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ORIGINAL ARTICLE

The use of medicaments in the management of symptomatic irreversible pulpitis: A community-based cohort study

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Abstract

Aim: To investigate patient outcomes from either pulpotomy or pulpectomy for the management of symptomatic irreversible pulpitis, with and without application of antibiotic/corticosteroid pastes in urgent primary dental care settings in the United Kingdom.

Methodology: All patients receiving intervention for symptomatic irreversible pulpitis in three different primary care settings were invited to participate. Pre-operatively, data regarding patients' numerical ratings scale (NRS), