that extend radially from the core. During the debridement phase, the brush rotates at a speed of 300 rpm, which causes bristles to deform. This causes the residual debris to be displaced, moving them out of the canal, towards the coronal section. Unfortunately, this equipment is not commercially available though it has been patented long before. (96)

Continuous Irrigation

The Quantec-E irrigation system is a self-contained fluid delivery unit that is attached to the Quantec-E Endo system. It makes use of a pump console, two reservoirs for irrigation and running, that provides continuous irrigation during the rotary instrumentation. The continuous irrigant agitation during the rotary instrumentation generates an increased volume of irrigant, which increases the contact time and greater depth of the irrigant penetration within the root canal. This approach leads to a more effective canal debridement when compared to the standard syringe technique. The research done on the use of these techniques have shown that, when compared to needle irrigation, the Quantec-E did provide a cleaner canal wall, and an increase in the debris and smear layer removal. (117) However, these advantages were not observed in the middle and apical thirds of the root canal. These findings were also confirmed in other studies which showed no significant differences that could promote the use of Quantec-E over the standard syringe-needle. (118)

Ultrasonic Irrigation

The ultrasonic devices are acknowledged to have been used long ago in periodontics, before Richman introduced the system in the field of endodontics, in 1957 as a method of debridement. (124) However, it was only in the 1980s that the first commercially available endodontic system was introduced. Ultrasonics are recognized to produce high frequencies, but low amplitudes. (125) The files operate between 25-30 kHz frequencies, which is known to be beyond the limit of human auditory perception. (126) They operate in a traverse vibration that sets a characteristic pattern for the nodes and antinodes along the length.

Nusstein has developed an adapter that hold a needle to the ultrasonic handpiece. (127, 128) During the activation, a 25-gauge irrigation needle is used in the place of an endosonic file. This enables the ultrasonic activation with a maximum power setting and ensure that the needle does not break. In this form of continuous ultrasonic irrigation system, the needle is activated simultaneously, while the irrigant is delivered in the canal through the needle under a continuous flow. Many studies have demonstrated the benefits of ultrasonic irrigation, as they were able to produce much cleaner canals and isthmus, both in vital and necrotic teeth. (88) However, such high-frequency leads to the disruption of the oscillating tip of the ultrasonic devices compromising the treatment, in the event that it provokes a blockage in the canal, compromising the outcome of the treatment. This factor may also explain the occasional inefficiency of ultrasonic activation, particularly in the apical part of the curved root canals. Moreover, UIA might be associated with apical zipping, canal deviation, and the root canal's perforation, particularly within a curved root canal. (129)

Sonic Irrigation

The use of sonic irrigation was first reported in 1985. (119) Sonic irrigation operates at a lower frequency than ultrasonic irrigation and the shear stress is also very low. Sonic energy generates higher amplitude or an increased back-and-forth of the tip movement. In addition, the oscillating patterns of sonic devices are recognized to be different from the ultrasonic. This technique has been shown to be an effective method when it comes to disinfecting the root canals. (120)

The conventional sonic irrigation is carried out with a Ripisonic file, attached to an MM1500 sonic handpiece, with the activation being done after the canal shaping is over. The Ripisonic files have non-uniform taper, and this would increase the file size. Considering that Ripisonic files are barbed, these files may inadvertently engage with the canal wall and damage the final canal preparation during the agitation stage.

Another method is the recently introduced EndoActivator® System, (121) which comprises a portable handpiece and disposable polymer tips of three types and different sizes. The tips are flexible but strong. Considering that they are smooth, they do not cut dentin, which is one of its great advantages, not damaging the root canal morphology. This system is reported to be capable of effectively removing the debris and removing the smear layer, and dislodge the clumps of biofilm (simulated) that is seen within the curved canals of the tooth. (122) The EndoActivator® tip produces a cloud that can be detected inside a fuel-filled pull chamber. The vibrating tip, along with the movement of the tip up and down, is known to create short vertical strokes that are capable to produce a powerful hydrodynamic phenomenon. (123) One disadvantage of using the polymer tip is their radiolucent properties, because it can be difficult to identify it, if part of the tip separates inside the canal. (124)

Sonic system EDDY® is powered at a high frequency which is close to 6 kHz. (Fig. 1.6) The vibration produced is transferred to the polyamide tip, which based on the qualities of the material, moves into a high amplitude oscillation. The three-dimension movement triggers cavitation and acoustic streaming, which is associated with characteristics required for higher cleaning efficiency. EDDY® tips are known to help bringing the same efficiency as ultrasonics (VDW Dental 2020). Based on studies carried out, it was seen that EDDY® was able to remove more debris when compared to manual irrigation. Additionally, EDDY® proved to be significantly better than EndoActivator®, and superior to manual irrigation. (125)

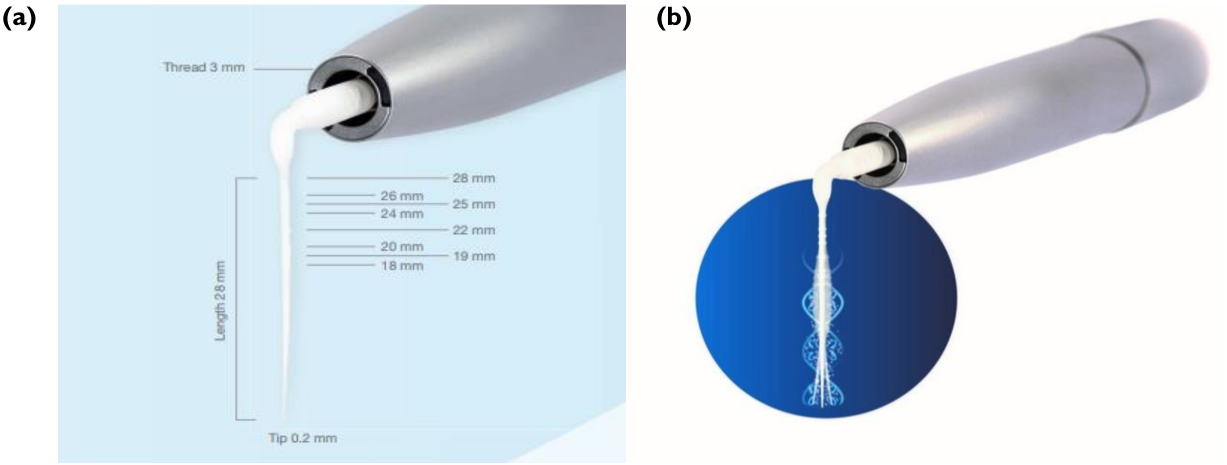

Figure 1.6 – (a) Schematic illustration of sonic system EDDY® and (b) tip motion.

Pressure Alteration Devices

Positive pressure irrigation is a method of irrigation that creates a positive apical pression in apical third of the root canal, and it occurs using syringe irrigation, when the irrigant is delivered by a syringe and a needle inserted near working length (WL) and it flows towards the root canal orifice where it is normally aspirated by a suction tip. On the other hand, negative pressure irrigation aims to decrease the risk of apical extrusion of irrigants beyond the apex. Root canal irrigants are delivered by a syringe and needle inside the pulp chamber and a fine suction tip placed near WL produces the necessary negative pressure that brings the irrigant into the canal. (126) Two examples of negative pressure alterations devices are the RinsEndo and the EndoVac™ irrigation systems. RinsEndo irrigate the root canal with a pressure-suction technology, and it consists in an handpiece with a cannula with a 7 mm-long exit aperture and along with it a syringe is used to carry the irrigant. (127) During the suction phase, the used solution and air are extracted from the root canal, and merged with the fresh rinsing solution. The pressure-suction cycles changes at least 100 times in a minute. (96) As per the manufacturers, this pulsing nature is recognized to effectively aids in rinsing the apical thirds of the canal, and the cannula is restricted to the coronal third due to the pulsating nature of the fluid flow. (113, 127) However, this system is less effective when it comes to removing stained collagen from the walls of the canal in comparison to the manual-dynamic technique, which was done by hand agitation of the instrumented canals.

EndoVac™ system, another negative pressure-based irrigation system, consists of a Master Delivery Tip (MDT), the microcannula and macrocannula. MDT is used to deliver the irrigant to the pulp chamber and to evacuate the irrigant concomitantly. Both the macro and microcannula are connected to the syringe of the irrigant, and to a highspeed suction unit. During the process, the MDT deliver the irrigant to the pulp chamber, and this helps in siphoning the excess irrigant and prevents any overflow. The cannula within the canal is filled with a negative pressure that would pull the irrigant from the fresh supply in the chamber from the MDT down the canal, to the tip of the cannula and then into the cannula, and then out with the help of a suction hose. This ensures that there is a constant and continuous flow of fresh irrigant, delivered with the help of negative pressure. (128, 129)

Laser Activated Irrigation

Laser activated irrigation (LAI) was first introduced as a powerful method for root canal irrigation. Under this, the laser radiation produces transient cavitation with the liquid, which is achieved due to the optical breakdown and strong adsorption of the laser energy. (130-132) LAI is capable to remove the smear layer from the walls, but can also lead to extrusion of the irrigant from the apex. The laser was first used by Weichman and Johnson in 1971 (133), who focused on using it to seal the apical foramen with the use of high power laser. (133) Lasers with different powers impact the cleaning in different ways, and the most suitable wavelengths to clean and disinfect is yttrium aluminum garnet (Er: YAG) 2940 nm and neodymium: yttrium aluminium garnet (Nd: YAG) 1064 nm. The impact of the laser on the root canal is dependent on the absorption of the wavelength in the biological components as well as the chromophores like apatite minerals, pigmented substances, and water. Wavelengths of visible and near-infrared radiation levels are known to have more bactericidal effects. (134) The initial research mentions that though specific lasers could help remove the smear layer and debris and modify the morphology, they still are not as effective as replacing the sodium hypochlorite, so it should be considered an adjunct to the current protocols. (135) In a study carried out by Groot *et al.,* in 2009 (136), it was seen that LAI was more effective in the removal of dentine debris in comparison to the ultrasonic irrigation as well as the hand irrigation, when the irrigant was activated for at least 20 seconds. (136)

Photon-induced Photoacoustic streaming (PIPS)

A newer technique introduced has been the photon-induced photoacoustic streaming (PIPS), which use the Er: YAG laser. (137-139) Photoacoustic pressure waves are generated with this technique as a result of laser irradiation. PIPS is known to induce fluidic movements that could lead to improved penetration into the root canal system. The tapered or stripped tip is used in the process for activation purpose. The side effects are largely prevented, because the root canal walls contact is avoided, and the melting of dentine is also minimized. The only side effect that has been mentioned is the apical extrusion of the irrigation solution. The concentration of the irrigant is known to impact the result of the irrigation solution on the tissue, and because of that, the extruded irrigation solution could also lead to inflammation. Thus, it is highly important to ensure that the pressure levels of the irrigation solutions are lower than the periapical tissue resistance (140) PIPS is considered safe and effective while debriding and decontaminating the root canal system. There is no thermal effect on the dentin wall, which could be a result of the decreased energy setting, placement of the tip and short pulse duration. (141) In another study, it was seen that there were significantly fewer bacterial counts with the use of PIPS when it was combined with NaOCl 5%. The measurement was performed 48 hours after the procedure was completed, and PIPS was effective in eradicating the bacterial biofilm and smear layer. (142)

10. POST ENDODONTIC PAIN

The pain after root canal treatment is considered one of the biggest challenges in endodontic treatment. The postoperative pain can range between 3 to 50% of the cases. (143) The mild postoperative pain is not considered to be rare even when the endodontic treatment follows all the protocols that have been established. (144, 145) The flare-up consists of an intense pain or swelling of the facial soft tissues as well as the oral mucosa in the area where the operation or endodontic treatment has been undertaken. The clinical symptoms can be severe, like pain during biting, and the patient might need to visit the clinic to relieve the pain. (146-148) After the treatment is completed, the flare-up manifests at different levels of pain and intensity over a period and may be accompanied by some swelling. The flare-up could be just for a few hours or could even last for few days. (145, 149) The pain could be a periapical inflammatory response to several factors like mechanical/instrumentation, apical extrusion of debris that affects the periapical tissues, chemical injury or psychological influences. (150, 151) One of the most significant risks associated to the irrigation procedure remains the extrusion of debris and irrigant solution into the periapical region, which may cause post-operative undesirable outcomes, as periapical inflammation, postoperative pain, and, eventually, compromise the success of root canal treatment. (152, 153) The leakage of NaOCl during treatment may cause sequelae such as pain, swelling, bruising, and numbness comparable to a chemical burn.(154) Due to the positive apical pressure generated during irrigation delivery, irrigant solutions may be pushed out into the periapical tissues, thereby inducing an inflammatory response and PEP.(155, 156) Therefore, safe and effective irrigation delivery systems are required to prevent the periapical inflammation associated with irrigants use. Factors like age, gender, tooth features, (*i.e.*, type, vitality and intracanal medication), are often associated with the flare-up. (157-159) Numerous reports have mentioned that pain between the two endodontic appointments might be a result of periapical lesion, and preoperative pain. The pain after root canal treatment is impacted by the exacerbation of a chronic lesion. The accumulation of the remnant materials in the final portion of the root is considered a typical occurrence that cause obliteration of the root canal, and this contributes to the presence of bacteria in the apical zone that may provoke pain. (160-162) It is said that the situation could be avoided if the patency for the apical foramen is maintained. (157, 163)

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CHAPTER II

OBJECTIVES

The complete debridement and disinfection of the canal is very difficult to reach, which can lead to an accumulation of tissue debris, bacteria and their products, resulting in persistent periradicular inflammation. Accordingly, it's of great importance the study of alternative approaches for cleaning and disinfecting the root canal.

Having that in mind, the following objectives were outlined:

- Conduct a systematic review comparing sonic and ultrasonic activation systems for irrigation during root canal treatment;
- Conduct an integrated analysis of sonic and ultrasonic activation systems for endodontic irrigation within distinct apical dimensions through an *ex vivo* study;
- Conduct a clinical study to evaluate the postoperative pain after irrigation with 5.25% NaOCl using endodontic needle and activation with EDDY® during root canal treatment.

Paixão S., Rodrigues C., Grenho L., Fernandes M.H., Efficacy of sonic and ultrasonic activation during endodontic treatment: a Meta-analysis *of in vitro* studies. Acta Odontologica Scandinavica. 2022

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CHAPTER III

EFFICACY OF SONIC AND ULTRASONIC ACTIVATION DURING ENDODONTIC TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS OF *IN VITRO* STUDIES

Chapter III. Efficacy of sonic and ultrasonic activation during endodontic treatment; a systematic review and meta-analysis of *in vitro* studies

Abstract

Objective: To ensure a successful endodontic treatment, it is important to have a proper disinfection of the root canal. The current study compares the root canal cleanliness and smear layer score between sonic and ultrasonic activation.

Method: Systematic literature review was implemented, using 12 databases. All *in vitro* studies comparing the efficacy of sonic and ultrasonic activation and reporting at least one outcome of interest were included.

Results: At the apical level, pooling the data in the random-effects model ($I^2=64\%$, $p=0.1$) revealed a statistically significant lower smear layer score within the sonic activation group (MD-0.48; 95% CI-0.92, -0.04; $p=0.03$). Furthermore, there was a statistically significant lower push-out bond strength value among the sonic group, in contrast to the ultrasonic group at the middle (MD-0.69; 95% CI-1.13, -0.25; $p=0.002$) and at the apical levels (MD-0.78; 95% CI-1.09, -0.46; $p<0.0001$) of the root canal.

Conclusions: Sonic activation accomplished advancement relative to ultrasonic agitation in removing the smear layer, while ultrasonic activation resulted in significant cohesion between the sealers and the dentin tubules, decreasing the vulnerability of apical leakage and tooth fracture.

Keywords: disinfection, endodontics, root canal irrigants, sodium hypochlorite, ultrasonics

1. INTRODUCTION

Endodontic treatment aims to thoroughly disinfect the root canal and to reduce the bacteriologic status. The accomplishment of such purposes entails an efficient chemo-mechanical preparation, as well as proper obturation of the root canal system. (1) Canal's complex anatomy, mainly accessory and irregular canals, makes it extremely difficult to completely clean and seal all the ramifications of the canal system through chemo-mechanical preparation. (2) Canal cleanliness consists in the complete cleaning of the complex anatomy of the root canal system (lateral canals, isthmuses, fins and accessory canals). This is influenced by proper removal of debris and smear layer. (3, 4) After preparation, a smear layer consists of organic and inorganic components, like dentin debris, microorganisms and necrotic tissue. This layer reduces the ability of root canal irrigants, and intracanal drugs to penetrate into the dentinal tubules adequately. (5, 6) Smear layer scores are used to measure the percentage of smear layer covering the dentinal tubules and measure if dentinal tubules are visible and open. (3) Also, there are debris scores, to evaluate the percentage of the canal wall covered by dentine chips, pulp remnants and particles loosely attached to the canal wall. (3) Furthermore, close to 60% of the root canal surface might remain untouched by endodontic instruments using rotary files, which lead to inconvenient debridement and disinfection of the entire canal system. (7) Employment of irrigant solutions alone is found to be inappropriate to accomplish the complete elimination of debris and to kill the microorganisms, remove the smear layer, and eliminate the pulp residues within the canal system. (8) To enhance the distribution and flow of the agitated solutions during endodontic treatment, several strategies have been advocated. (9)

To date, various mechanical, chemical, and thermal techniques have been proposed to achieve the desired cleaning. (10) On the contrary, none of these approaches alone or in combination succeeded in perfectly cleaning the root canal system. Additionally, such methods might be associated with adverse events such as periapical inflammation and irritation, along with postoperative flare-up. Accordingly, adjunct methods such as ultrasonic and sonic devices have been reported to alleviate/improve the cleaning efficacy and disinfection ability of the different irrigants. (11, 12)

Ultrasonic irrigant activation (UIA) is an irrigation protocol that uses files or smooth wires oscillating freely in the root canal producing powerful acoustic microstreaming. It enhances noticeably the efficacy of irrigants in eliminating inorganic and organic debris from the root canal, and promotes cavitation and acoustic transmission through operating at high frequency (25 to 30 kHz). (13) However, such high-frequency leads to the disruption of the oscillating tip of the ultrasonic devices compromising the treatment, in the event that it provokes a blockage in the canal, compromising the outcome of the treatment. This factor may also explain the occasional inefficiency of ultrasonic activation, particularly in the apical part of the curved root canals. Moreover, UIA might be associated with apical zipping, canal deviation, and the root canal's perforation, particularly within a curved root canal. Sonic activation operates through low-frequency vibration (1-6 kHz) using flexible tips linked to an air sealer handpiece. These factors contribute to the increased penetration ability of the irrigants into the apical and lateral canals. (14) Further, the flexible plastic-like points don't deform the canal walls like metal files in UIA, but as sonic devices operate at a lower level than ultrasonic devices, this may be linked to lower efficacy levels.

Despite the dentists' efforts to clean the root canal system and improve endodontic treatment outcomes, the optimal activation methods remain a challengeable question in the literature. Although there are some *in vitro* studies comparing both techniques and several systematic reviews about ultrasonic irrigant activation (15-19), there is no meta-analysis comparing sonic and ultrasonic activation during endodontic treatment. Based on this, the current study was conducted to compare the root canal cleanliness, smear layer score, debris score, total amount of debris removed, penetration depths of irrigants and push-out bond strength values between sonic and ultrasonic activation during endodontic treatment.

2. METHOD

This meta-analysis was carried out following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines, (20) and the recommendations of Cochrane collaboration. (21) The methodology of the study was documented in a protocol which was registered at http://www.crd.york.ac.uk/prospero/ (**Registration number**; CRD42020197779).

Pico Question: Are sonic activation outcomes better than ultrasonic for endodontic treatment in human extracted teeth?

Data source

An extensive literature review was implemented, until 20 July 2020, by 2 independent reviewers, using the following databases; PubMed, Google Scholar, Web of Science, Scopus, SIGLE, Virtual Health Library, NYAM, Clinical trials, Controlled Trials, EMBASE, WHO and International Clinical Trials Registry Platform. No restrictions were employed on patients' age, sex, ethnicity, language, race or place/region.

A further extensive search of each database using related articles' function was carried out. Subsequently, manual scanning of references and bibliographies of all related studies was performed to retrieve all possible relevant articles that were not indexed. The cross-referencing approach was executed until no additional relevant articles were discovered.

Study selection

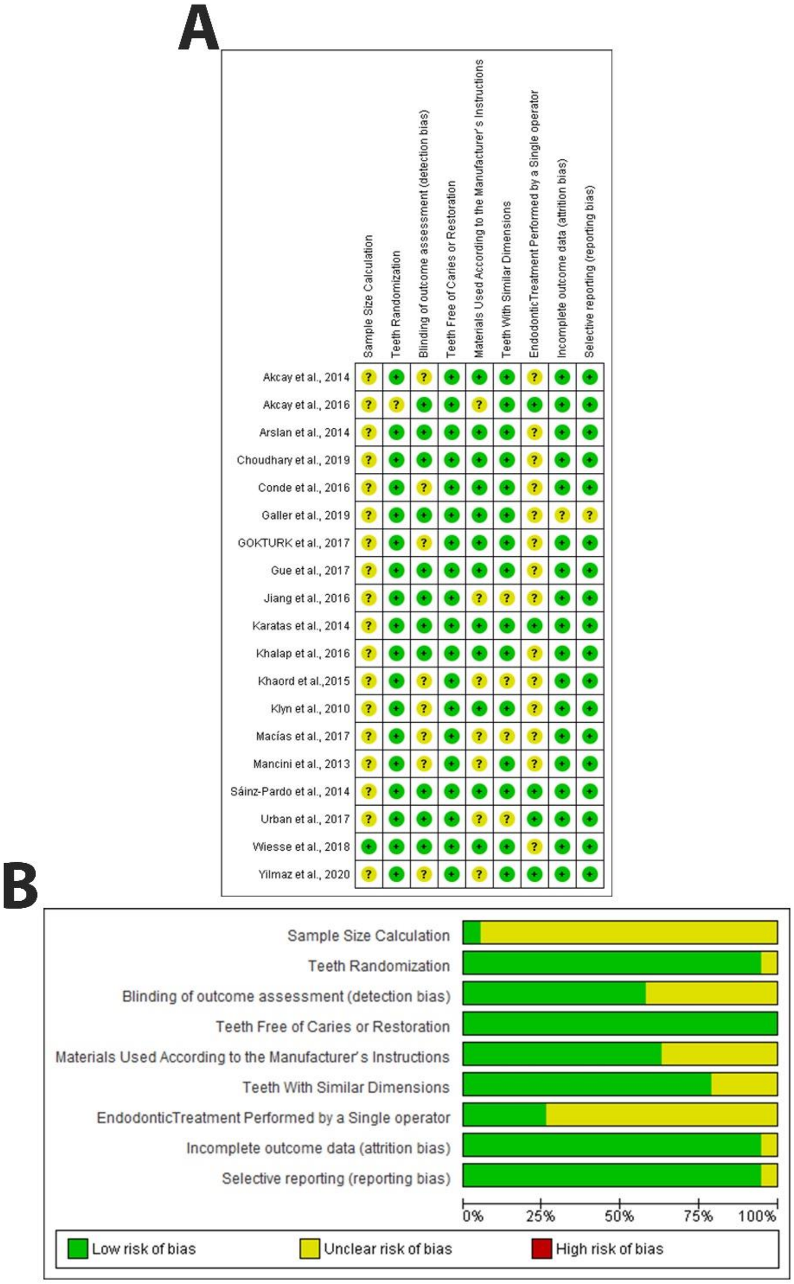
All *in vitro* and *ex vivo* studies comparing the outcomes of interest (total amount of debris removed, remaining debris scores, penetration depths of irrigants, total smear layer score, push-out bond strength values, percentage of canal cleanliness) between sonic and ultrasonic activation during endodontic treatment and reported at least one outcome of interest were included in the current meta-analysis. There was no restriction on the age or site of the extracted teeth. Studies including teeth with calcification, resorption, or cracks were ousted. Similar to that, non-comparative studies and studies in which data unattainable to be extracted, review articles, animal studies, case reports, comments, letters, editorials, posters, and book chapters were excluded. Taking into account that these outcomes are not possible to verify *in vivo*, only *in vitro* articles were included.

The screening process of the title, abstract, and the full text was performed independently to reveal the potentially relevant articles that met the inclusion criteria. The discussion dissolved the contradiction between the reviewers.

Data extraction and quality assessment

The following data were extracted from the finally included articles, independently by two reviewers (SP & LG): study characteristics (the title of the included study, the second name of the first author, year of publication, study design, study period, number of centers, and study region), teeth related data (number of teeth, age of patients, and source of the extracted teeth), endodontic treatment and root canal preparation (filling methods, irrigants, irrigation time, protocols of sonic and ultrasonic irrigation techniques, time of activation, and methods of outcomes assessment) and outcomes (total amount of debris removed, remaining debris scores, penetration depths of irrigants, total smear layer score, push-out bond strength values, percentage of canal cleanliness). The effect sizes were extracted from data reported as graphs using Web Plot Digitizer software (https://automeris.io/WebPlotDigitizer/).

The quality of the included studies was assessed based on the Checklist for Reporting *In Vitro* Studies (CRIS Guidelines) (22) and as demonstrated by Sarkis-Onofre *et al.,* 2014 (23) Moraes *et al.*, 2015, (24) and Valente *et al.*, 2016 (25) studies. The following parameters, like seen in Fig. 2.1 were put in consideration: sample size calculation, teeth randomization, blinding of outcome assessment (detection bias), teeth free of caries or restoration, materials used according to the manufacturer's instructions, teeth with similar dimensions, endodontic treatment performed by a single operator, incomplete outcome data (attrition bias), and selective reporting (reporting bias). If the parameter was controlled, the domain was considered "low risk" and vice versa. If it was not reported, the domain was classified as "unclear".



	Sample Size Calculation	Teeth Randomization	Blinding of outcome assessment (detection bias)	Teeth Free of Caries or Restoration	Materials Used According to the Manufacturer's Instructions	Teeth With Similar Dimensions	EndodonticTreatment Performed by a Single operator	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Akcay et al., 2014	?	+	?	+	+	+	?	+	+
Akcay et al., 2016	?	?	+	+	?	+	+	+	+
Arslan et al., 2014	?	+	+	+	+	+	?	+	+
Choudhary et al., 2019	?	+	+	+	+	+	?	+	+
Conde et al., 2016	?	+	?	+	+	+	?	+	+
Galler et al., 2019	?	+	+	+	+	+	?	?	?
GOKTURK et al., 2017	?	+	?	+	+	+	?	+	+
Gue et al., 2017	?	+	+	+	+	+	?	+	+
Jiang et al., 2016	?	+	+	+	?	?	?	+	+
Karatas et al., 2014	?	+	+	+	+	+	+	+	+
Khalap et al., 2016	?	+	+	+	+	+	?	+	+
Khaord et al.,2015	?	+	?	+	?	?	?	+	+
Klyn et al., 2010	?	+	?	+	+	+	?	+	+
Macías et al., 2017	?	+	?	+	?	?	?	+	+
Mancini et al., 2013	?	+	?	+	?	+	?	+	+
Sáinz-Pardo et al., 2014	?	+	+	+	+	+	+	+	+
Urban et al., 2017	?	+	+	+	?	?	+	+	+
Wiesse et al., 2018	+	+	+	+	+	+	?	+	+
Yilmaz et al., 2020	?	+	?	+	?	+	+	+	+

Figure 2.1 (A) Risk of bias summary: review authors' judgements about each risk of bias item for each included study. **(B)** Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Statistical analysis

Weighted mean difference (WMD) or standardized mean difference (SMD) was used for analyzing the continuous variables. Mean and standard deviation (SD) were calculated from studies reported data using mean and range or median and range based on the equations exemplified by Hozo *et al*., (26) The fixed-effect model was implemented when a fixed population effect size is assumed; otherwise, the random-effects model was used. Statistical heterogeneity was appreciated using Higgins I^2 statistic, at the value of $> 50\%$, and the Cochrane Q (Chi^2 test), at the value of $p < 0.10$. (27) To account for this heterogeneity, the random-effects model was employed, and subgroup analysis was implemented concerning the anatomical considerations. Publication bias was assumed in the presence of an asymmetrical funnel plot and based on Egger's regression test (*p-value* <0.10). Herein, the trim and fill method of Duvall and Tweedie was used. (28) Data analysis was performed using Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The significant difference was established at the value of $p < 0.05$.

3. RESULTS

The extensive literature review yielded an overall 365 articles. After duplicates removal, 224 reports were selected for title, abstract, and full-text screening. Amongst them, 16 articles were identified for review and meta-analysis besides three studies recognized throughout the manual search. A flow diagram illustrated the process of the literature search is shown in Fig. 2.2.

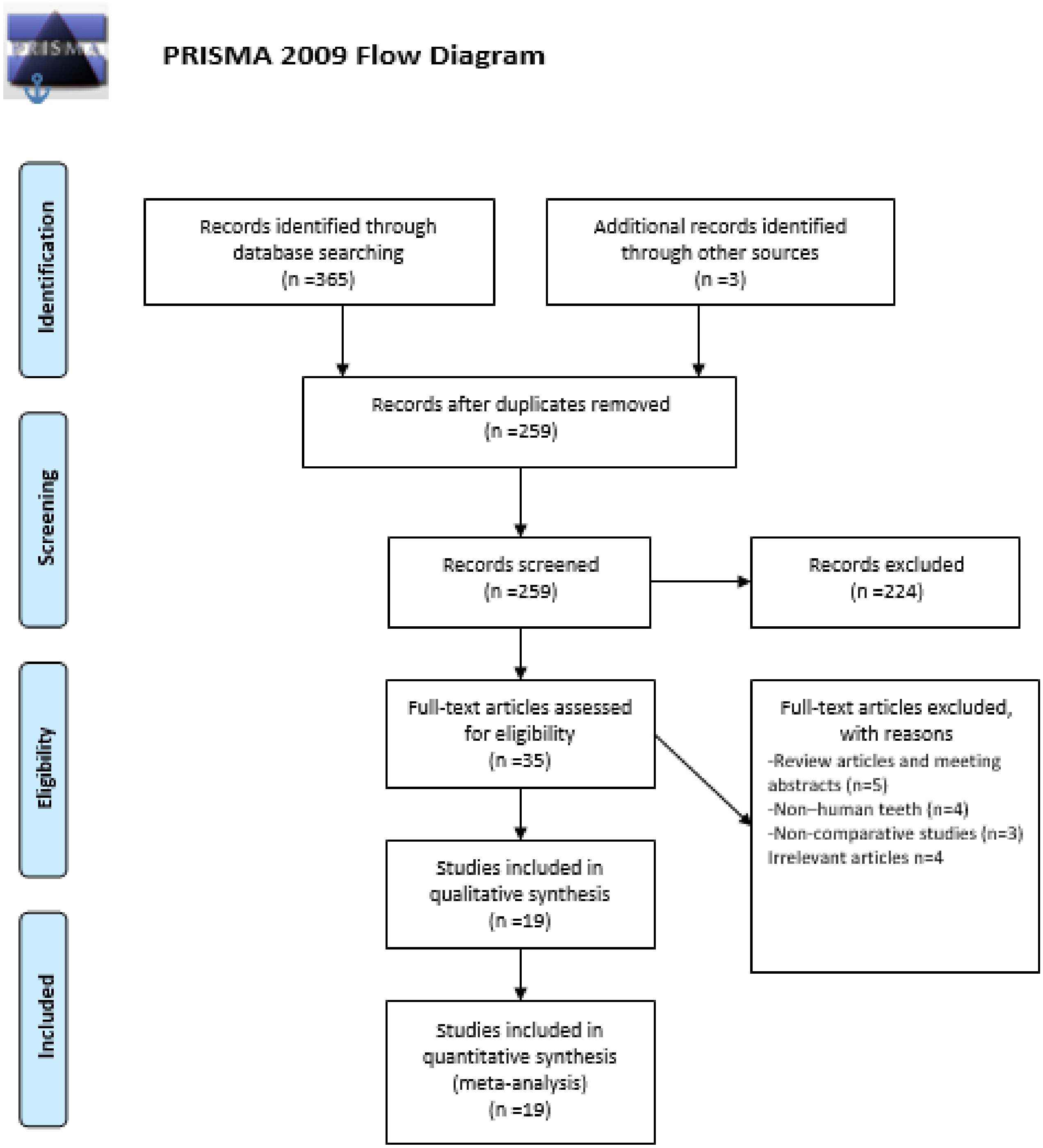


Figure 2.2 PRISMA Flow chart showing the process of the literature search, title, abstract, and full text screening, systematic review, and meta-analysis. (20)

Characteristics of the included studies

This meta-analysis included a total of 19 articles. (3, 4, 29-45) These articles encompassed an overall 570 extracted teeth with an equal proportion of teeth (285 teeth) among sonic and ultrasonic groups. Regarding the studies distribution, six studies included teeth from Turkey, while three studies included extracted teeth from Indian patients. Out of the included studies, five and three studies included mandibular premolars and mandibular molars, respectively. Additionally, three studies included maxillary incisors. Having the sonic activation protocols, EndoActivator® was employed among 15 studies whereby EDDY® (VDW, Munich, Germany) and Vibringe® devices were implemented within two studies, separately. The irrigation time ranges from one to five minutes.

Apart from Wiesse *et al*., 2018 study (44), no study reported the method of sample size calculation, showing unclear risk of bias. All the included studies showed a low risk of bias regarding the teeth randomization domain apart from Akcay *et al*., 2016. (30) Out of the included studies, 11 studies showed a low risk of detection bias whilst seven studies showed unclear risk of bias regarding materials used according to the manufacturer's instructions. Furthermore, 15 and five studies depicted low risk of bias regarding teeth with similar dimensions and endodontic treatment performed by a single operator domain, respectively. Only one study showed unclear risk of attribution and reporting biases.

Study endpoints:

Amount of Debris Removed

Three studies, including 114 teeth, assessed the difference between sonic and ultrasonic irrigation regarding the mean amount of removed debris. In the random-effects model (I^2=91%, $p < 0.001$), pooling the data revealed no statistically significant difference between both groups (MD -0.00; 95 %CI -0.71, 0.70; $p=1.000$).

As for the change in root weight before and after irrigation, pooling two studies' effect sizes showed no statistically significant difference between sonic and ultrasonic irrigation (MD -0.12; 95 %CI -0.59, 0.35; *p=0.62*).

Mean Debris scores

Two studies, including 54 teeth, evaluated the mean debris score between sonic and ultrasonic activation at the coronal level. In the random-effects model, there was no statistically significant difference between both groups (MD -0.00; 95 %CI -0.24, 0.24; *p=1.000*). At the middle level, pooling the data from two studies, including 64 extracted teeth, showed no statistically significant difference between sonic and ultrasonic activation (MD -0.23; 95 %CI -0.72, 0.26; *p=0.35*), as seen in Figure 2.3 A. At the apical level, there was no statistically significant difference between both groups (MD -0.00; 95 %CI -0.24, 0.24; *p=1.000*).

Mean Smear layer scores

The mean smear layer score was reported within two studies, including a total of 64 extracted teeth. At the middle level, pooled analysis, in the random effects-model (I^2=78%, *p=0.03*), showed no statistically significant difference between sonic and ultrasonic irrigation techniques (MD -0.34; 95 %CI -0.92, 0.25; *p=0.26*).

At the apical level, pooling the data in the random-effects model (I^2=64%, *p=0.1*) revealed a statistically significant lower smear layer score within the sonic activation group, relative to the ultrasonically activated group (MD -0.48; 95 %CI -0.92, -0.04; *p=0.03*), as in Figure 2.3 B.

Percentage of canal cleanliness

Two studies, including 50 extracted teeth, assessed the percentage of canal cleanliness after sonic and ultrasonic activation. At one mm from the apex, there was no statistically significant difference between both groups (MD 0.46; 95 %CI -2.32, 3.24; $p=0.75$). In this concern, there was no statistically significant difference between sonically activated and ultrasonically activated teeth regarding the percentage of canal cleanliness at three mm (MD -0.36; 95 %CI -1.83, 1.10; $p=0.63$) and at five mm (MD -0.16; 95 %CI -0.95, 0.62; $p=0.68$) from the apex.

Irrigants penetration depth

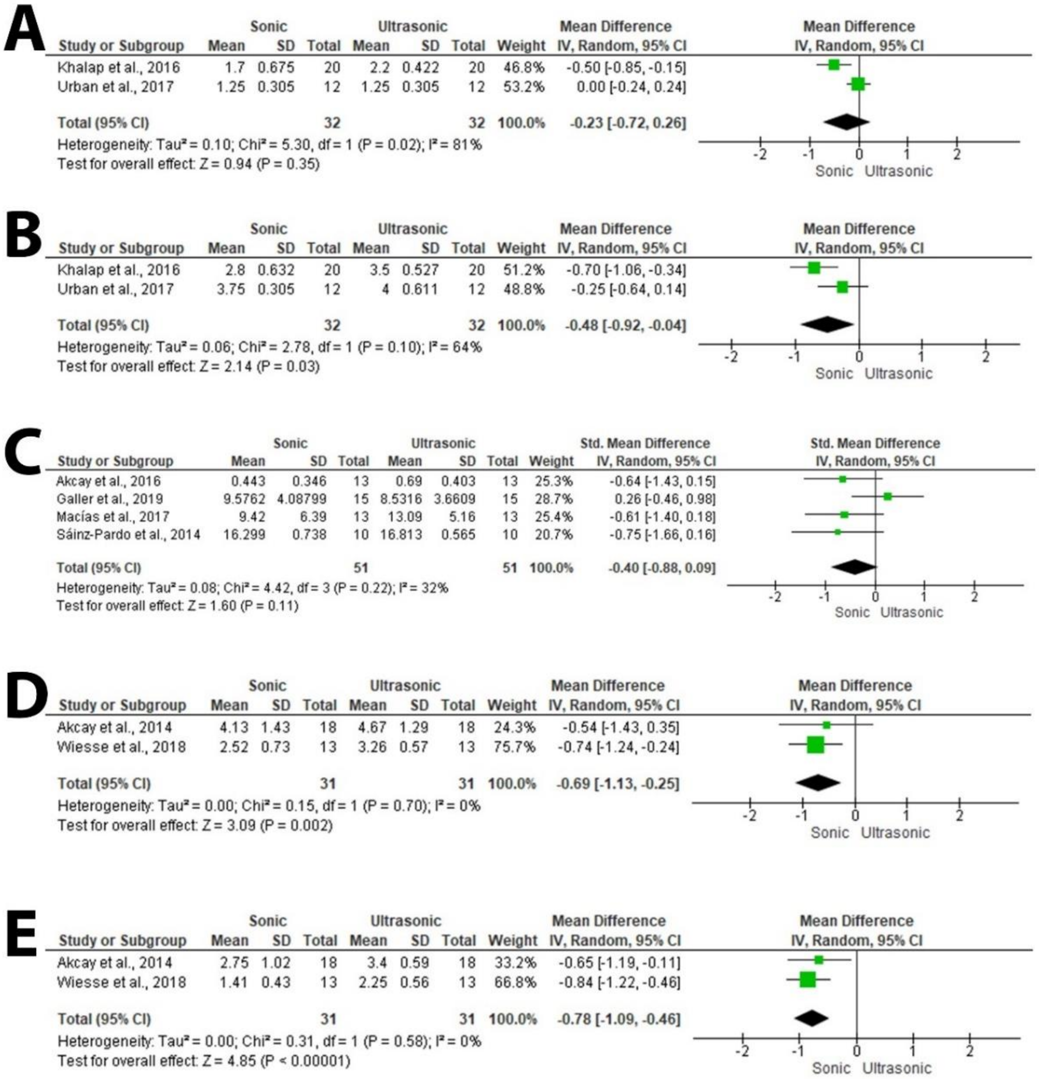
The total irrigants penetration depth was assessed within four studies, including a total of 102 extracted teeth. Pooling the data revealed no statistically significant difference between sonically activated and ultrasonically activated teeth (MD -0.40; 95 %CI -0.88, 0.09; $p=0.11$), as seen in Figure 2.3 C.

At the coronal level, pooling the data in the random-effects model (I^2=78%, $p=0.003$) showed no statistically significant difference between sonic and ultrasonic groups regarding the irrigants penetration depth (MD 0.01; 95 %CI -0.85, 0.86; $p=0.99$). In this respect, there was no statistically significant difference between sonically and ultrasonically activated groups regarding the irrigants penetration depth at the middle (MD -0.10; 95 %CI -0.66, 0.46; $p=0.73$) and apical levels (MD -0.40; 95 %CI -0.99, 0.19; $p=0.18$).

Push-out bond strength values

The mean push-out bond strength value was reported within two studies, including 62 extracted teeth. At the coronal level, pooling the data in the random-effects model (I^2=85%, $p=0.001$) displayed no statistically significant difference between sonic and ultrasonic activation (MD -1.22; 95 %CI -2.87, 0.44; $p=0.15$).

In the random-effects model, pooling the data showed a statistically significant lower push-out bond strength value among the sonic activation group, in contrast to the ultrasonically activated group at the middle (MD -0.69; 95 %CI -1.13, -0.25; *p=0.002*) and at the apical levels (MD -0.78; 95 %CI -1.09, -0.46; *p<0.0001*), as in Figure 2.3 D-E.



A

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Khalap et al., 2016	1.7	0.675	20	2.2	0.422	20	46.8%	-0.50 [-0.85, -0.15]
Urban et al., 2017	1.25	0.305	12	1.25	0.305	12	53.2%	0.00 [-0.24, 0.24]
Total (95% CI)			**32**			**32**	**100.0%**	**-0.23 [-0.72, 0.26]**

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 5.30$, df = 1 (P = 0.02); $I^2 = 81\%$
Test for overall effect: Z = 0.94 (P = 0.35)

B

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Khalap et al., 2016	2.8	0.632	20	3.5	0.527	20	51.2%	-0.70 [-1.06, -0.34]
Urban et al., 2017	3.75	0.305	12	4	0.611	12	48.8%	-0.25 [-0.64, 0.14]
Total (95% CI)			**32**			**32**	**100.0%**	**-0.48 [-0.92, -0.04]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 2.78$, df = 1 (P = 0.10); $I^2 = 64\%$
Test for overall effect: Z = 2.14 (P = 0.03)

C

	Sonic			Ultrasonic				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2016	0.443	0.346	13	0.69	0.403	13	25.3%	-0.64 [-1.43, 0.15]
Galler et al., 2019	9.5762	4.08799	15	8.5316	3.6609	15	28.7%	0.26 [-0.46, 0.98]
Macías et al., 2017	9.42	6.39	13	13.09	5.16	13	25.4%	-0.61 [-1.40, 0.18]
Sáinz-Pardo et al., 2014	16.299	0.738	10	16.813	0.565	10	20.7%	-0.75 [-1.66, 0.16]
Total (95% CI)			**51**			**51**	**100.0%**	**-0.40 [-0.88, 0.09]**

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 4.42$, df = 3 (P = 0.22); $I^2 = 32\%$
Test for overall effect: Z = 1.60 (P = 0.11)

D

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2014	4.13	1.43	18	4.67	1.29	18	24.3%	-0.54 [-1.43, 0.35]
Wiesse et al., 2018	2.52	0.73	13	3.26	0.57	13	75.7%	-0.74 [-1.24, -0.24]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.69 [-1.13, -0.25]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.15$, df = 1 (P = 0.70); $I^2 = 0\%$
Test for overall effect: Z = 3.09 (P = 0.002)

E

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2014	2.75	1.02	18	3.4	0.59	18	33.2%	-0.65 [-1.19, -0.11]
Wiesse et al., 2018	1.41	0.43	13	2.25	0.56	13	66.8%	-0.84 [-1.22, -0.46]
Total (95% CI)			**31**			**31**	**100.0%**	**-0.78 [-1.09, -0.46]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.31$, df = 1 (P = 0.58); $I^2 = 0\%$
Test for overall effect: Z = 4.85 (P < 0.00001)

Figure 2.3 (A) Mean amount of removed debris. **(B)** Mean smear layer score at the apical level. **(C)** Total irrigants penetration depth. **(D)** Push-out bond strength value at the middle level **(E)** Push-out bond strength value at the apical level.

4. DISCUSSION

Irrigants penetration into a considerable area of the root canal system is a critical factor for successful endodontic therapy. It is essential to maximize the efficacy of irrigants penetration by combining solutions with different activation devices. (46-48) Being anatomically complex, finding the best agitation technique during root canal treatment is a doubtful question in the literature due to contradictory outcomes. (49) Therefore, this meta-analysis was conducted to reveal the outcomes of sonic and ultrasonic irrigations during endodontic treatment.

The evidence obtained in the current study showed that sonically activated teeth had a significantly lower smear layer scores, particularly at the apical level of the root canal. On the contrary, root canals with irrigant solution ultrasonically activated had a remarkedly high push-out bond strength value. The push-out bond strength was measured between root canal sealers and root canal dentin. There was no superiority of either technique regarding the amount of removed debris, percentage of canal cleanliness, and irrigants penetration depth during endodontic therapy.

The apical third of the root canal has the utmost impact on the outcomes of endodontic therapy, being the communication part between periapical tissues and the pulp cavity. (50) In the present study, the employment of sonic activation during endodontic treatment decreased the smear layer score considerably at the apical level. As the lateral canals and ramifications are frequently presented in the apical region, their cleansing is crucial for effective endodontic treatment. In concordance with our findings, Shahravan *et al*., 2017 stated that removing the smear layer noticeably improved the cleanliness and fluid-tight obturation of the root canal. (51)

This finding might be attributed to the ineffective delivery of the irrigant solutions into the apical region of the root canal in the ultrasonically activated group. Additionally, the resultant acoustic microstreaming of the ultrasonic devices generates shear stress for dislodging debris from the operated canals. This mechanism produced unfavorable dampening alterations when the device tip comes in contact with the root canal's lateral walls, whereby sonic activation was not influenced by lateral wall contact as it uses less truculent tips. (52-54)

According to the finding of the current study, UIA was more effective than sonic activation regarding the adhesion strength between the sealers and root dentin. This might be attributed to the high frequency and small oscillation amplitude of the ultrasonic devices, which generate adequate energy for the sealer for the more homogenous distribution. (55) Besides that, the generated heat from the previous process allows the better blending of the sealer particles and the root dentin, improving the cohesive strength between them. (56) The more the increase in the bond cohesion between the root dentin and the root canal sealer, the less the tendency of apical canal leakage. Such factors also keep the root canal sealer's position under different dislocating forces, such as the mechanical exertion of the operative procedures and tooth function. These factors impacted dramatically on the longevity of the endodontic treated root canals. (57, 58)

Regarding the root canal cleanliness, the current study showed no difference between sonically and ultrasonically activated groups, which was parallel with Silva *et al*., 2019 study. Their systematic review announced that UIA achieved bacterial disinfection ability as non-activated irrigation. (15)

This meta-analysis results should be interpreted cautiously due to the limitations in translating *in vitro* studies to *in vivo* circumstances. The included studies' sample size ranged from 14 to 60 teeth, which might impair the evidence. Additionally, there was significant heterogeneity among the included studies, stemming from difference in outcomes assessment methods, source of the extracted teeth, irrigant solutions, endodontic preparation, and activation protocols. Such heterogeneity was also statistically established for the employed random-effects model. Furthermore, the lack of optimal follow-up periods constringed the assessment of long-term outcomes.

5. Conclusions

Sonic activation accomplished advancement relative to ultrasonic agitation in removing the smear layer, mainly at the apical area, during endodontic therapy. Furthermore, ultrasonic activation of the irrigants resulted in significant cohesion between the sealers and the dentin tubules, decreasing the vulnerability of apical leakage and tooth fracture. The integration of these findings in endodontic therapy protocols will help dentists to improve root canal therapy outcomes by stratifying the patients to the most appropriate and effective agitation technique. However, further randomized clinical trials are needed to address the limitations of the current meta-analysis, because it is hard to conclude by this research that one technique is better than the other.

Table 2.1 Demographic characteristics of the included studies

<table>
<tr><th colspan="2" rowspan="3">Study ID</th><th rowspan="3">Region</th><th colspan="2">Sample size</th><th rowspan="3">Source of the teeth</th><th rowspan="3">Root Canal Preparation</th><th colspan="2">Activation Protocol</th><th rowspan="3">Methods of outcome assessment</th></tr>
<tr><th>Sonic</th><th>Ultrasonic</th><th rowspan="2">Sonic</th><th rowspan="2">Ultrasonic</th></tr>
<tr><th>Number</th><th>Number</th></tr>
<tr><td rowspan="2">**1**</td><td rowspan="2">(29)</td><td rowspan="2">Turkey</td><td rowspan="2">18</td><td rowspan="2">18</td><td rowspan="2">Mandibular premolars</td><td rowspan="2">ProTaper rotary instruments were used to shape the root canals. The instrumentation sequence was as follows: Sx, S1, S2, F1, F2, F3, and F4.</td><td colspan="2">A total of 5 mL of 17 % EDTA (30 s) followed by 5 mL of 2.5 % NaOCl (30 s) was agitated</td><td rowspan="2">Stereomicroscope</td></tr>
<tr><td>EndoActivator handpiece, which was set at 10,000 cycles per minute with a red (25/04) tip, inserted 2 mm short of the working length.</td><td>Ultrasonic device (Anthos u-PZ6, Imola, Italy)</td></tr>
<tr><td rowspan="2">**2**</td><td rowspan="2">(30)</td><td rowspan="2">Turkey</td><td rowspan="2">13</td><td rowspan="2">13</td><td rowspan="2">Mandibular premolars</td><td rowspan="2">A size 10-K file was inserted in the canal until it was apparent at the major apical foramen. Root canals were prepared by using ProTaper Universal rotary instruments up to size F4</td><td colspan="2">0.5 mL of labeled NaOCl was placed into the root canal via a blunt-tip needle; a red tip (size 25, 0.04 taper) was placed within 2 mm of the working length.</td><td rowspan="2">Confocal laser scanning microscope analysis</td></tr>
<tr><td>Sonic handpiece was used for 1 min at 10,000 cycles/min in short 2–3-mm vertical strokes.</td><td>Ultrasonic device was activated for 1 min at the recommended power setting.</td></tr>
<tr><td rowspan="2">**3**</td><td rowspan="2">(31)</td><td rowspan="2">Turkey</td><td rowspan="2">12</td><td rowspan="2">12</td><td rowspan="2">Mandibular premolar</td><td rowspan="2">ProTaper rotary instruments (Dentsply Maillefer) were used for root canal shaping procedures. The instrumentation sequence was as</td><td colspan="2">A total of 5 mL of 17% EDTA was agitated for 60 s.</td><td rowspan="2">Stereomicroscope</td></tr>
<tr><td>Using the EndoActivator (Dentsply Tulsa Dental Specialties, Tulsa, OK, USA) handpiece set at</td><td>Ultrasonic device (Anthos u-PZ6; Imola, Italy). 1 mL 17% EDTA was placed into the root canal, and</td></tr>
</table>

						follows: Sx, S1, S2, F1, F2, F3, and F4 (size 40, 0.06 taper).	10,000 cycles/min, with a red (25/04) tip inserted 2 mm short of the working length.	then an ultrasonic file (size 20, 0.02 taper) was placed into the canal.	
4	(32)	India	30	30	Mandibular molars	The initial filling was done with hand files #15 and #20 K. Followed by hand filing the ProTaper rotary system was used for endodontic preparation.	The canals and pulp chambers were filled with 5.25% NaOCl. The EndoActivator sonic handpiece was set at 10,000 cycles per minute	Acivato tip was selected that fits passively when placed 2-3 mm short of working length. The solution was agitated using short vertical strokes for around 30s.	Stereomicroscope and Paque *et al.*, criteria
5	(33)	Australia	20	20	Maxillary central incisor	Manual preflaring using size 15 and 20 K-Files (ReadySteel), root canal shaping was carried out to size 40, taper 0.6 using the Reciproc system and an R40 instrument	The canals were irrigated as follows: 3 mL 2.5% NaOCl per 30 seconds, activation for 30 seconds, 1 mL 17% EDTA 30 seconds, activation for 30 seconds, 3 mL 2.5% NaOCl per 30 Seconds.		NR
							EndoActivator: with a size 25, .04 taper tip, 22 mm, set at 10000 cycles per minute, placed at WL-2 mm.	A size 20 tip, no taper, 21 mm length, mounted on an ultrasonic unit at a power setting of 4	
6	(34)	Germany	15	15	NR	A glide path was prepared with hand files size 08, .02 taper to size 20, .02 taper (K-files, VDW, Munich, Germany). Root canals were instrumented in a	1. NaOCl (5 mL, 1 min) 2. Ultrapure water (5 mL, 1 min) 3. EDTA (5 mL, 1 min), activation for 30 s 4. Ultrapure water (5 mL, 1 min) 5. NaOCl (5 mL, 1 min), activation for 30 s, resting phase 30 s, activation for 30 s		Light microscope
							EDDY®	IRRI K 25/25 (VDW GmbH,	

						crown-down manner with rotary files		Munich, Germany and the appendant	
7	(35)	Turkey	15	15	Maxillary incisors	Roots were prepared with Reciproc rotary files up to size R40 at WL (VDW GmbH, Germany). Next, roots were placed in Eppendorf tubes (Labosel, İstanbul, Turkey) filled with a silicone material (Zetaplus soft; Zhermack Clinical, Badia Polesine, Italy).	A 10 mL 2.5% NaOCl was delivered and sonically activated via the Vibringe system (Vibringe B. V. Corp, Amsterdam, Netherlands). The needle tip was placed 1 mm short of the WL without touching the canal walls, enabling it to vibrate freely for 2 min.	Irrisafe ultrasonic tip (size 25, 0.02 taper) (Satelec Acteon group, France) that was placed 1 mm short of the WL. A power setting of 9 was used for duration of 1 min. A 10 mL 2.5% NaOCl solution continuously delivered at a flow rate of approximately 0.16 mL s-1through the unit.	Stereomicroscope
8	(36)	Republic of Korea	12	12	Single-rooted maxillary premolars	The canals were instrumented in a crown-down technique with ProTaper Next NiTi rotary files (Dentsply Maillefer) up to an X4 (apical size 40) at working length.	Rhodamine B-labeled 5.25% NaOCl was sonically activated for 30 sec with a #15 K-file mounted in the EndoMaster (ENC System) at H mode setting	Rhodamine B-labeled 5.25% NaOCl was ultrasonically activated for 30s with an ISO #15 stainless steel ultrasonic file The ultrasonic device (PerioScan; Sirona Dental System GmbH)	Confocal laser scanning microscope

								was set at PERIO 3 mode	
9	(37)	China	7	7	Maxillary premolar	ProTaper NiTi rotary instruments and obturated with guttapercha and AH Plus sealer using the continuous wave of condensation technique. The root canal was filled with 2 mL of 3% NaOCl solution. During irradiation or activation, the pulp chamber was refreshed using 3% NaOCl solution when the coronal reservoir level became low.	EndoActivator (The sonic tip was placed into the canal 1 mm short of the WL without touching the walls and activated for 20s (3x20 s).	Ultrasonic device on a 25% power setting in E mode 28 kHz (EMS, Le Sentier, Switzerland) and delivered using an ultrasonic tip (size 20, taper 0.02) (ESI Instrument, EMS, Le Sentier, Switzerland).	A high-resolution micro-CT
10	(38)	Turkey	15	15	Maxillary incisors	ProTaper Universal rotary files to a size 40, .06 taper using a crown-down technique. Apical patency was maintained by passing a size 15 file to WL after the use of each file.	The irrigation needle was placed 1 mm short of the predetermined working length. The root canals were irrigated with the Vibringe for 1 minute, and following Use of the last instrument it was used for 2 minutes as a final rinse.	U-file ultrasonic tip (size 15, 0.02 taper) was placed to 1 mm short of the working length. It was activated at a frequency cycle of 28-32 kHz per second for 1 minute, and after the last irrigation it was used for 2 minutes.	Electronic weigh machine

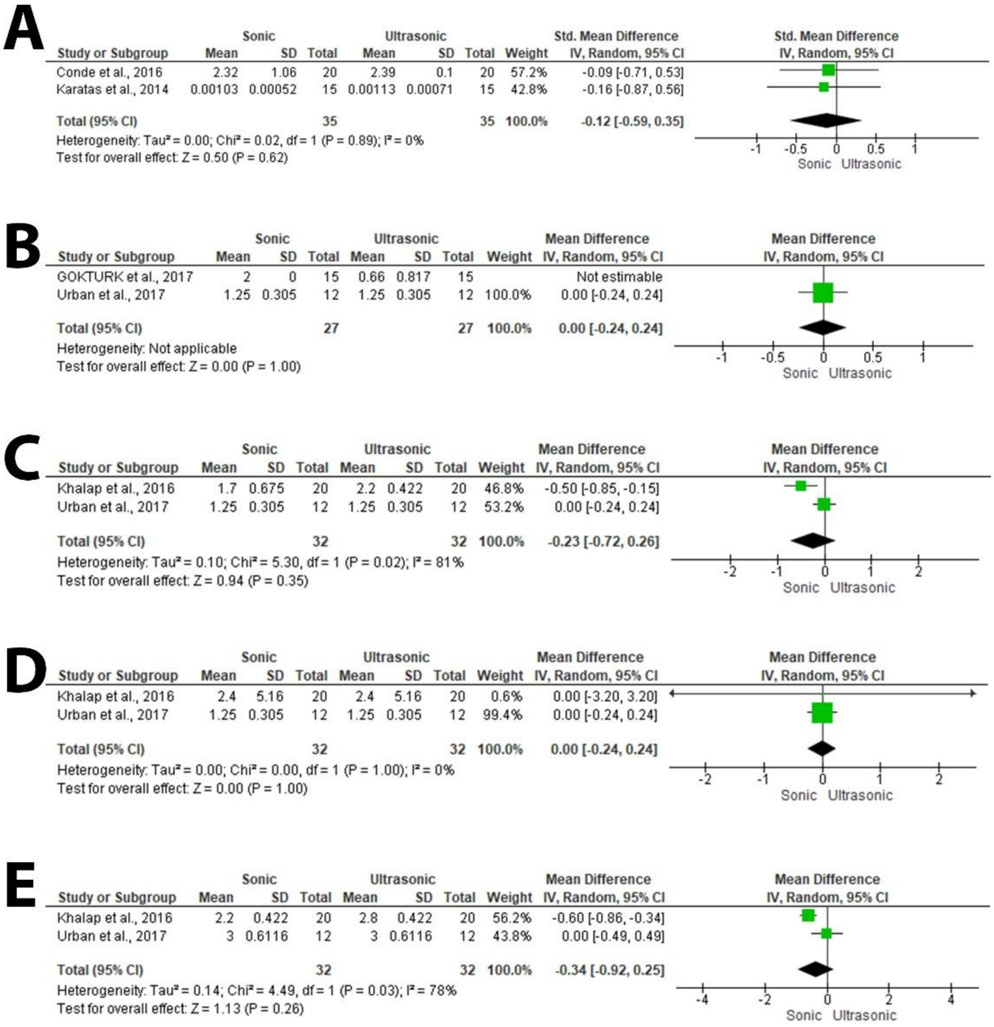
11	(39)	India	20	20	Mandibular premolars	Specimens were instrumented by PTN files until full sequence X4 (40/.06). These files were used in outward brushing mode at 300 rpm/2.6 nm.	The EndoActivator (Dentsply, Maillefer) sonic handpiece with a size #25/0.04 taper activator tip was passively inserted to within 2 mm of the working length and used in a pumping action to move the tip for 1 min in short, 2–3 mm vertical strokes.	An ultrasonic tip 20/.04 (Satellec, Acteon) was passively inserted into the canal 1 mm short of working length and driven by an ultrasonic device (Satellec, Acteon) with power set at 5 for 1 min.	Scanning electron microscopy
12	(40)	India	20	20	Mandibular permanent first molars	Each canal was prepared up to an apical preparation of F1 size because the use of the rotary files	1 ml of 17% EDTA solution for 1 min was applied, followed by 3 ml of 3% NaOCl solution for 30 s, with PUI, followed by 3 ml of normal saline with a 26-gauge needle. The same procedure was followed for the sonic group at 10,000 rpm.		Scanning electron microscope
13	(41)	USA	10	10	Mandibular molars	ProFile 0.04 rotary files (Dentsply-Tulsa Dental) using a crown-down technique to a master apical file size #40. Between each rotary file, 0.5 mL of 6% NaOCl was used to irrigate each canal by using a 30-gauge	The canals and chamber were filled with 2 mL of 6% NaOCl before treatment. The EndoActivator sonic handpiece was set at 10,000 cpm, and a size #15/0.02 taper activator tip was passively inserted to within 2 mm of the WL.	Canals and chamber were filled with 2 mL of 6% NaOCl, and a 30K PEC Endosonic size #20 file (Dentsply) was passively inserted into the canals.	Digital camera attached to a stereomicroscope

						Max-i-ProbeTM (Dentsply).			
14	(42)	Chile	13	13	NR	Manual preflaring using size 15 and 20 K-Files (ReadySteel), root canal shaping was carried out to size 40, taper 0.6 using the Reciproc system and an R40 instrument. the endodontic access of the instrumented teeth was filled with Chinese ink using an irrigation needle until completely filling the crown access.	Each file was used with balanced strong movements and between each file, 1.5ml of Na OCl 2.5% was used to irrigate. After that, 10% EDTA was used to irrigate during 1 minute Followed by rinsing with 3ml distilled water.		Stereomicroscope
							EndoActivator with a blue tip was used (Dentsply Maillefer, Switzerland), at 10kHZ.	Varios 350 equipment (NSK Nakanishi, Japan) was used at medium power (30 kHz), together with a 25mm 15/02 stainless steel ultrasonic file with an E10 insert (NSK).	
15	(4)	Italy	15	15	Mandibular premolars	A #10 K-file was inserted before the apex was sealed. The Pro-Train (Simit Dental, Mantova, Italy) was used during the experimental protocol to standardize the procedures for tooth preparation	5 mL 5.25% NaOCl 37°C activated for 1 minute with the EA system with a 15/.02 point at 2 mm from the WL	Final rinse with 5 mL 5.25% NaOCl 37C activated with PUI; a #.15 K-file (Dentsply Maillefer) was used driven by an ultrasonic device (MiniEndo II; SybronEndo, West Collins, Orange, CA) with power set at 5 for 1 minute at	Field emission scanning electron microscopy, micrographs

								1 mm from the WL	
16	(43)	Australia	10	10	Upper incisor	Root canal shaping was performed to a working length (WL) of 17 mm, using Profile rotary files (Maillefer) of up to 30 size 0.06 taper. All samples received 1.5 mL of 4.25% NaOCl, using a 30G Max-i-Probe	EndoActivator (Advanced Endodontics, Santa Barbara, CA, USA) with a 25/.04 tip, set at 10000 cycles per minute per 30 s, placed at WL-2 mm.	Using an untapered Irri-S tip size 25 (VDW GmbH, Munich, Germany) mounted on an Ultra ultrasonic unit (VDW), set at power 25 (Irri-mode) for 30 s, placed at WL-2 mm.	A radiograph and software Photoshop Extended CS5.1. version
17	(3)	Germany	12	12	Mandibular premolars	Using Reciproc R40 instruments (VDW) using the VDW-Silver motor and the setting BRECIPROC ALL.^	All root canals were irrigated with 2.5 ml of 3% NaOCl with a 30-g open-ended needle (NaviTip, Ultradent, South Jordan, UT, USA) inserted into the root canal.		Scanning electron microscopy
							EndoActivator (166 Hz, size 25.04)	PUI (Irri S size 25; VDW-Ultra device; VDW; setting 30% resulting in about 30 kHz)	
18	(44)	Brazil	13	13	Permanent maxillary canines	The root canals was prepared with Ni-Ti rotary instruments under irrigation with 2.5% NaOCl and 17% EDTA and filled by lateral condensation of gutta-percha and	The sealer was activated using the size 20 .02 taper tip of a sonic device (EndoActivator, Dentsply Tulsa Dental Specialties, Tulsa, OK, USA) at 10,000 cycles/min.	It was performed with the insertion of a size 20 .02 taper ultrasonic device (EMS, Le Sentier, Switzerland) at power level.	Fluorescence confocal laser scanning microscopy

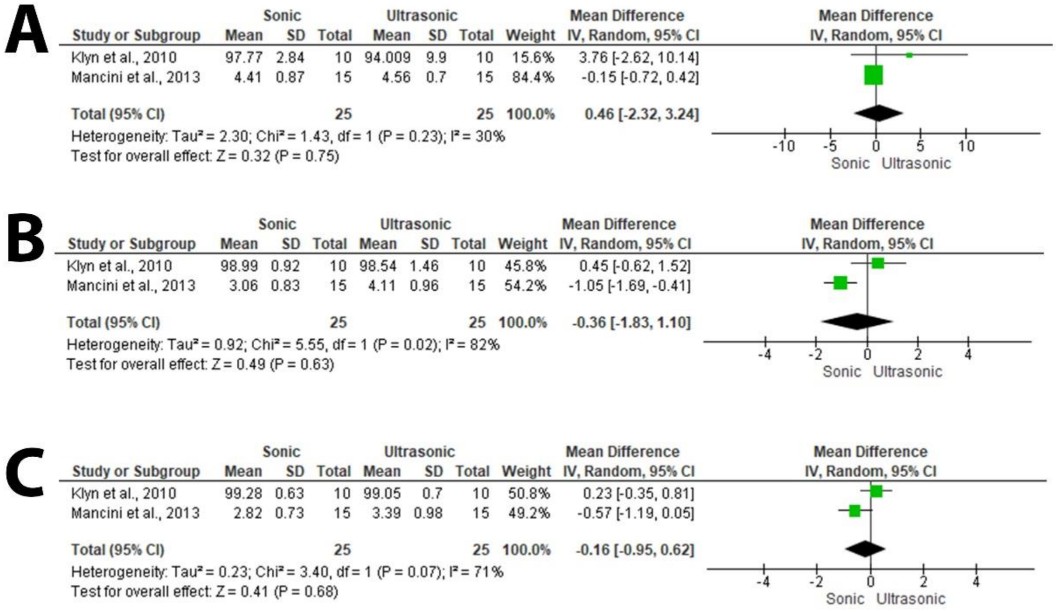
						AH Plus or MTA Fillapex.			
19	(45)	Turkey	15	15	Maxillary first molar teeth	The mesiobuccal canals were prepared using ProTaper Next rotary instruments. The canals were irrigated with 1 ml of 5.25% NaOCl after each file removal	EndoActivator System (Dentsply Maillefer) set at 10,000 cycles per minute (cpm) for 1 minute by using the tip 25/.04 placed within 2 mm of the WL.	EndoUltra handpiece (Vista, Racine, Wisconsin, USA) with a noncutting NiTi tip 15/.02 was used at a frequency of 40 kHz at 2 mm short of the WL. Each irrigant was passively agitated using the intermittent flush technique, with a total irrigation volume of 3 ml for 3 cycles of 20 seconds.	Image measurement tool

Abbreviations; EA=Endoactivator, EDTA= Ethylenediaminetetraacetic acid, NR=Non-reported



Supporting Information:

Supplementary Figure.1 (A) Standardized mean difference of the change in root weight. **(B)** Mean difference of the mean debris score at the coronal level, **(C)** middle level, **(D)** apical level. **(E)** Mean difference of mean smear layer score at the middle level.



A

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Klyn et al., 2010	97.77	2.84	10	94.009	9.9	10	15.6%	3.76 [-2.62, 10.14]
Mancini et al., 2013	4.41	0.87	15	4.56	0.7	15	84.4%	-0.15 [-0.72, 0.42]
Total (95% CI)			**25**			**25**	**100.0%**	**0.46 [-2.32, 3.24]**

Heterogeneity: $Tau^2 = 2.30$; $Chi^2 = 1.43$, df = 1 (P = 0.23); $I^2 = 30\%$
Test for overall effect: Z = 0.32 (P = 0.75)

B

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Klyn et al., 2010	98.99	0.92	10	98.54	1.46	10	45.8%	0.45 [-0.62, 1.52]
Mancini et al., 2013	3.06	0.83	15	4.11	0.96	15	54.2%	-1.05 [-1.69, -0.41]
Total (95% CI)			**25**			**25**	**100.0%**	**-0.36 [-1.83, 1.10]**

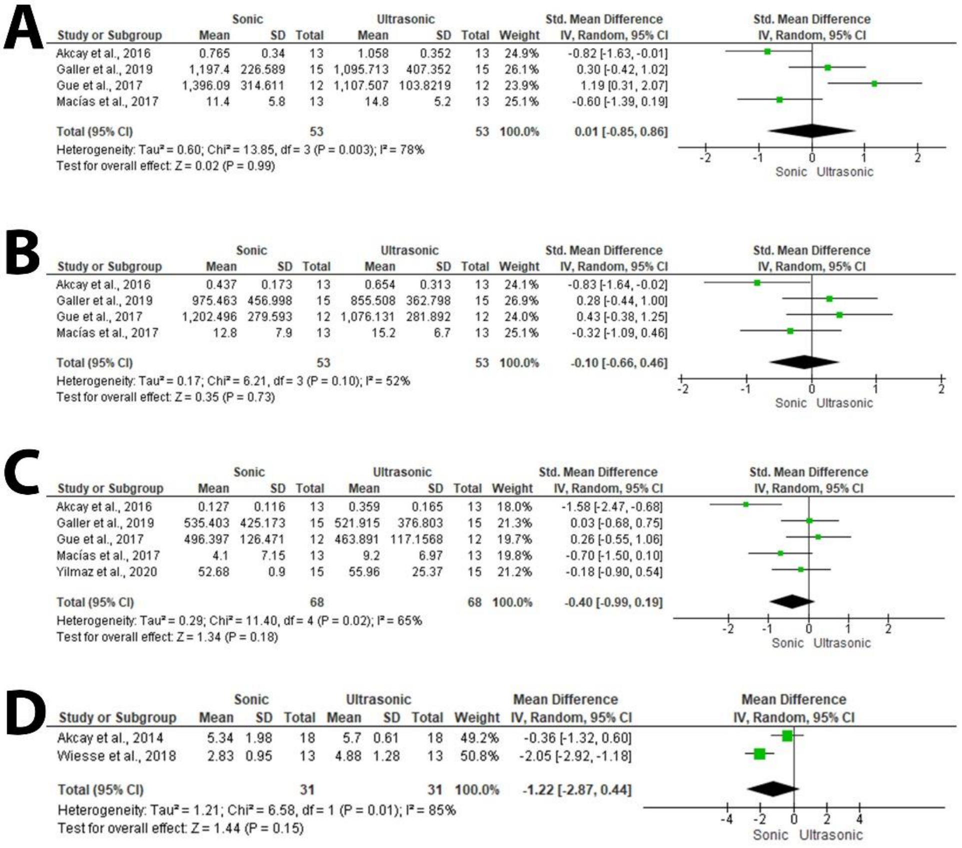
Heterogeneity: $Tau^2 = 0.92$; $Chi^2 = 5.55$, df = 1 (P = 0.02); $I^2 = 82\%$
Test for overall effect: Z = 0.49 (P = 0.63)

C

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Klyn et al., 2010	99.28	0.63	10	99.05	0.7	10	50.8%	0.23 [-0.35, 0.81]
Mancini et al., 2013	2.82	0.73	15	3.39	0.98	15	49.2%	-0.57 [-1.19, 0.05]
Total (95% CI)			**25**			**25**	**100.0%**	**-0.16 [-0.95, 0.62]**

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 3.40$, df = 1 (P = 0.07); $I^2 = 71\%$
Test for overall effect: Z = 0.41 (P = 0.68)

Supplementary Figure.2 (A) The percentage of canal cleanliness at 1mm between activation groups. **(B)** The percentage of canal cleanliness at 3mm between activation groups. **(C)** The percentage of canal cleanliness at 5mm between activation groups.



A

	Sonic			Ultrasonic				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2016	0.765	0.34	13	1.058	0.352	13	24.9%	-0.82 [-1.63, -0.01]
Galler et al., 2019	1,197.4	226.589	15	1,095.713	407.352	15	26.1%	0.30 [-0.42, 1.02]
Gue et al., 2017	1,396.09	314.611	12	1,107.507	103.8219	12	23.9%	1.19 [0.31, 2.07]
Macías et al., 2017	11.4	5.8	13	14.8	5.2	13	25.1%	-0.60 [-1.39, 0.19]
Total (95% CI)			**53**			**53**	**100.0%**	**0.01 [-0.85, 0.86]**

Heterogeneity: Tau² = 0.60; Chi² = 13.85, df = 3 (P = 0.003); I² = 78%
Test for overall effect: Z = 0.02 (P = 0.99)

B

	Sonic			Ultrasonic				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2016	0.437	0.173	13	0.654	0.313	13	24.1%	-0.83 [-1.64, -0.02]
Galler et al., 2019	975.463	456.998	15	855.508	362.798	15	26.9%	0.28 [-0.44, 1.00]
Gue et al., 2017	1,202.496	279.593	12	1,076.131	281.892	12	24.0%	0.43 [-0.38, 1.25]
Macías et al., 2017	12.8	7.9	13	15.2	6.7	13	25.1%	-0.32 [-1.09, 0.46]
Total (95% CI)			**53**			**53**	**100.0%**	**-0.10 [-0.66, 0.46]**

Heterogeneity: Tau² = 0.17; Chi² = 6.21, df = 3 (P = 0.10); I² = 52%
Test for overall effect: Z = 0.35 (P = 0.73)

C

	Sonic			Ultrasonic				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2016	0.127	0.116	13	0.359	0.165	13	18.0%	-1.58 [-2.47, -0.68]
Galler et al., 2019	535.403	425.173	15	521.915	376.803	15	21.3%	0.03 [-0.68, 0.75]
Gue et al., 2017	496.397	126.471	12	463.891	117.1568	12	19.7%	0.26 [-0.55, 1.06]
Macías et al., 2017	4.1	7.15	13	9.2	6.97	13	19.8%	-0.70 [-1.50, 0.10]
Yilmaz et al., 2020	52.68	0.9	15	55.96	25.37	15	21.2%	-0.18 [-0.90, 0.54]
Total (95% CI)			**68**			**68**	**100.0%**	**-0.40 [-0.99, 0.19]**

Heterogeneity: Tau² = 0.29; Chi² = 11.40, df = 4 (P = 0.02); I² = 65%
Test for overall effect: Z = 1.34 (P = 0.18)

D

	Sonic			Ultrasonic				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Akcay et al., 2014	5.34	1.98	18	5.7	0.61	18	49.2%	-0.36 [-1.32, 0.60]
Wiesse et al., 2018	2.83	0.95	13	4.88	1.28	13	50.8%	-2.05 [-2.92, -1.18]
Total (95% CI)			**31**			**31**	**100.0%**	**-1.22 [-2.87, 0.44]**

Heterogeneity: Tau² = 1.21; Chi² = 6.58, df = 1 (P = 0.01); I² = 85%
Test for overall effect: Z = 1.44 (P = 0.15)

Supplementary Figure.3 (A) Meta-analysis of the standardized mean difference of irrigants penetration depth between groups at coronal level, **(B)** at middle level, **(C)** at apical level. **(D)** Meta-analysis of the mean difference of the push-out bond strength value at the coronal level.

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Paixão S., Sousa Gomes P., Fernandes M.H., Rodrigues C., Grenho L. Effectiveness of ultrasonic and sonic irrigation systems on extrusion risk, canal debridement and biofilm removal within distinct apical dimensions – an *ex vivo* study in human teeth. Submitted to Clinical Oral Investigations

CHAPTER IV

EFFECTIVENESS OF ULTRASONIC AND SONIC IRRIGATION SYSTEMS ON EXTRUSION RISK, CANAL DEBRIDEMENT AND BIOFILM REMOVAL WITHIN DISTINCT APICAL DIMENSIONS – AN *EX VIVO* STUDY IN HUMAN TEETH

Chapter IV. Effectiveness of ultrasonic and sonic irrigation systems on extrusion risk, canal debridemenet and biofilm removal within distinct apical dimensions – an *ex vivo* study in human teeth

Abstract

Objectives: To compare the effectiveness of ultrasonically and sonically activated irrigation on extrusion risk, root canal debridement and biofilm removal within distinct apical preparation sizes, through an *ex vivo* study in human teeth.

Materials and Methods: Human premolar teeth, with single straight roots, were instrumented to an apical size of 35/.06 or 50/.06, and assigned to one of the irrigation procedures: ultrasonically activated irrigation (UAI), sonically activated irrigation using EDDY® tips (ED), and manual irrigation (MI). After irrigation, apical extrusion risk was evaluated by quantification of irrigant and debris extrusion. The removal of debris and smear layer from root canal wall were rated by scanning electron microscopy (SEM), and the elimination of a mature 21-days biofilm of *Enterococcus faecalis* was assessed by resazurin assay and SEM.

Results: Sonic and ultrasonic activation exhibited higher risk of both irrigant and debris extrusion for larger apical size, *i.e.*, 50/.06, while for manual irrigation the risk of extrusion was independent of the apical preparation size. Regarding the debridement and disinfection of the root canal area, less residual debris and smear layer were detected after activation of the irrigant, as well as a significant increase in the elimination of a mature biofilm of *E. faecalis*, comparatively to manual irrigation. Nevertheless, the effectiveness was improved for root canals prepared to a size 50/.06, particularly for UAI procedure.

Conclusions: Both irrigation activations procedures have a significant impact on the effectiveness of root canal disinfection and debridement, particularly for larger apical size, attended by increased risks of extrusion.

Clinical Relevance: The study proves, through evaluation of multiple clinical-relevant parameters, the adequacy of ultrasonic and sonic irrigation activations for larger apical sizes.

Keywords: Debridement, Disinfection, Extrusion, Irrigation, Sonic EDDY, Ultrasonic activated irrigation.

1. INTRODUCTION

An appropriated instrumentation and irrigation of the root canal system are widely considered critical procedures for a successful endodontic treatment. Instrumentation of root canals facilitates the removal of vital and/or necrotic tissue and microbial biofilms, assures the flow of irrigants, and allows the structural preparation that enables the subsequent filling within the cleaned and shaped root canal space. (1, 2) Yet, more than 50% of the root canal surface area may remain untouched by mechanical instrumentation alone, due to the complex anatomy of the root canal system, with its oval extensions, isthmuses and apical deltas. (3-5) Therefore, irrigation with antimicrobial and tissue-dissolving solutions is an essential part of root canal treatment, as it further enhances the cleaning and chemical disinfection beyond the instrumentation procedures. (6) During standard manual needle irrigation, replenishment and fluid exchange only extend shortly beyond the tip of the irrigating needle. (7) Trapped air in any part of the root canal, the vapor lock effect, may hinder the replacement of irrigants and therefore, the efficiency of irrigation may be limited. (8) To mitigate this pitfall, activation of the irrigation solutions was introduced to maximize the efficacy of irrigants, *i.e.*, to improve the debridement and disinfection of the full extent of the root canal system following mechanical instrumentation. (9)

Over the last decades, a broad range of irrigant activating systems have been developed and some of these techniques encompass ultrasonic and sonic devices. Aforesaid techniques are based on the transmission of acoustic energy to the irrigation solution that causes an increase in flow velocity and, consequently, improves the distribution of the irrigant inside the complex root canal system. (10) Among them, ultrasonically activated irrigation (UAI) is likely the most widespread technique among endodontists due to its improved cleaning efficiency, which relies on cavitation and acoustic streaming of the oscillatory motion of the file at ultrasonic frequencies of 25-30 kHz. (11-13) Alternatively, sonic systems, which operate at lower frequencies than ultrasonic devices, are composed of flexible non-cutting polymer tips. Strategically, these flexible tips aim to prevent modifications of the root canal morphology and dentin cutting during sonic activation at frequencies of 2-3 kHz. (14, 15) Recently, a new sonic powered irrigation activation device, referred as EDDY® (VDW, Munich, Germany), has been released to the market and has been disclosed as superior to other sonic devices due to the higher frequency attained (6 kHz) in combination with the increased amplitude of the polyamide tip. (16) The manufacturer claims that this system creates a three-dimensional movement that triggers cavitation and acoustic streaming which, up to now, have only been obtained by ultrasonic devices. (17)

Numerous published studies report the increased efficacy of these irrigation activation devices, as compared to conventional needle irrigation, regarding the removal of pulp tissue remnants (18), microorganisms (planktonic or biofilm) (19-21), as well as smear layer and dentin debris (17, 22), but through the assessment within distinct experimental setups, substantiating the lack of an integrative analysis.

Of particular relevance, previous studies have used distinct apical preparation sizes, which makes data comparison difficult, further precluding translational application into the clinical setting. The issue of apical preparation size is a relevant matter with clinical implications, and still a debatable issue. Several studies have shown that canals need to be significantly enlarged for adequate irrigation, while others argue that larger preparation sizes raise the risk of apical transportation and/or apical zipping. (23, 24) Despite that, there is a universal agreement that the ideal apical size varies between teeth and depends on anatomical, microbiological and mechanical factors. (25)

To the best of the authors’ knowledge, there is no published study addressing relevant clinical outcomes, in an integrative way, on the efficacy of different irrigant activating systems for different apical preparation sizes. Therefore, the aim of the present *ex vivo* study was to compare the effectiveness of UAI, sonic EDDY® tips, and standard manual needle irrigation, when applied to premolars instrumented at two apical sizes *i.e.*, 35/.06 and 50/.06. In the same experimental setting, the activation systems outcomes were evaluated regarding irrigant and debris extrusion, removal of debris and smear layer, as well as the elimination of a mature biofilm of *Enterococcus faecalis*, a commonly isolated pathogen from root canal system in failing endodontic cases.

2. MATERIALS AND METHODS

Teeth selection and root canal preparation

Permanent human anterior and premolar teeth, with single straight roots, fully formed apices without signs of apical resorption and clinically intact crowns were selected to this study. Tooth and root canal system anatomy was analyzed by digital radiography in the buccal and proximal directions to confirm a single canal and apical foramen, and the absence of a complex root canal anatomy. The crowns of the teeth were adjusted to a standardized working length (WL) of 18 mm and access openings were prepared using diamond burs under air-water spray and patency was established using a size 15 K-file (Dentsply®). The teeth were divided into 2 large groups according to the apical preparation size. Half of the samples were instrumented to an apical size of 35/.06 taper and the other half to an apical size of 50/.06 taper. Briefly, WL was set at 1 mm short of the apical foramen by visual inspection with a size 15 K-file (Dentsply®). Canals were instrumented using Wave One® Gold files with ISO size 35/.06 taper and Protaper Next (Dentsply®) X1, X2, X3, X4, X5 to an apical ISO size 50/.06 taper. Copious irrigation with 5.25% sodium hypochlorite (NaOCl) was performed between each preparation cycle, using a 27-gauge endodontic needle (Monoject®). All procedures were performed by a single experienced endodontist.

Irrigant activation

Irrigant activation procedures were performed as follows: Group Manual Irrigation (MI): root canal was irrigated with 1.5 mL NaOCl, during 30 seconds in an up-and-down motion, with a 27-gauge endodontic needle 1 mm short of the WL, without binding, followed by a 30-seconds pause. This procedure was repeated once again (26). Group Ultrasonically Activated Irrigation (UAI): root canal was irrigated with 1.5 mL NaOCl and the irrigant was activated using R&S® Tri Scaler Compact (R&S, Paris, France), in endodontic mode with power level 6, with Satelec® ET20 ultrasonic tip 1 mm short of the WL without binding. The activation was performed for 30 seconds, followed by a 30-seconds pause. The cycle was repeated once again (26). Group EDDY® (ED): root canal was irrigated with 1.5 mL NaOCl and the irrigant was activated using EDDY® tips (VDW, Munich, Germany), at 6 kHz, 1 mm short of the WL without binding. The activation was performed for 30 seconds as indicated by the manufacturer, followed by a 30-seconds pause. The cycle was repeated once again. (26)

Apical extrusion of irrigant

After instrumentation, each tooth was fixed with composite resin in a clear container. The container was filled to the cervical level of the tooth with 1% agarose (Liofilchem) containing 0.1% (w/v) M-cresol purple (Sigma-Aldrich), which undergoes a colour change from yellow to purple, in the presence of NaOCl. The teeth were randomly divided into three groups (n=10/group) and root canal irrigation was performed as aforementioned. The tooth/gel set-up was examined with transillumination and was digitally photographed in the buccal/lingual direction, at a fixed distance. Each sample was photographed before the irrigation cycle and 10 minutes after irrigation. The extent of colour change was analysed with Image J software, upon calibration, to determine the total area of extrusion.

Apical extrusion of debris

To evaluate the apical extrusion of debris, a previously described experimental model was employed. (27) Briefly, the stoppers were separated from 1.5 mL tubes, and their initial weight was determined using an analytical balance (ALS 160-4A, Kern). Each tube was weighed three times and the mean value calculated. Each tooth was inserted up to the cementoenamel junction (CEJ), and a 27-gauge needle was placed alongside the stopper to balance the air pressure inside and outside. Then, each stopper with the tooth and the needle was attached to its tube. The teeth were randomly divided into three groups (n=10/group) and the irrigation protocols previously described were performed, with distilled water. Finally, the stopper, needle and the tooth were separated from the tube and the debris adhered to the root surface were collected by washing the root with distilled water into the tube. The tubes were stored in an incubator at 68 °C for 5 days to completely dry. The tubes were weighed again to obtain the final weights. Each tube was weighed in triplicate, and the mean value was calculated. The amount of the extruded debris was obtained by weight difference calculation.

Removal of debris and smear layer

After root canal irrigation procedures, specimens (n=5/group) were longitudinally split in a vestibular-lingual direction using a chisel, and the morphology of the canal surface (medium third) was accessed by scanning electron microscopy (SEM, FEI Quanta 400 FEG/ESEM). A previously published 4-score index system was adapted for the present work to evaluate the amount of superficial debris and the presence of smear layer. (28) Succinctly, index used for debris evaluation: score 1, none to slight presence of superficial debris covering up to the 25% of the dentinal surface; score 2, little to moderate presence of debris covering between 25% - 50% of the surface; score 3, moderate to heavy presence of residual debris covering between 50% - 75% of the surface; score 4, heavy amount of aggregated or scattered debris covering over 75% of the surface. Index used for smear layer evaluation: score 1, little or no smear layer, covering less than 25% of the specimen with tubules visible and patent; score 2, little to moderate or patchy amounts of smear layer, covering between 25% - 50% of the specimen with many tubules visible and patent; score 3, moderate amounts of scattered or aggregated smear layer, covering between 50% - 75% of the specimen with minimal to no tubules visible or patent; score 4, heavy smear layer covering over 75% of the specimen with no tubule orifices visible or patent. Analysis was conducted by calibrated observers.

Removal of bacterial biofilm

To assess the efficacy of the endodontic activation systems on biofilm removal, the apical foramen of instrumented teeth was sealed with self-cure glass ionomer and the root surfaces were covered with two layers of nail varnish. Prior to bacteria inoculation, the teeth were sterilized by autoclave. A standard suspension of *E. faecalis* ATCC 29212 at 10^8 cells/mL was prepared from an exponential bacterial culture grown in brain heart infusion (BHI, Liofilchem) broth. Each canal was filled to the orifice level with *E. faecalis* suspension and individually submerged in tubes containing BHI broth. The tubes were incubated at 37 °C for 21 days to allow bacterial colonization of the root canals and dentinal tubules. Every two days, the culture medium was replaced by fresh medium. After incubation, the BHI broth in the canal space was first aspirated and the canal was washed once with phosphate buffer saline (PBS, Sigma Aldrich). The teeth were randomly gathered into 4 groups (n=10/group) and root canal irrigation procedures, namely manual (MI), UAI and EDDY®, were performed as previously described. An additional control group (C) was created in which the root canals were not subjected to any irrigation procedure. The remaining metabolic active bacteria in the root canal and dentinal tubules after each procedure were assessed by the resazurin assay. Briefly, root canals were filled with BHI broth supplemented with 10 % resazurin (0.1 mg/mL, Sigma-Aldrich) and incubated for 3 hours at 37 °C. The medium in the canal space was collected and its fluorescence intensity (excitation: 530 nm; emission: 590 nm) was measured in a microplate reader (Synergy HT, BioTek). Results are presented as relative fluorescence units (RFU). Additionally, the biofilm remaining on root canal surface, after each irrigation procedure, was accessed by SEM (FEI Quanta 400 FEG/ESEM). Briefly, biofilms were fixed with 1.5 % glutaraldehyde in sodium cacodylate buffer (both from Sigma-Aldrich) for 30 minutes. Then, teeth were longitudinally split using a chisel to expose the colonized root canals and the specimens were dehydrated in sequential graded ethanol solutions, critical point dried (CPD 7501, Polaron Range) and sputter-coated (SPI-Module) with a thin conductive film of Au-Pd alloy for subsequent visualization.

Statistical analysis

Results are presented as mean ± standard deviation. For statistical analyses, the Student's paired *t*-test was used to assess the intragroup differences and the one-way analysis of variance (ANOVA) with post-hoc Tukey HSD for comparisons between groups. The level of significance was set at $p < 0.05$, and IBM® SPSS® Statistics software (vs. 26.0, SPSS Inc., USA) was used as the analytical tool.

3. RESULTS

Apical extrusion of irrigant

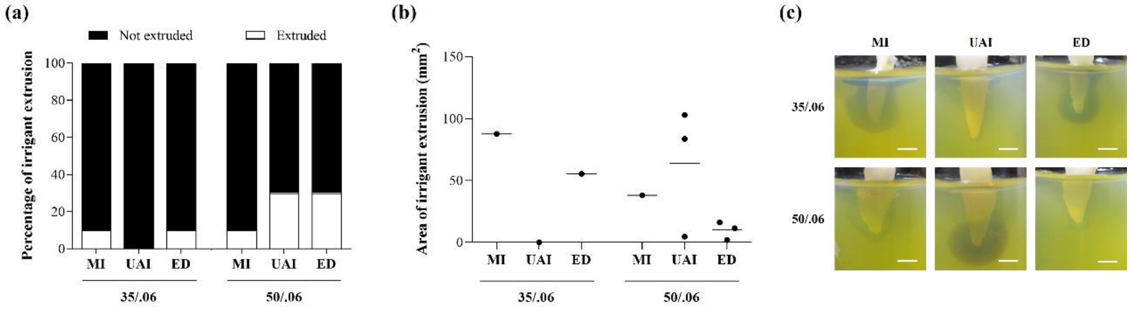

Figure 3.1 (A) Frequency of irrigant extrusion under different root canal irrigation procedures and apical preparation size. **(B)** Extension of irrigant extrusion in positive samples and **(C)** representative photographs of irrigant extrusion, 10 minutes after root canal irrigation procedures (scale bar 0,5 cm), in apical sizes of 35/.06 and 50/.06.

Irrigant extrusion presented a tendency to occur more frequently in teeth with an apical preparation size of 50/.06, as compared to an apical size of 35/.06, except for manual group, which exhibited similar results for both apical preparation sizes (Fig. 3.1a). Regarding teeth prepared to an apical size of 50/.06, sonic and ultrasonic activation systems presented a similar frequency of irrigant extrusion and, despite the absence of significant differences, higher than standard manual needle irrigation (MI). The extent of extrusion in positive samples is shown in Figure 3.11b and c. Apical preparation size influenced the extent of extrusion for all groups but in different ways. Both manual (MI) and EDDY® (ED) groups presented lower extrusion areas for an apical size of 50/.06, as compared to 35/.06 taper (Fig. 3.1b). On the other hand, UAI lead to higher extent of extrusion for an apical size of 50/.06 (Fig. 3.1b). Representative images of the extrusion for all groups are presented in Figure 3.1c.

Apical extrusion of debris

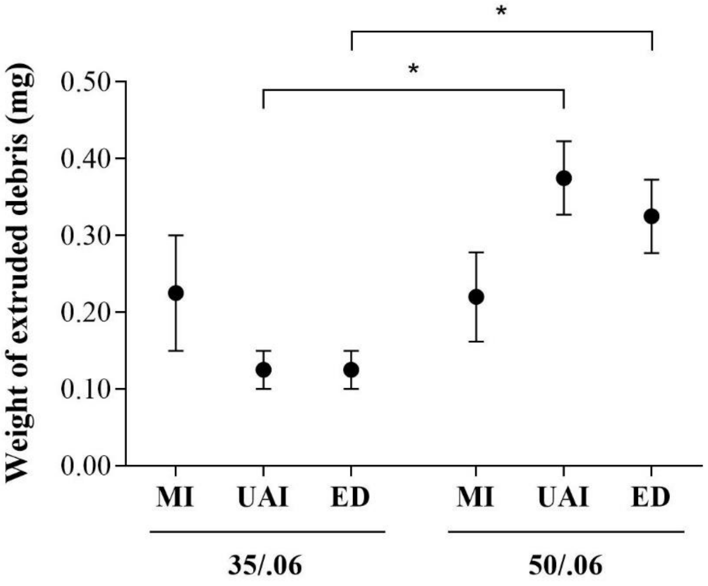

Figure 3.2 Amount of apically extruded debris under different root canal irrigation procedures and apical preparation sizes. *Significantly different between apical sizes. $p \leq 0.05$.

The results showed that all the activation protocols caused apical debris extrusion (Fig. 3.2). Manual irrigation group (MI) exhibited a similar mass of extruded debris for both apical preparation sizes. While for sonic and ultrasonic activation, the mass of extruded debris was significantly higher in teeth with an apical preparation size of 50/.06, as compared to an apical size of 35/.06. For the same apical size there were no significant differences in the mass of apical extruded debris between the different groups.

Removal of debris and smear layer

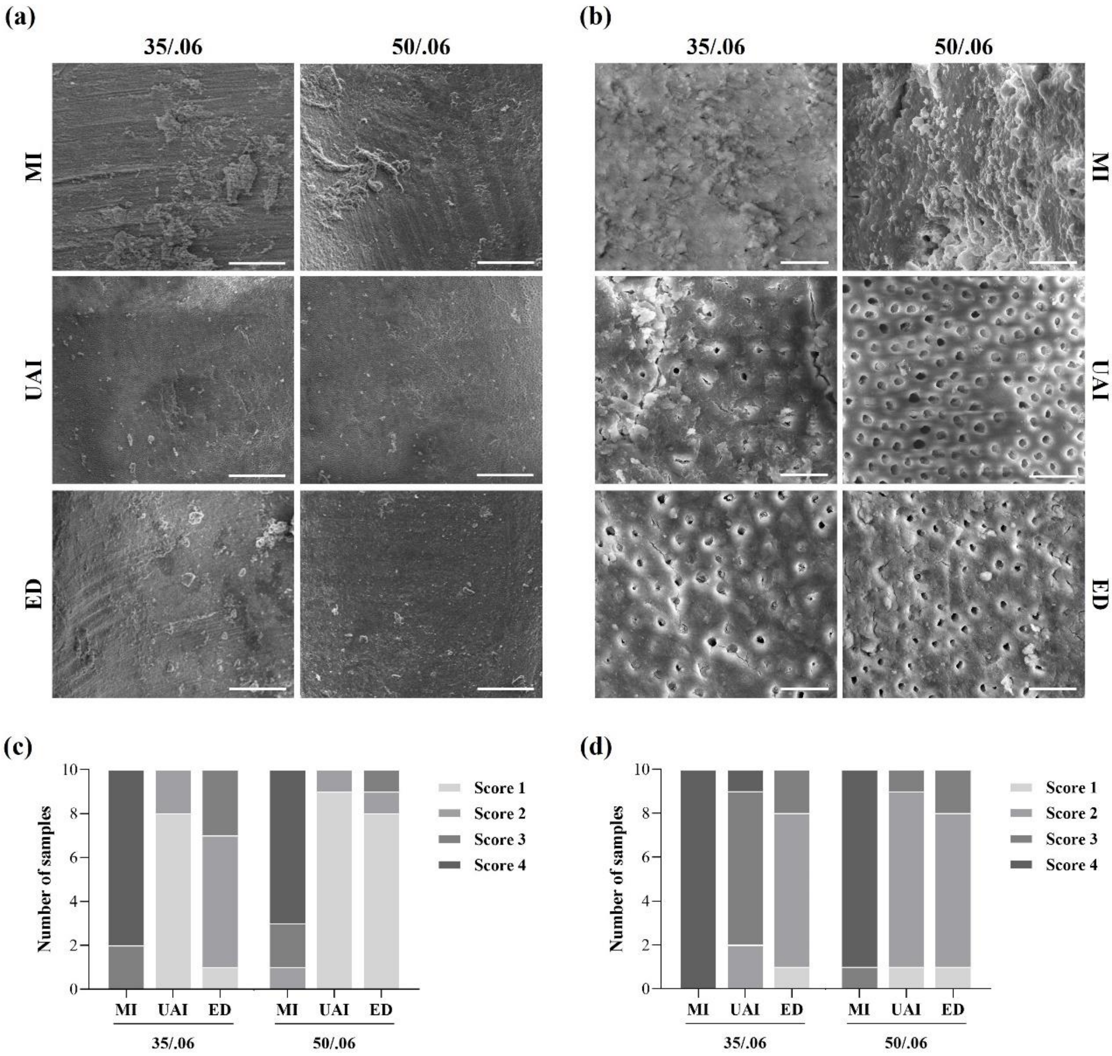

Figure 3.3 Representative SEM images of the root canal walls at **(a)** lower magnification for debris evaluation (scale bar 100 µm); and at **(b)** higher magnification for smear layer evaluation (scale bar 10 µm). Number of samples indexed for each score in the evaluation of **(c)** residual debris and **(d)** smear layer, after selected irrigation procedure, in apical sizes of 35/.06 and 50/.06.

The removal of debris and smear layer upon irrigation procedures were analysed by SEM and both the representative images and the number of samples indexed for each score are presented in Figure 3.3. For manual needle irrigation (MI), in the assayed root canal preparation sizes, the amount of superficial debris and the presence of smear layer were detected covering the entire root canal walls with no visible openings of the dentinal tubules. After ultrasonic irrigant activation (UAI), root canals prepared at 35/.06 exhibited a diminutive presence of debris and a thin smear layer covering the walls with a low frequency of visible/patent dentinal tubules. For root canals prepared at 50/.06, the presence of debris and smear layer were diminutive and related to the identification of the opening of many dentinal tubules. As for sonic activation of irrigant by EDDY® tips (ED), root canals prepared at lower apical size presented a diminutive to moderate presence of debris and smear layer, with many dentinal tubules exposed. For larger apical size, a decrease in the amount of superficial debris was noted, but the smear layer remained diminutive to moderate, with many dentinal tubules being identified. Overall, less debris and smear layer were reported for specimens with an apical size of 50/.06, for which the irrigant were sonic or ultrasonically activated, as comparing to manual irrigation.

Removal of bacterial biofilm

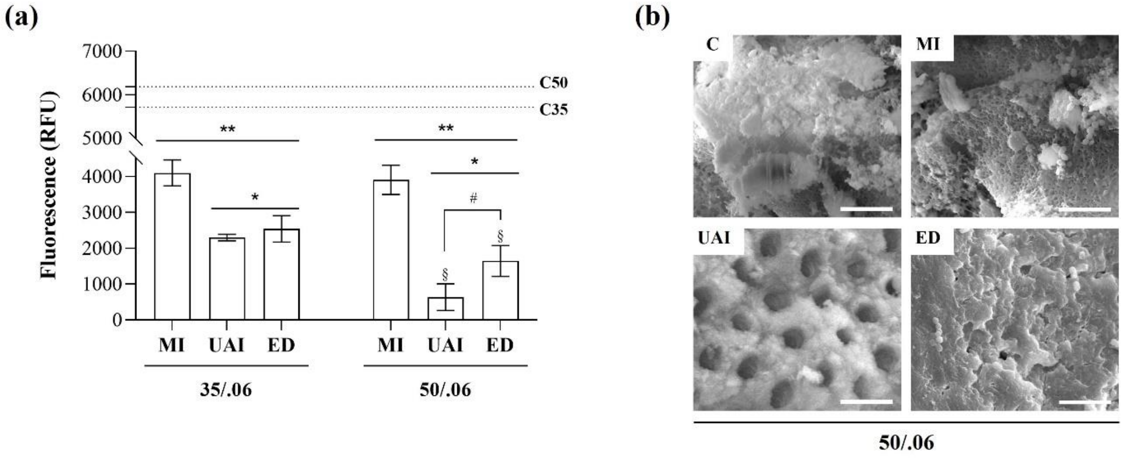

Figure 3.4 (a) Metabolic activity of the 21-day *E. faecalis* biofilm after selected irrigation procedure, quantified by the resazurin assay. *Significantly different to the manual group (MI), for the same apical size; **Significantly different to the control group **(**C), for the same apical size; $^{\#}$Significant differences between UAI 50/.06 and ED 50/.06 groups; §Significant differences between the same irrigation procedure at different apical sizes; for all $p \leq 0.05$. **(b)** Representative SEM images of the root canal walls after selected irrigation procedure, in apical size of 50/.06 (scale bar 5 μm).

The metabolic activity of the bacterial biofilm established for 21 days within the canal system, following irrigant activation procedure is presented in Figure 3.4a. In comparison to the control (C35 and C50, with no irrigation procedure), the three irrigation procedures significantly reduced the metabolic activity of the biofilm, in both sizes of apical preparation. Additionally, ultrasonic UAI and sonic EDDY® (ED) activations induced a significant reduction as compared to manual irrigation (MI), for both apical sizes. For an apical size of 35/.06 no differences were noticed between UAI and EDDY® activations (mean reduction of 41%, compared to MI), while for the larger preparation size (50/.06), the UAI group induced a significant reduction of the 21-day biofilm (84%, compared to MI), as compared to EDDY® group (58%, compared to MI). Furthermore, a significantly higher reduction of the metabolic activity of the biofilm was achieved in the apical size 50/.06, over the 35/.06. For manual group (MI), metabolic activity reduction was similar for both apical preparation sizes (mean reduction of 33%, as compared to C). Representative images of the biofilm remaining on root canal surface, after each procedure, on teeth instrumented to an apical size 50/.06, are presented in Figure 3.4b.

4. DISCUSSION

The chemo-mechanical preparation is one of the key steps in root canal treatment. Accordingly, an adequate instrumentation and irrigation must be combined to decrease the microbial load and their by-products within the root canal system and to enhance the cleaning process, minimizing the risk of re-infection and inflammation of the periapical tissue, allowing for the subsequent sealing of the root canal system with filling materials. For effective action, the irrigant must directly contact the canal wall, and its flushing action should be enhanced to reach intricate areas of the entire root canal system. Nowadays, different irrigation delivery and activating devices are available to improve the disinfection and debridement. A survey among members of the American Association of Endodontists reported that almost half used these devices, with 48% using ultrasonic activation and 34% using sonic activation to improve irrigation efficacy. (29) UAI is regarded as the gold standard for irrigant activation throughout the present literature, mainly due to the acoustic streaming and cavitation produced by the ultrasonically activated file. (11, 12) As an alternative, sonic EDDY® tips have been recently introduced with a remarkable potential to improve fluid flow, as compared with other sonic irrigation devices, due to the higher frequency and higher amplitude of tip movement. (14) Published investigations have addressed and compared the effectiveness of UAI and EDDY® in irrigant activation, against standard manual needle irrigation, but through the independent analysis of different settings, neglecting the impact of root canal preparation size on the irrigating procedures outcomes. (17, 19-22) In this context, the present study addresses, through multiple clinical-relevant parameters, the efficacy of different irrigation procedures on two apical sizes, *i.e.,* 35/.06 and 50/.06, using an *ex vivo* study in human teeth.

One of the most significant risks associated to the irrigation procedure remains the extrusion of debris and irrigant solution into the periapical region, which may cause post-operative undesirable outcomes, as periapical inflammation, postoperative pain, and, eventually, compromise the success of root canal treatment. (30, 31) Although all procedures have an associated risk of apical extrusion, the extension of extrusion may differ according to the instrumentation techniques and devices. (32, 33) In the present study the extrusion risk with standard needle irrigation was independent of apical size. On the contrary, ultrasonic and sonic procedures exhibited a trend to a higher risk of both irrigant and debris extrusion within larger apical size, *i.e.*, 50/.06, and these values tended to be higher in the ultrasonic group. These results are consistent with a previous study (32) in which the frequency of extrusion was reduced in teeth with apical preparation 35/.06, as compared to 50/.06, with the extent of extrusion being further reduced with a sonic device as compared to UAI. In another study, authors suggested that larger apical preparations result in a high risk of canal transportation and perforation, which raises concerns in preparing canals with larger sizes. (24)

On the other hand, root canal preparation to a size 50/.06 resulted in significantly less residual debris and smear layer as compared to a size 35/.06, after activation of the irrigant either by UAI or EDDY® tips. In another study, it has also been reported that a basic preparation to a size 25/.06 produced significantly less clean root canal walls than a size 40/.04. (34) In fact, an enlargement of the apical preparation has been advanced for improved cleaning, through better acoustic streaming and penetration of irrigants, which is a critical aspect considering that the remaining tissue and debris can negatively impact endodontic treatment outcomes by interfering with root filling materials and by serving as a niche and nutritional source for microorganisms, potentially contributing to the development of a secondary infection. (25, 35) Additionally, both sonic and ultrasonic procedures enhanced the removal of dentin debris and smear layer, as compared to standard manual needle irrigation, to any specific size. These results are in accordance with most of the literature which advises that irrigant activation exhibits enhanced canal debridement efficacy over the use of needle irrigation alone. (17, 22, 36) Comparing both sonic and ultrasonic activations, UAI proved to remove more debris and smear layer than EDDY® tips. The outperformance of UAI may be justified by the driving frequency of ultrasound, which is higher than that of the sonic device – EDDY®. (12) Theoretically, higher frequency results in higher velocity of the flow, which allows the irrigant to reach otherwise inaccessible regions inside the complex root canal system and increase the shear stress that can disrupt debris. (7, 13) However, potent ultrasonic irrigation may also entail some limitations. It has been shown that even in noncomplicated root canal geometries, ultrasonic instruments collide with the wall during 20% of the activation time. (37) File-to-wall contact dampens the energy and constrains the file movement, which may lead to accidental removal of small amounts of dentin, changing root canal morphology, even with a noncutting design. (38) Instead, sonic activation with soft polymer tips minimizes the risk of unintentional dentin removal and root canal alterations. (39) Regarding apical preparation size, a previous study reported significantly longer file-to-wall contact time in #35 root canal size, as compared to #50. (37) The resulting surface alterations may hamper the proper adhesion of filling materials and offer favorable niches for bacterial adhesion and proliferation.

Microbial biofilms play a central role in the development of pulpal and periapical diseases and, accordingly, the reduction of the microbial load in the root canal is a major clinical aim and a relevant parameter to be evaluated in experimental studies of endodontic irrigation. (40) In this context, *E. faecalis* is the primary pathogen isolated, in part due to its ability to bind to dentin and invade dentinal tubes, where it can survive for long periods of time. (41) Perseverance of intraradicular microorganisms within the root canal system is the major cause of post-treatment failure, namely reinfection and inflammation of the periapical tissues. (42) Although endodontic microbiological studies are entangled with some methodological difficulties, they can partly predict healing/prevention of pulpitis and apical periodontitis. (43) Then again, in the present investigation, sonic and ultrasonic activation of irrigant presented a significantly higher capability in the elimination of a mature biofilm of *E. faecalis* than standard manual needle irrigation, to any specific apical size, which is in accordance with published data. In another study, it has been confirmed that sonic activation with EDDY® tips surpasses the antimicrobial effect of manual needle irrigation. (14) The differences between procedures may be explained by the fact that conventional needle syringe irrigation provides far lower fluid dynamics as compared to the investigated activation techniques.(44) For an apical size of 35/.06, antibacterial efficacy was similar for both sonic and ultrasonic activation procedures, which is in accordance with other studies. For example, authors demonstrated equivalent antimicrobial performance for both sonic and ultrasonic irrigation, and enhanced efficacy when compared with syringe needle irrigation. (20) For an apical size of 50/.06, the high-power ultrasonic irrigation system exhibited significantly improved results, as compared to EDDY® tips. The enhanced effectiveness of UAI has been associated to acoustic streaming and cavitation effects that increase shear stress and, consequently, enhance the rupturing of intraradicular biofilm. (20) Overall, an improved performance in eliminating a 21-day biofilm was attained for larger apical size, for any procedure assayed, in accordance with other studies that proposed the preparation of the canal to larger apical sizes for a greater reduction in the root canal biomass and increased effectiveness of the irrigation procedure. (18, 45)

The *ex vivo* model used in this study has some limitations. The use of straight single-rooted teeth precludes possible variations, as WL loss or nonstandard preparation and irrigation in curved root canals. However, this model provided a standardized and reproducible setup to determine the adequacy between root canal preparation size and irrigating procedure, through an integrative analysis of the major' clinical-relevant settings in the medical practice. Next step will be to evaluate if the results of the present study are replicable in multi-rooted teeth, with curved roots and/or more complex root canal anatomies.

5. CONCLUSIONS

Thoughtful conclusions that can be drawn based on the results of this study are that (1) both sonic and ultrasonic activation might be associated to higher risk of extrusion for larger apical preparation sizes, as compared to manual irrigation; however (2) higher efficiency of debris and smear layer removal, as well as (3) biofilm elimination was obtained for EDDY® and UAI procedures, for both apical preparation sizes, as compared to manual needle irrigation. (4) UAI applied to root canals at 50/.06 exhibited the best combined outcomes.

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CHAPTER V

COMPARATIVE EVALUATION OF POSTOPERATIVE PAIN AFTER USING MANUAL IRRIGATION AND EDDY DURING ROOT CANAL IRRIGATION

Abstract

Objectives: Post-endodontic pain (PEP) represents a significant challenge for dentists and patients. This pain could worsen patients' quality of life and teeth function. This study compared the risk of PEP between irrigations using an EDDY® device and a conventional endodontic needle among patients seeking initial non-surgical root canal treatment.

Methods: This was a prospective single center randomized controlled clinical trial, conducted at the Faculdade de Medicina Dentária Dental Clinic at Porto University, Portugal. Patients diagnosed with irreversible pulpitis or pulp necrosis were included. This study included 80 single-rooted teeth that were randomly assigned to EDDY® group or manual syringe irrigation with needles with up-and-down movement (control group). PEP was assessed at 8, 24, and 48 hours postoperatively using Visual Analogue Scale. Student's T-test; Kruskal-Wallis test; Pearson's chi-square test with Fisher's exact test; and. Friedman's post-hoc sign test were used.

Results: Eight hours after irrigation, EDDY® group experienced a statistically significant higher incidence of pain (P=0.041) (52.5%) relative to the manual irrigation group (30%). There was no statistically significant difference between groups regarding the PEP 24 hours (P=0.068) and 48 hours (P=0.433) after RCT.

Conclusion: EDDY® irrigation during initial RCT is associated with a high incidence of PEP, principally in the 24 hours following treatment, relative to manual irrigation. After, the rate of PEP was similar between groups, with a gradual decline in pain intensity.

Keywords: Disinfection, Post-Operative Pain, Randomized Controlled Trial, Root Canal Therapy

1. INTRODUCTION

Root canal treatment (RCT) involves the elimination of necrotic or vital pulp tissue as well as dental pain management. These outcomes are usually accomplished through proper mechanical preparation and the use of irrigation solutions.(1) However, post-endodontic pain (PEP) is reported after treatment among between 1.9% and 28.8% of patients subjected to non-surgical RCT. This experience originates from the periapical inflammatory response, provoked by biting and palpation, and persists from a few hours to many days. However, 7% of patients experienced persistent PEP for more than six months.(2-5)

The factors associated with PEP include patients general health status, patients' gender, periapical and pulp condition, apical patency, preoperative pain, obturation technique, instrumentation, and irrigants.(6) Several preoperative procedures and pharmacotherapeutic agents have been proposed to diminish PEP. This includes placement of intracanal medicaments, occlusal reduction, and oral or parenteral administration of anti-inflammatories and analgesics. However, the effectiveness of these interventions in reducing PEP has not been comprehensively evaluated.(7-9)

Irrigation techniques are critical for successful endodontic therapy.(10) Whereas several substances have been advocated for canal irrigation, the most frequently used irrigant is

NaOCl.(11-15) It has a significant antibiofilm activity, antimicrobial efficacy, and high ability to dissolve organic matter. The severity of NaOCl cytotoxicity depends on the solution concentration, pH, and duration of tissue exposure to the agent.(16, 17) The leakage of NaOCl during treatment may cause sequelae such as pain, swelling, bruising, and numbness comparable to a chemical burn.(18) Due to the positive apical pressure generated during irrigation delivery, irrigant solutions may be pushed out into the periapical tissues, thereby inducing an inflammatory response and PEP.(13, 19)

Safe and effective irrigation delivery systems are required to prevent the periapical inflammation associated with NaOCl use, and many irrigation devices have been developed using sonic or ultrasonic energy and apical negative pressure.(20) EDDY® (VDW, Munich, Germany) is a recently developed sonic irrigation activation device made with flexible polyamide. It is activated with 5000 to 6000 Hz using an air scaler.(21) There is no available literature claiming whether the activation of NaOCl with an EDDY® device provides more favorable outcomes in terms of PEP during initial non-surgical RCT. Therefore, this study was conducted in order to compare the risk of PEP and periapical damage between irrigation using EDDY® and manual syringe irrigation with needles with up-and-down movements (using 27-gauge side-vented needle) among patients seeking initial non-surgical RCT. The null hypothesis of the study is that there would be no difference in pain levels between manual irrigation and EDDY® irrigation groups.

2. MATERIALS AND METHODS

Accordingly to a previous study (22), 40 patients per group were recruited to compensate for participant dropouts during the follow-up period.

This was a prospective single center randomized controlled clinical trial, conducted at the Faculdade de Medicina Dentária Dental Clinic at Porto University, Portugal, from February 13, 2020 to February 27, 2021. The study protocol was approved by the University of Porto Ethics Committee, and it was documented at **www.clinicaltrials.gov** (ClinicalTrials.gov. Identifier: NCT03946306). The study was reported following the Consolidated Standards of Reporting Trials (CONSORT) guidelines. (23)

The clinical interventions were elucidated clearly for all patients and they were aware of the potential adverse events associated with RCT. Informed consents were assigned prior to study processing. The steps of the study were implemented following the guidelines of the Declaration of Helsinki. (24)

Patient selection

Our patient selection followed the following criteria: Inclusion criteria: Patients aged more than 12 years who had been diagnosed with irreversible pulpitis or pulp necrosis. A total of 80 single-rooted anterior and premolar teeth with fully formed apices were selected.

Exclusion criteria: Patients less than 12 years old, pregnant women, patients receiving prophylactic antibiotics, or taking antibiotics or non-steroidal anti-inflammatory drugs, cases with uncontrolled hypertension or diabetes mellitus, patients with chronic renal failure, hematologic diseases, human immunodeficiency virus, osteoporosis treated with bisphosphonates, receiving steroid therapy > 5mg/day, or who had a history of head and neck irradiation therapy. Teeth with abnormal root canal anatomy and those with advanced periodontal disease were also ruled out.

Randomization and blinding

A computer random sequence generated table was used to assign the included teeth to either group randomly. Randomization was performed using random block sizes (http://www.randomization.com/) with an allocation ratio of 1:1. The sequentially numbered, opaque, sealed envelopes (SNOSE) method was applied to conceal the sequence until the patients were assigned to their respective interventions. Patients were assigned to either intervention as they sequentially entered this study. The investigators and the patients were unaware of the assigned treatment arms during the study period.

Preoperative evaluation

A dental assessment was performed to retrieve the pulp status, tooth type, and tooth location, and preoperative pain was recorded using the visual analogue scale (VAS). This is a 10-point scale in which the left side corresponds to no pain, while the right side corresponds to the worst pain ever. This was the chosen technique, as it is a method with a high response rate and high levels of completion and it takes less than one minute to complete. This method requires almost no training to manage and is well received by patients. (25, 26) There is also empirical evidence of inter-rater reliability and test–retest reliability. (25) It is considered accurate, valid, reliable, and reproducible.(27) The pain was assorted into five categories in which no pain was considered a zero, while mild pain was considered a 1-2. Scores of 3-4 and 5-6 points were considered moderate and severe pain, respectively, while very severe pain was given a 7-8, and the worst pain ever was considered to be 9-10. The diagnosis was obtained with the use of pulp sensibility cold testing. Periapical radiographs were taken to evaluate the status of the periapical structures.

Endodontic treatment

All patients were treated by a single experienced endodontist and received local infiltration anesthesia (Xilonibsa: lidocaine, with 1:80000 epinephrine, Inibsa*) before RCT. Each tooth was isolated using a rubber dam and the access cavity was made. Working length (WL) was determined using stainless steel hand files, confirmed by periapical radiographs. The root canals were instrumented with a preflaring of the canals with #10 and #15 k-files and Protaper Next® files X1, X2, and X3.

Irrigation protocol

The selected root canals were irrigated continuously with 5.25% NaOCl, with a conventional endodontic syringe with a side-vented 27-gauge needle. In the control group, the final irrigation was made with was with manual syringe irrigation with needles, made with 1.5 mL of NaOCl per canal for 30 seconds in an up-and-down motion, with the needle 1 mm short of the WL without binding. After this, a 30-second pause was taken, and then irrigation was repeated once again. In the intervention group, the final irrigation was made with 1.5 ml of 5.25% NaOCl per canal. The irrigant was activated using EDDY® tips, 1 mm short of the WL without binding. The activation was performed for 30 seconds, followed by 30 seconds pause, and this cycle was repeated according to manufacture instructions.

After the final irrigation protocol, the canals were dried, and sterile cotton pellets were placed in the pulp chamber with a provisional restoration. No intracanal medicament was placed, in order to diminish variables. The obturation was executed in the following appointment.

Assessment of post-endodontic pain

VAS was implemented and none of the patients had analgesics prescribed immediately after the treatment. Patients were advised not to take any analgesics at any point before the follow-up. PEP was assessed at 8, 24, and 48 hours postoperatively, by phone. If any patient mentioned substantial pain, they were advised to take 600 mg of Ibuprofen every 6 hours until the pain went away. Patients allergic to non-steroidal anti-inflammatory drugs (NSAIDs) were advised to take paracetamol.

Statistical analysis

Continuous normally distributed data were reported in the form of mean and standard deviation (SD) and were compared using the student's T-test. Non-normally distributed data were reported using median and range and its related groups were compared using the Kruskal-Wallis test. Categorical variables were expressed in the form of the number and percentage, and their particular groups were compared using Pearson's chi-square test with Fisher's exact test. Friedman's post-hoc sign test was implemented to reveal the difference in visual analogue scale levels at different time intervals within the EDDY® and manual groups. The significance is established when *P*<0.05. Statistical analysis was performed using SPSS software version 25 for Windows (SPSS Inc., Chicago, IL, USA) [Corporation, I., *IBM SPSS Statistics (Version 25)[Computer Software]*. 2017]. Figures were renovated using GraphPad Prism (GraphPad Software, Inc, San Diego) software version 8.

3. **RESULTS**

Patients’ demographic characteristics

A total of 89 patients were assessed for eligibility to be included in this study. Out of those, 80 patients were randomly assigned to EDDY® or manual groups. The mean age of the included patients was 54.40±16.45 and 52.90±15.95 in EDDY® and manual groups, respectively (P=0.68). There was no statistically significant difference between both groups regarding the number of irrigated teeth (P=0.324), types of irrigated teeth (P=0.421), and teeth location (P=0.404). (Fig. 4.1 and Table 3.1**)**

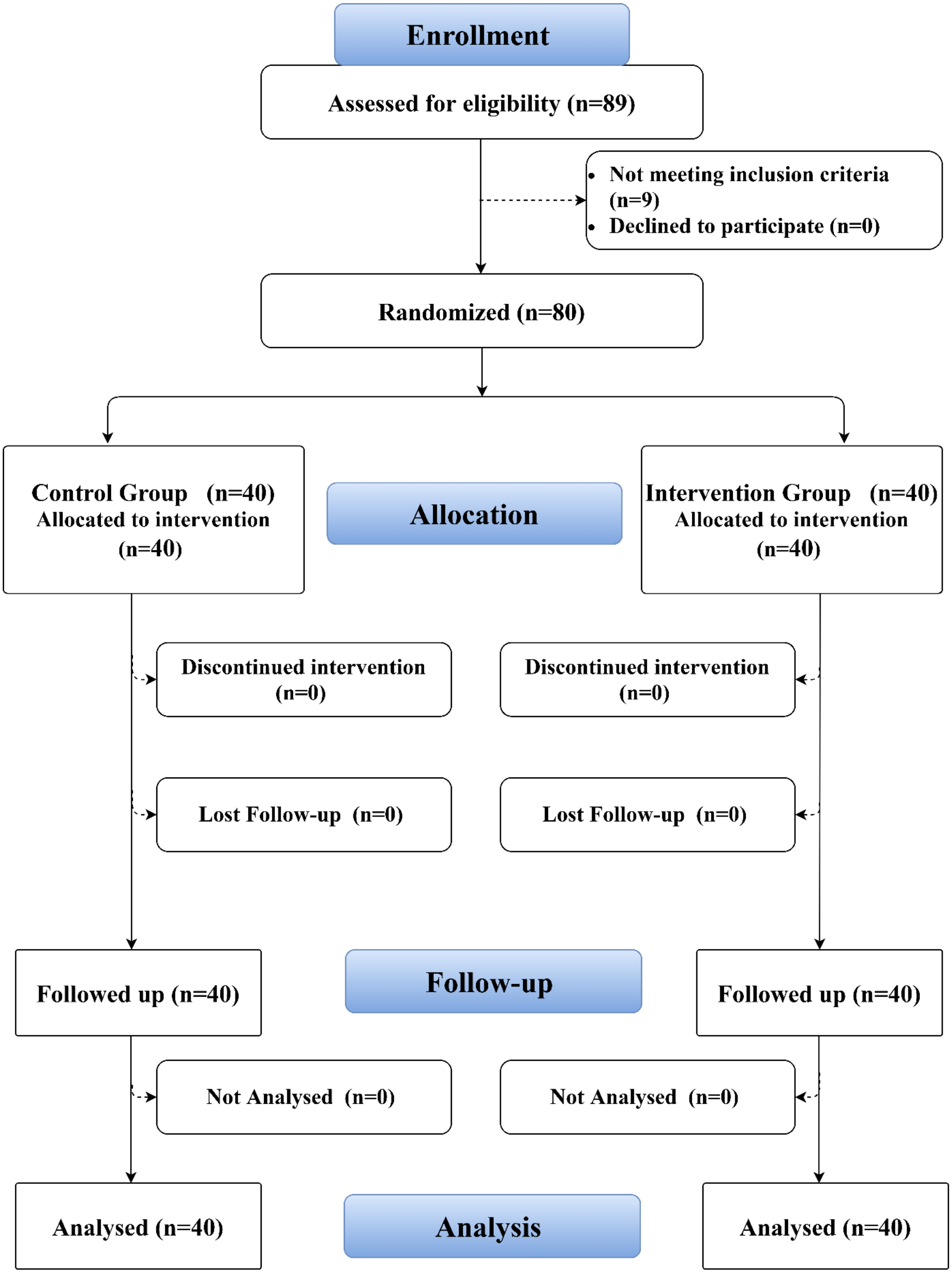

Figure 4.1 CONSORT flowchart showing flow of participants along the study

Pulp status

18 (45%) patients were diagnosed with pulp necrosis in the EDDY® group, in contrast to 17 (42.5%) patients in the manual group. Irreversible pulpitis was diagnosed in 22 (55%) and 23 (57.5%) cases among EDDY® and manual groups, respectively. (Table 3.2)

Incidence and intensity of post-endodontic pain

Eight hours after irrigation, the median levels of VAS were 1 (0-10) and 0 (0-10) among EDDY® and manual groups, respectively (P=0.113). Patients who received EDDY® experienced a statistically significant higher incidence (P=0.041) of PEP (52.5%) relative to the manual group (30%). 13 (32.5%) and 7 (17.5%) cases experienced mild pain among EDDY® and manual groups, respectively (P=0.196). There was no statistically significant difference between both groups regarding the number of analgesics taken (P=0.967). (Tables 3.2, 3.3 and Fig. 4.2)

Twenty-four hours post-irrigation, there was no statistically significant difference between both groups regarding the median levels of pain, with a median of 0 (0-3) and 0 (0-1), respectively. Post-irrigation pain occurred in 20 (50%) and 12 (30%) cases within EDDY® and manual groups (P=0.068), respectively. The number of patients who experienced mild pain was 14 (35%) in the EDDY® group and 6 (15%) in the manual group (P=0.069). The difference in the median number of analgesics taken was not statistically significant between both groups (P=0.724). (Tables 3.2, 3.3 and Fig. 4.3)

Forty-eight hours after irrigation, the median levels of post-endodontic treatment pain were 0 (0-9) and 0 (0-10) in EDDY® and manual groups, respectively (P=0.433). Then, 12 (30%) patients developed PEP in the EDDY® irrigation group, in contrast to 9 (22.5%) patients in the manual

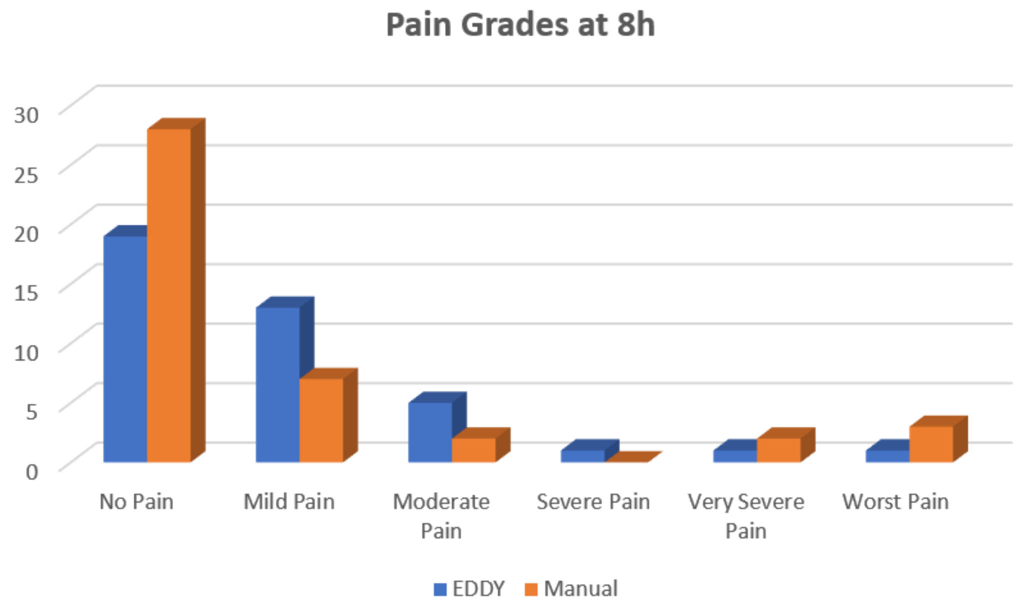

Figure 4.2 Bar chart showed median levels of Visual Analogue Scale for pain severity between EDDY® irrigation and Manual Irrigation groups at eight hours.

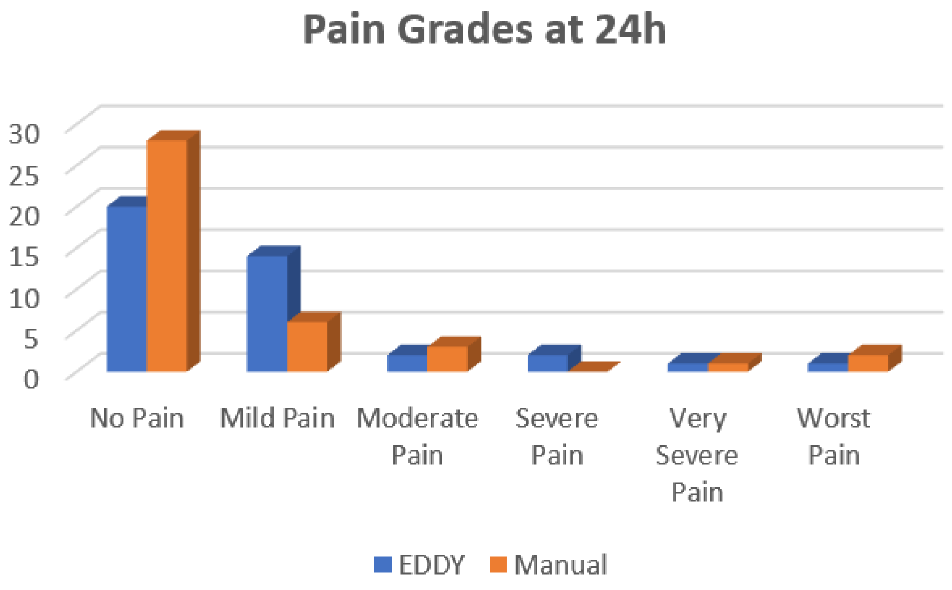

Figure 4.3 Bar chart showed median levels of Visual Analogue Scale for pain severity between EDDY® irrigation and Manual Irrigation groups at twenty-four hours.

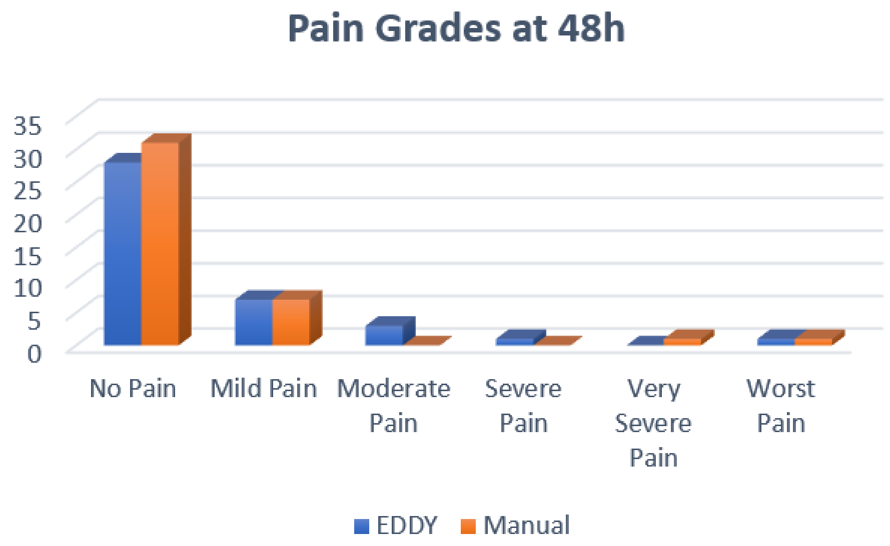

Figure 4.4 Bar chart showed median levels of Visual Analogue Scale for pain severity between EDDY® irrigation and Manual Irrigation groups at forty-eight hours.

group (P=0.446). There was a similar proportion of mild pain, accounting for 7 (17.5%) cases within both groups (P=1). In this concern, there was a similar median number of analgesics taken, 0 (0-2), among EDDY® and manual groups (P=1). (Tables 3.2, 3.3 and Fig. 4.4)

Among patients who received EDDY®, there was a statistically significant difference between VAS levels at 24 hours and 48 hours (P<0.001) and at 8 hours and 48 hours (P<0.001). There was no statistically significant difference between the pain scores at 8 and 24 hours (0.375). As for the manual irrigation group, the median levels of pain decreased significantly at 24 hours to 48 hours (P=0.004) and 8 hours to 48 hours (P=0.021). The median levels of pain were similar at 8 and 24 hours (P=1). (Fig. 4.5 and 4.6)

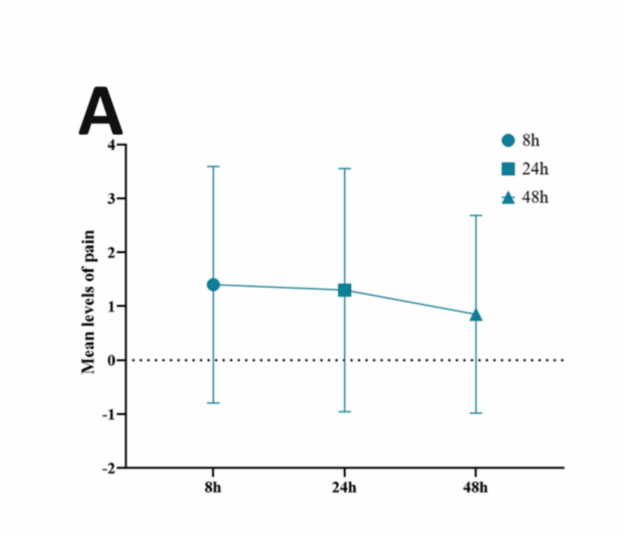

Figure 4.5 Line graph with error bars showed the mean levels of visual analogue scale at 8, 24, and 48 hours among patients received EDDY® irrigation.

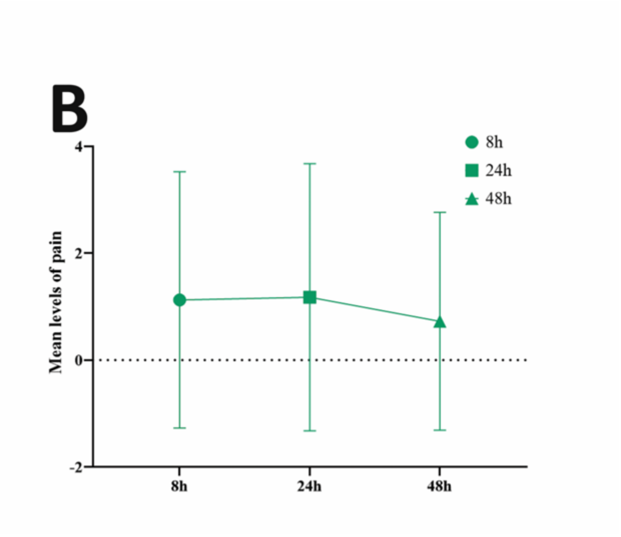

Figure 4.6 Line graph with error bars showed the mean levels of visual analogue scale at 8, 24, and 48 hours among patients received Manual irrigation.

4. DISCUSSION

Methods to prevent PEP include proper selection of instruments, techniques of instrumentation, and irrigants and devices used during RCT.(6, 28, 29) A safe irrigation delivery system is desirable to prohibit the damage of periapical tissues and to lessen PEP. Conversely, the available evidence is limited, with few studies assessing the impact of using different irrigation devices on PEP during RCT.

This clinical trial was conducted to reveal the safety and efficacy of EDDY® during initial non-surgical RCT on periapical damage and PEP. This study showed patients who received EDDY® experienced a higher rate of PEP, particularly during the first 24 hours after endodontic therapy. After such time, the pattern of PEP was similar between EDDY® and manual groups. It is noteworthy that subjects were randomly assigned to each group and the degree of preoperative pain was not taken into account for this distribution.

There was a gradual descending trend in the PEP rate with time, in which the pain decreased noticeably at 48 hours post RCT relative to pain at 8 hours. There was no difference between the number of analgesics taken at the end of the follow-up between EDDY® and manual irrigations. This finding was coincident with Pak and White (2011), who reported an approximate drop of 30% in pain prevalence from the first to the seventh day of endodontic treatment.(30) In this concern, Gündoğar *et al.,* (2021) reported a similar pattern of PEP after 24 hours of EDDY® and side-port endodontic needles irrigation. They also reported no significant difference between EDDY® and needle irrigation regarding the number of analgesics used. Contrary to the present study's findings, they reported a significantly lower PEP associated with EDDY® compared to side-port endodontic needle irrigation during the first 24 hours. (22)

The possible explanation for why more PEP was associated with EDDY® might be related to the concentration of NaOCl used (5.25%) relative to a concentration of 3% in Gündoğar *et al.,* (2021). (22) According to Marion *et al.,* (2012), it was observed 5.25% NaOCl has better effectiveness in dissolving organic tissue, greater antibacterial action, a more alkaline pH, and shorter effectiveness time, which led us to choose this concentration. Conversely, it is more irritating to the periapical tissues. (18) In agreement with this finding, Mostafa *et al.,* (2019) revealed a significantly higher PEP intensity associated with the application of 5.25% NaOCl in mandibular molars with non-vital pulp, relative to 1.3% NaOCl. (31) The NaOCl cytotoxic effect may be further augmented by the rotating tips of EDDY®, resulting in more debris extrusion and inflammation. (32, 33)

5. CONCLUSIONS

EDDY® during initial RCT is associated with a higher incidence of PEP, principally in the 24 hours following treatment, relative to manual irrigation. After, the rate of PEP was similar between EDDY® and manual irrigation, with a gradual decline in pain intensity. It is important to emphasize the importance of this randomized clinical trial because there are little information about these topic; however, there are some limitations regarding the results evaluation, because of the inclusion of random cases of pulp necrosis and irreversible pulpitis, with different levels of perioperative pain. Further randomized clinical trials with adequate sample sizes and longer follow-up periods are necessary to reveal the efficacy and safety of EDDY® during initial RCT.

Table 3.1 Baseline demographic characteristics

	EDDY$^{®}$ irrigation	**Manual Irrigation**	**P-Value**
	Mean (SD)/ N (%)	**Mean (SD)/ N (%)**	
Age (Years)	54.40 ± 16.45	52.90 ± 15.95	0.68
Gender			
Males	17 (42.5%)	17 (42.5%)	1
Females	23 (57.5%)	23 (57.5%)	
Number of irrigated teeth	25.42 ± 11.18	23.10 ± 9.73	0.324
Types of irrigated teeth			
Central incisor	7 (17.5%)	3 (7.5%)	0.421
Canine	8 (20%)	13 (32.5%)	
Premolar	21 (52.5%)	20 (50%)	
Lateral incisor	4 (10%)	4 10%)	
Teeth location			
Mandibular	13 (32.5%)	11 (27.5%)	0.404
Maxillary	27 (67.5%)	29 (72.5%)	
Preoperative pain incidence [n (%)]			
Yes	9 (22.5%)	9 (22.5%)	1
No	31 (77.5%)	31 (77.5%)	
Preoperative pain incidence in Irreversible Pulpitis			
Yes	6 (27.3%)	5 (21.7%)	0.666
No	16 (72.7%)	18 (78,3%)	
Preoperative pain incidence in Pulp Necrosis			
Yes	3 (16.7%)	4 (23.5%)	0.612
No	15 (83.3%)	13 (76.5%)	
Pulp status			1
Pulp Necrosis	18 (45%)	17 (42.5%)	
Irreversible Pulpitis	22 (55%)	23 (57.5%)	

Abbreviations; SD=Standard deviation, N=Number

Table 3.2 Pain scores and analgesics taken at 8 h, 24 h, and 48 h post-irrigation

	EDDY® irrigation	**Manual Irrigation**	**P-Value**
	Median (Range)	**Median (Range)**	
Visual analogue scale			
8 h post-irrigation	1 (0 - 10)	0 (0 - 10)	0.113
24 h post-irrigation	0.5 (0 - 10)	0 (0 - 10)	0.212
48 h post-irrigation	0 (0 - 9)	0 (0 - 10)	0.433
Number of taken analgesics			
8 h post-irrigation	0 (0 - 3)	0 (0 - 1)	0.967
24 h post-irrigation	0 (0 - 2)	0 (0 - 1)	0.724
48 h post-irrigation	0 (0 - 2)	0 (0 - 2)	1

Table 3.3 Visual analogue scale severity at 8h, 24h, and 48h

	EDDY® irrigation	Manual Irrigation	P-Value
	Number (%)	Number (%)	
At 8 h			
No Pain	19 (47.5%)	28 (70%)	0.069
Mild	13 (32.5%)	7 (17.5%)	0.196
Moderate	5 (12.5%)	2 (5%)	0.432
Severe	1 (2.5%)	0 (0%)	1
Very Severe	1 (2.5%)	2 (5%)	1
Worst pain possible	1 (2.5%)	1 (2.5%)	1
At 24 h			
No Pain	20 (50%)	28 (70%)	0.110
Mild	14 (35%)	6 (15%)	0.069
Moderate	2 (5%)	3 (7.5%)	1
Severe	2 (5%)	0 (0%)	1
Very Severe	1 (2.5%)	1 (2.5%)	1
Worst pain possible	1 (2.5%)	2 (5%)	1
At 48 h			
No Pain	28 (70%)	31 (77.5%)	0.612
Mild	7 (17.5%)	7 (17.5%)	1
Moderate	3 (7.5%)	0 (0%)	0.241
Severe	1 (2.5%)	0 (0%)	1
Very Severe	0 (0%)	1 (2.5%)	1
Worst pain possible	1 (2.5%)	1 (2.5%)	1

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CHAPTER VI

DISCUSSION

1. DISCUSSION

Root canal treatment is an endodontic procedure that involves treating an inflammation/infection in the dental pulp, preventing its reinfection while preserving the natural teeth. Failed root canal symptoms include swelling or development of fistula on the gum, tooth discoloration, sensitivity, pain, or swelling of the neck. (1) Once these symptoms have manifested, a patient needs to seek intervention.

Endodontic treatment should aim at conserving the outer structure of the tooth and maintaining the original canal geometry, as well as remove bacteria, pulp tissue and smear layer, achieving a proper canal debridement and, consequently, a proper root canal filling. This will require adopting the appropriate chemo-mechanical mechanism with minimum preparation. It should reduce bacterial infection as much as possible by creating contact with the canal wall to reach the intricate part of the root canals. (2) Another goal in endodontic treatment is pain management, notably, eliminating pain after treatment. One of the main factors contributing to postoperative pain is the chemical injury to periradicular tissues by irrigating solutions, when extrusion beyond the apical constriction occurs.

Many techniques and devices have been proposed to increase the effect of chemical disinfection within the root canal system, due to the inability of endodontic irrigants to penetrate the complexities of the root canal system allowing bacterial biofilms to persist after the cleaning and shaping procedures. Residual debris and smear layer may act as a barrier, decreasing the antimicrobial effectiveness of intracanal medicaments.

The introduction of disinfectants into the root canal system during root canal process is called irrigation. This process is essential as it ensures minimal or no friction between the dentine and the instruments, dissolves the tissues, and cools the endodontic instruments. (3) This is regarded as one of the most important steps of root canal treatment, because it indorses the killing and removal of bacteria, pulp tissue and smear layer. The most used irrigant is sodium hypochlorite; due to its ability to dissolve organic material and its strong activity against root canal microorganisms. A rinsing chelant is also applied after the canal instrumentation, to remove the existing smear layer. (4) The process of root canal irrigation can be conducted through various techniques, but the ones addressed in this work are the following: standard needle irrigation, sonic activation and ultrasonic activation. (5) Ultrasonic activation is the most used technique of irrigant activation used, and sonic activation it's an alternative technique to ultrasonics, without the risk of accidental dentin removal during activation. (6) The focus of these concerns revolved around the lack of researched or clearly defined evidence regarding the comparison between sonic and ultrasonic activation. Therefore, this thesis addresses the outcomes for endodontic treatments provided by the use of EDDY® (VDW, Munich, Germany), a sonic powered irrigation activation system, in order to evaluate the level of canal cleanliness, bacterial disinfection, periapical damage and pain through *ex vivo* and clinical studies.

EDDY® system is a sonic device which operates at lower frequencies, thus preventing file-to-wall contact minimizing the risk of dentin removal. EDDY® has a soft flexible polyamide tip that is incorporated in an air scaler and it does not cut, preventing canal damage and works at a frequency of 5-6 kHz. (5) Its structure, reduces the chances of unintentional dentine removal, and its antimicrobial efficacy applies to both straight and curved root canals. This is possible due to its flexible structure that is able to enter in any type or root canal anatomy. EDDY® power modes are essential in ensuring the effectiveness of endodontic disinfection, so it must work at its highest power setting. EDDY® operates at 5-6kHz, a much higher frequency than other sonic systems like EndoActivator® that operates at 0.166–0.3 kHz, and with his vibration it is able to generate "cavitation" and "acoustic streaming", two physical effects which have only been known to be triggered by UIA. (2)

Initially, a meta-analysis was performed to address if sonic activation outcomes were better than ultrasonic for endodontic treatment. The performed analysis established no statistically significant difference in the amount of debris removal for both sonic and ultrasonic irrigation procedures as well as the amount of residual debris for both the sonic and ultrasonic activation. There was no significant difference between the two in the middle level concerning the smear layer score, but a considerably lower smear layer score was noted in the apical level for sonic activation group. In relation to the percentage of canal cleanliness, there was no statistically significant difference for both treatments at one, three, and five mm. The study also revealed no statistically significant difference in irrigant penetration depth between coronal and middle levels treatments. This meta-analysis results should be interpreted cautiously due to the limitations in translating *in vitro* studies to *in vivo* circumstances. The included studies' sample size ranged from 14 to 60 teeth, which might impair the evidence. Additionally, there was significant heterogeneity among the included studies, stemming from difference in outcomes assessment methods, source of the extracted teeth, irrigant solutions, endodontic preparation, and activation protocols. Such heterogeneity was also statistically established for the employed random-effects model. Furthermore, the lack of optimal follow-up periods constringed the assessment of long-term outcomes.

Sonic activation accomplished advancement relative to ultrasonic agitation in removing the smear layer, mainly at the apical area, during endodontic therapy. Furthermore, ultrasonic activation of the irrigants resulted in significant cohesion between the sealers and the dentin tubules, decreasing the vulnerability of apical leakage and tooth fracture.

The *ex vivo* study focused on the comparison of the efficacy of sonic and ultrasonic activation on root canal disinfection and debridement using distinct apical enlargement. The study proved that mechanical activation of irrigants is more advantageous than manual activation and larger apical sizes make it more effective for UAI and EDDY® activation.

Weine (1972) (10), defined the master apical file (MAF) size as enlarging the apical portion of the root canal system three sizes larger than the first file that bound at working length, but it is unsure where this binding occurred and, if in fact, it reflected the true pre-instrumented apical diameter of the root canal system. Having said that, it is difficult to assume a preparation size as ideal, after searching the published literature. (11) Studies show that irrigation has better effect if the taper and size are larger. The preparation process usually involves a tip size of 25 and a continuous .06 taper. (2) Some systems also implement additional instrumental sizes for an extra phase called "apical enlargement and refinement". Hereupon, our *ex vivo* study used 35 and 50 apical sizes to establish a comparison between medium and wider canals.

Lastly, through a clinical study, it was addressed the risk of PEP between irrigation using EDDY® and conventional endodontic needles among patients seeking initial non-surgical RCT. This study showed patients who received EDDY® experienced a higher rate of PEP, particularly during the first 24 hours after endodontic therapy. After such time, the pattern of PEP was similar between EDDY® and manual groups. There was a gradual descending trend in the PEP rate with time, in which the pain decreased noticeably at 48 hours post RCT relative to pain at 8 hours. There was no difference between the number of analgesics taken at the end of the follow-up between EDDY® and manual irrigations. This finding was coincident with Pak and White (2011), who reported an approximate drop of 30% in pain prevalence from the first to the seventh day of endodontic treatment.(8) In this concern, Gündoğar *et al.,* (2021) reported a similar pattern of PEP after 24 hours of EDDY® and side-port endodontic needles irrigation. They also reported no significant difference between EDDY® and needle irrigation regarding the number of analgesics used. Contrary to the present study's findings, they reported a significantly lower PEP associated with EDDY® compared to side-port endodontic needle irrigation during the first 24 hours.(9)

Future work

There are many different types of teeth anatomy with varied morphological characteristics, therefore, future researches should test on different canal morphologies to better understand their characteristics and the vantages and disadvantages of EDDY® in these anatomical groups. Different anatomy will give varying results that will be useful to the dental research.

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CHAPTER VII

CONCLUSIONS

1. CONCLUSIONS

Key findings in Chapter III

- This systematic review suggested that sonic activation accomplished advancement relative to ultrasonic agitation in removing the smear layer, while ultrasonic activation resulted in significant cohesion between the sealers and the dentin tubules, decreasing the vulnerability of apical leakage and tooth fracture.

Key findings in Chapter IV

- The conclusions that can be drawn based on the results of this *ex vivo* study are that (1) both sonic and ultrasonic activation might be associated to higher risk of extrusion for larger apical preparation sizes, as compared to manual irrigation; however (2) higher efficiency of debris and smear layer removal, as well as (3) biofilm elimination was obtained for EDDY® and UAI procedures, for both apical preparation sizes, as compared to manual needle irrigation; (4) UAI applied to root canals at 50/.06 exhibited the best combined outcomes.

Key findings in Chapter V

- The conclusions that were achieved with this clinical study are: EDDY® during initial RCT is associated with a higher incidence of PEP, principally in the 24 hours following treatment, relative to manual irrigation. After, the rate of PEP was similar between EDDY® and manual irrigation, with a gradual decline in pain intensity. Further randomized clinical trials with adequate sample sizes and longer follow-up periods are necessary to reveal the efficacy and safety of EDDY® during initial RCT.

Concluding remarks

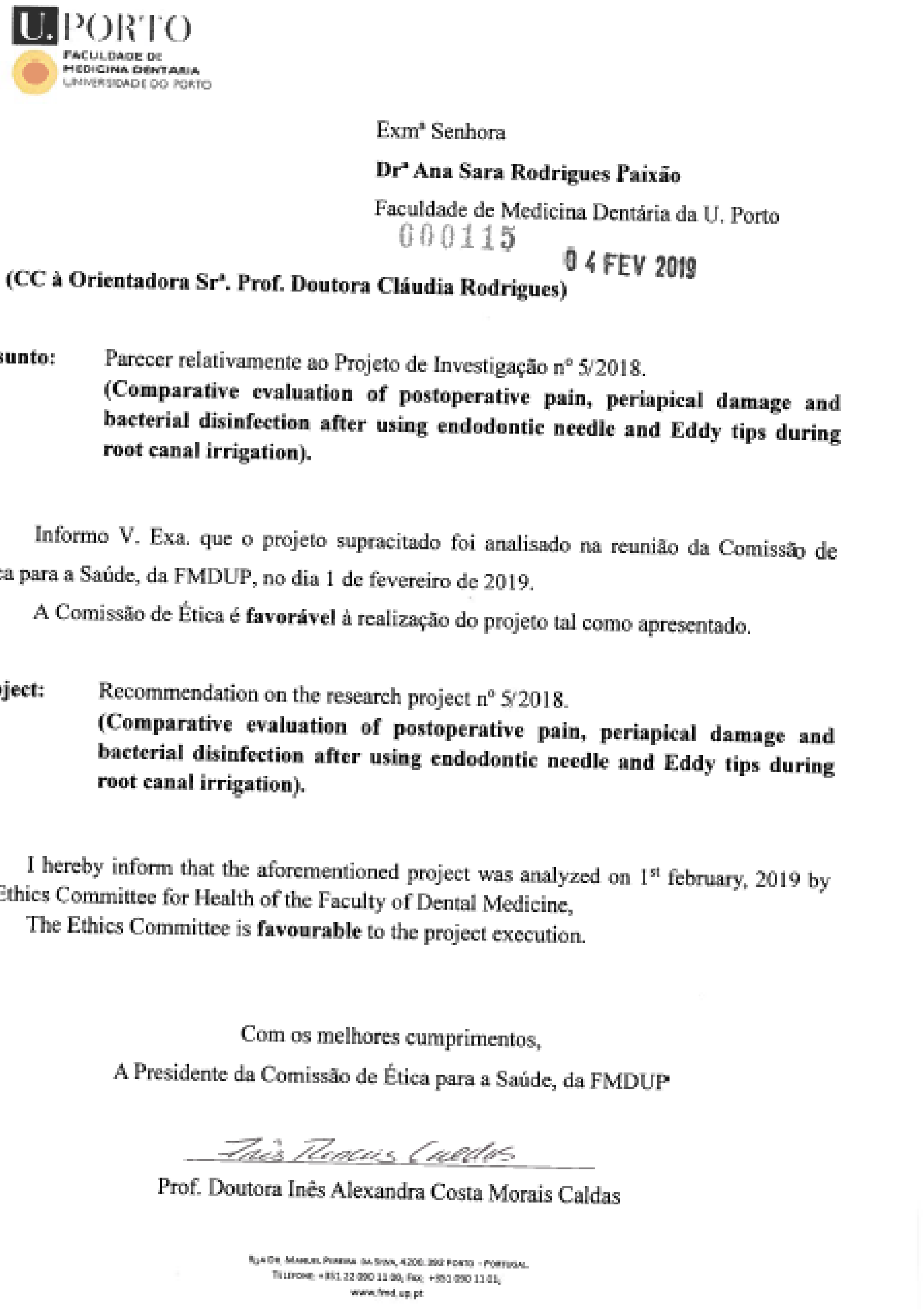
EDDY® appears to be a reliable sonic irrigant activator, with better results than manual syringe irrigation and similar results to ultrasonic irrigant activation, but with less downsides than the latter.

Supplementary files

Appendix I – Literature search / keywords of the systematic review

Database	Keywords	Results
PubMed	((((((((Endodontic[Title]) OR (Root Canal[Title])) AND (Ultrasonic[Title])) OR (Ultrasonically[Title])) AND (Activation[Title])) OR (Activating[Title])) OR (Agitation[Title])) OR (Irrigation[Title])) AND (Sonic[Title])	46
Google Scholar	allintitle: Sonic ultrasonic endodontic Activation OR Activating OR Agitation OR Irrigation	3
	allintitle: Sonic ultrasonic root canal Activation OR Activating OR Agitation OR Irrigation	17
Web of Science	TITLE: (Root Canal) AND TITLE: (Ultrasonic) OR TITLE: (ultrasonically) AND TITLE: (Activation) OR TITLE: (Agitation) AND TITLE: (Sonic)	143
	TITLE: (Endodontic) AND TITLE: (Ultrasonic) OR TITLE: (ultrasonically) AND TITLE: (Activation) OR TITLE: (Agitation) AND TITLE: (Sonic)	57
Scopus	TITLE ("Endodontic" OR " Root Canal" AND " Ultrasonic" OR " Ultrasonically" AND " Activation" OR " Activating" OR " Agitation" OR "Irrigation" AND "Sonic")	17
EMBASE	(((endodontic:ti OR 'root canal':ti) AND ultrasonic:ti OR ultrasonically:ti) AND activation:ti OR agitation:ti OR activating:ti OR irrigation:ti) AND sonic:ti	47
SIGLE	"Root Canal" OR " Endodontic" AND "Ultrasonic" AND "Sonic" AND "Activation"	34
Virtual Health Library	(ti:(Endodontic)) OR (ti:(Root Canal)) AND (ti:(Ultrasonic)) OR (ti:(Ultrasonically)) AND (ti:(Activation)) OR (ti:(Irrigation)) OR (ti:(Agitation)) AND (ti:(Sonic))	0
NYAM	"Root Canal" OR " Endodontic" AND "Ultrasonic" AND "Sonic" AND "Activation"	0
Clinical Trials.Gov	Root Canal | endodontic | Sonic | ultrasonic	0
Controlled Trials (mRCT)	"Ultrasonic AND (Condition: Endodontic AND Interventions: Sonic AND Public title: Ultrasonic AND Trial acronym: Root Canal)"	0
ICTRP	Endodontic AND Ultrasonic AND Sonic	1

Appendix 11 – Ethics Committee



U.PORTO
FACULDADE DE
MEDICINA DENTÁRIA
UNIVERSIDADE DO PORTO

Exmª Senhora
Drª Ana Sara Rodrigues Paixão
Faculdade de Medicina Dentária da U. Porto

000115

04 FEV 2019

(CC à Orientadora Srª. Prof. Doutora Cláudia Rodrigues)

Assunto: Parecer relativamente ao Projeto de Investigação nº 5/2018.
(Comparative evaluation of postoperative pain, periapical damage and bacterial disinfection after using endodontic needle and Eddy tips during root canal irrigation).

Informo V. Exa. que o projeto supracitado foi analisado na reunião da Comissão de Ética para a Saúde, da FMDUP, no dia 1 de fevereiro de 2019.

A Comissão de Ética é **favorável** à realização do projeto tal como apresentado.

Subject: Recommendation on the research project nº 5/2018.
(Comparative evaluation of postoperative pain, periapical damage and bacterial disinfection after using endodontic needle and Eddy tips during root canal irrigation).

I hereby inform that the aforementioned project was analyzed on 1st february, 2019 by the Ethics Committee for Health of the Faculty of Dental Medicine,

The Ethics Committee is **favourable** to the project execution.

Com os melhores cumprimentos,

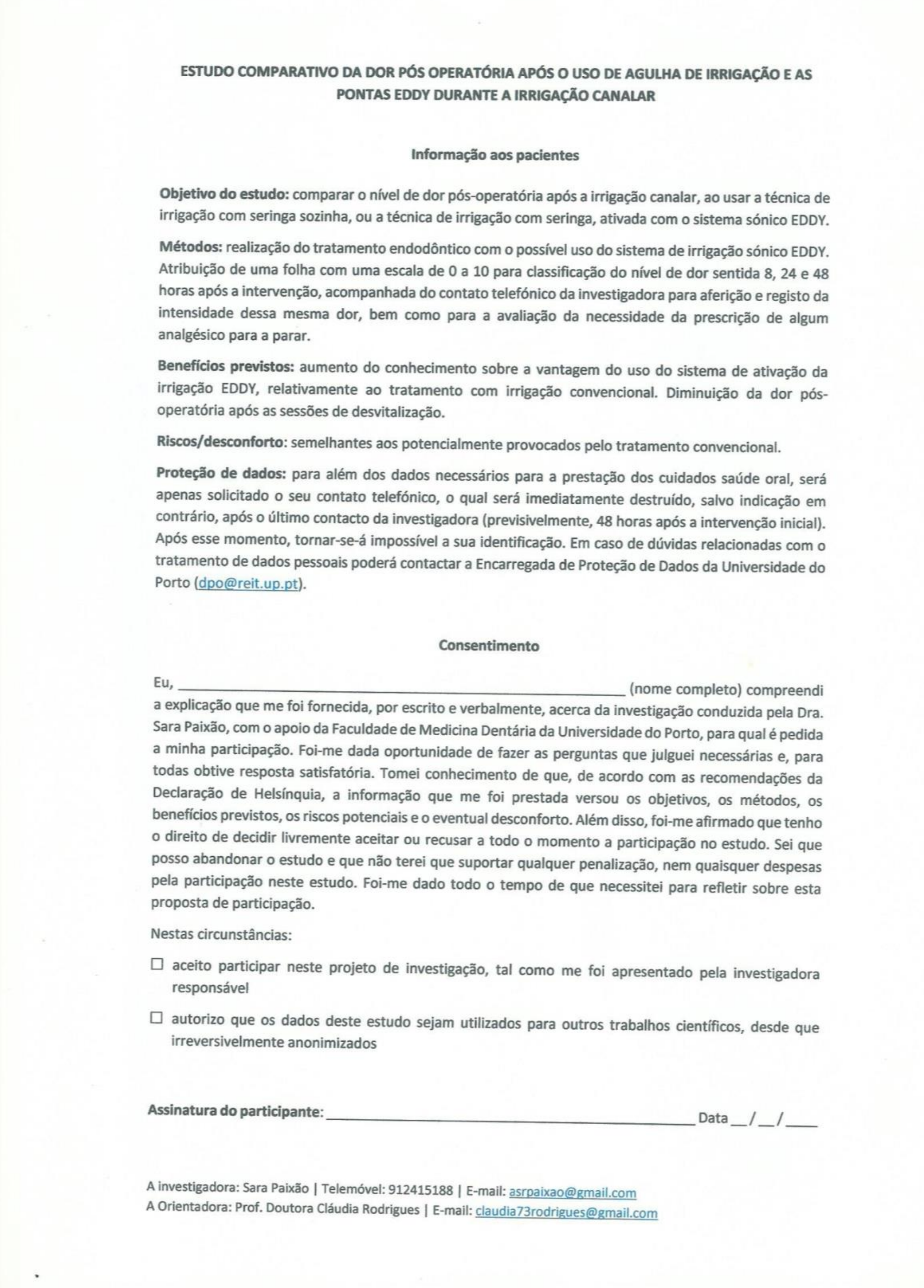
A Presidente da Comissão de Ética para a Saúde, da FMDUP

Inês Morais Caldas

Prof. Doutora Inês Alexandra Costa Morais Caldas

www.fmd.up.pt

Appendix II – Informed Consent (Adults)



ESTUDO COMPARATIVO DA DOR PÓS OPERATÓRIA APÓS O USO DE AGULHA DE IRRIGAÇÃO E AS PONTAS EDDY DURANTE A IRRIGAÇÃO CANALAR

Informação aos pacientes

Objetivo do estudo: comparar o nível de dor pós-operatória após a irrigação canalar, ao usar a técnica de irrigação com seringa sozinha, ou a técnica de irrigação com seringa, ativada com o sistema sónico EDDY.

Métodos: realização do tratamento endodôntico com o possível uso do sistema de irrigação sónico EDDY. Atribuição de uma folha com uma escala de 0 a 10 para classificação do nível de dor sentida 8, 24 e 48 horas após a intervenção, acompanhada do contato telefónico da investigadora para aferição e registo da intensidade dessa mesma dor, bem como para a avaliação da necessidade da prescrição de algum analgésico para a parar.

Benefícios previstos: aumento do conhecimento sobre a vantagem do uso do sistema de ativação da irrigação EDDY, relativamente ao tratamento com irrigação convencional. Diminuição da dor pós-operatória após as sessões de desvitalização.

Riscos/desconforto: semelhantes aos potencialmente provocados pelo tratamento convencional.

Proteção de dados: para além dos dados necessários para a prestação dos cuidados saúde oral, será apenas solicitado o seu contato telefónico, o qual será imediatamente destruído, salvo indicação em contrário, após o último contacto da investigadora (previsivelmente, 48 horas após a intervenção inicial). Após esse momento, tornar-se-á impossível a sua identificação. Em caso de dúvidas relacionadas com o tratamento de dados pessoais poderá contactar a Encarregada de Proteção de Dados da Universidade do Porto (dpo@reit.up.pt).

Consentimento

Eu, ____ (nome completo) compreendi a explicação que me foi fornecida, por escrito e verbalmente, acerca da investigação conduzida pela Dra. Sara Paixão, com o apoio da Faculdade de Medicina Dentária da Universidade do Porto, para qual é pedida a minha participação. Foi-me dada oportunidade de fazer as perguntas que julguei necessárias e, para todas obtive resposta satisfatória. Tomei conhecimento de que, de acordo com as recomendações da Declaração de Helsínquia, a informação que me foi prestada versou os objetivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto. Além disso, foi-me afirmado que tenho o direito de decidir livremente aceitar ou recusar a todo o momento a participação no estudo. Sei que posso abandonar o estudo e que não terei que suportar qualquer penalização, nem quaisquer despesas pela participação neste estudo. Foi-me dado todo o tempo de que necessitei para refletir sobre esta proposta de participação.

Nestas circunstâncias:

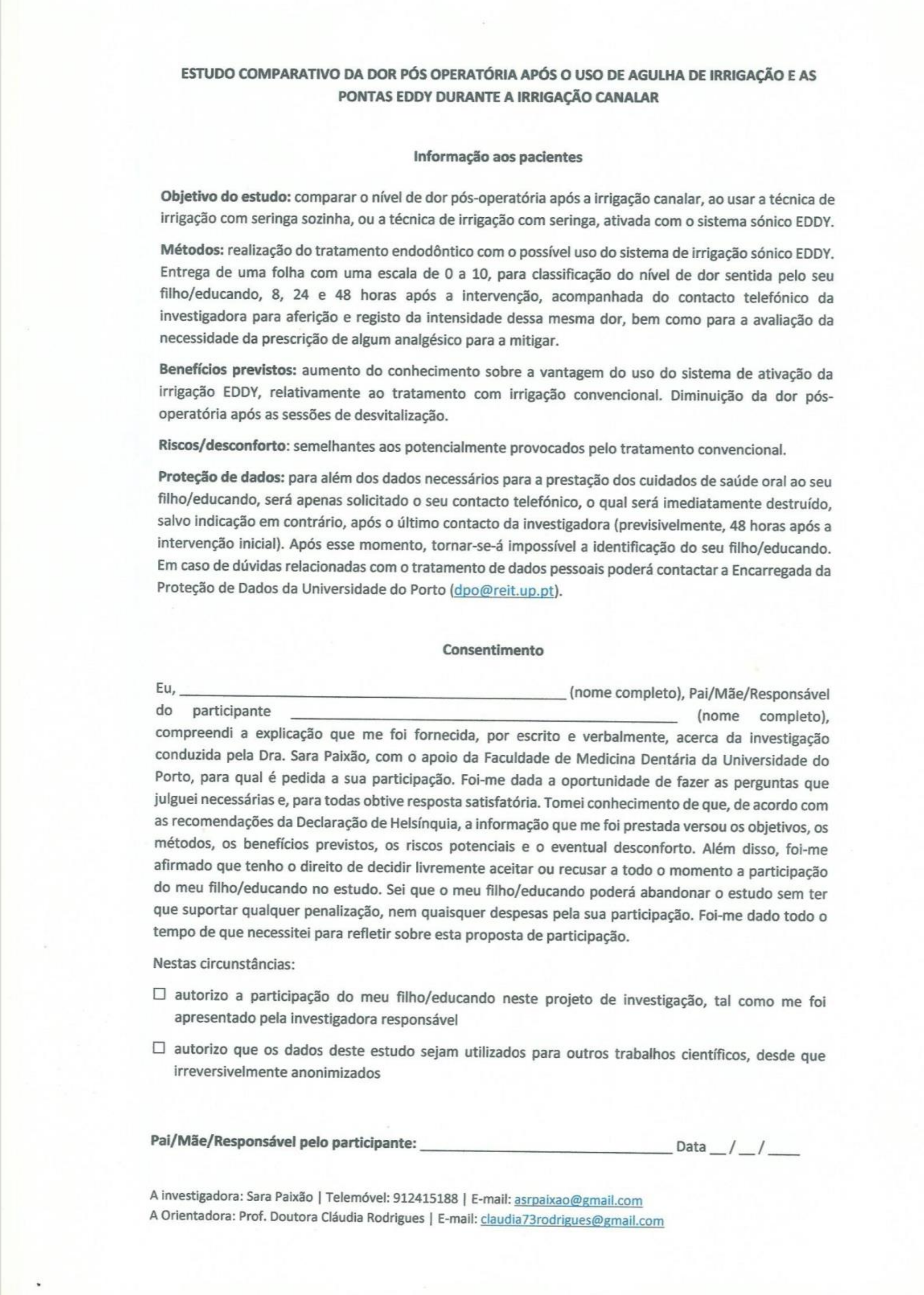
☐ aceito participar neste projeto de investigação, tal como me foi apresentado pela investigadora responsável

☐ autorizo que os dados deste estudo sejam utilizados para outros trabalhos científicos, desde que irreversivelmente anonimizados

Assinatura do participante: ____ Data __/__/____

A investigadora: Sara Paixão | Telemóvel: 912415188 | E-mail: asrpaixao@gmail.com
A Orientadora: Prof. Doutora Cláudia Rodrigues | E-mail: claudia73rodrigues@gmail.com

Appendix III – Informed Consent (underage)



ESTUDO COMPARATIVO DA DOR PÓS OPERATÓRIA APÓS O USO DE AGULHA DE IRRIGAÇÃO E AS PONTAS EDDY DURANTE A IRRIGAÇÃO CANALAR

Informação aos pacientes

Objetivo do estudo: comparar o nível de dor pós-operatória após a irrigação canalar, ao usar a técnica de irrigação com seringa sozinha, ou a técnica de irrigação com seringa, ativada com o sistema sónico EDDY.

Métodos: realização do tratamento endodôntico com o possível uso do sistema de irrigação sónico EDDY. Entrega de uma folha com uma escala de 0 a 10, para classificação do nível de dor sentida pelo seu filho/educando, 8, 24 e 48 horas após a intervenção, acompanhada do contacto telefónico da investigadora para aferição e registo da intensidade dessa mesma dor, bem como para a avaliação da necessidade da prescrição de algum analgésico para a mitigar.

Benefícios previstos: aumento do conhecimento sobre a vantagem do uso do sistema de ativação da irrigação EDDY, relativamente ao tratamento com irrigação convencional. Diminuição da dor pós-operatória após as sessões de desvitalização.

Riscos/desconforto: semelhantes aos potencialmente provocados pelo tratamento convencional.

Proteção de dados: para além dos dados necessários para a prestação dos cuidados de saúde oral ao seu filho/educando, será apenas solicitado o seu contacto telefónico, o qual será imediatamente destruído, salvo indicação em contrário, após o último contacto da investigadora (previsivelmente, 48 horas após a intervenção inicial). Após esse momento, tornar-se-á impossível a identificação do seu filho/educando. Em caso de dúvidas relacionadas com o tratamento de dados pessoais poderá contactar a Encarregada da Proteção de Dados da Universidade do Porto (dpo@reit.up.pt).

Consentimento

Eu, ____________________________________ (nome completo), Pai/Mãe/Responsável do participante ____________________________________ (nome completo), compreendi a explicação que me foi fornecida, por escrito e verbalmente, acerca da investigação conduzida pela Dra. Sara Paixão, com o apoio da Faculdade de Medicina Dentária da Universidade do Porto, para qual é pedida a sua participação. Foi-me dada a oportunidade de fazer as perguntas que julguei necessárias e, para todas obtive resposta satisfatória. Tomei conhecimento de que, de acordo com as recomendações da Declaração de Helsínquia, a informação que me foi prestada versou os objetivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto. Além disso, foi-me afirmado que tenho o direito de decidir livremente aceitar ou recusar a todo o momento a participação do meu filho/educando no estudo. Sei que o meu filho/educando poderá abandonar o estudo sem ter que suportar qualquer penalização, nem quaisquer despesas pela sua participação. Foi-me dado todo o tempo de que necessitei para refletir sobre esta proposta de participação.

Nestas circunstâncias:

☐ autorizo a participação do meu filho/educando neste projeto de investigação, tal como me foi apresentado pela investigadora responsável

☐ autorizo que os dados deste estudo sejam utilizados para outros trabalhos científicos, desde que irreversivelmente anonimizados

Pai/Mãe/Responsável pelo participante: ____________________________ Data __/__/____

A investigadora: Sara Paixão | Telemóvel: 912415188 | E-mail: asrpaixao@gmail.com
A Orientadora: Prof. Doutora Cláudia Rodrigues | E-mail: claudia73rodrigues@gmail.com

Appendix IV – Pain Scale

Faculdade de Medicina Dentária da Universidade do Porto

QUESTIONÁRIO AOS PACIENTES

	Intensidade de Dor (de 0 a 10)	Comprimidos tomados
8H		
24H		
48h		

ESCALA DE DOR

0 1 2 3 4 5 6 7 8 9 10

sem dor · dor ligeira · dor moderada · dor intensa · dor máxima

Investigadora: Dra. Sara Paixão **Orientadora:** Prof. Dra. Cláudia Rodrigues

If I have seen further it is by standing on the shoulders of giants.

Isaac Newton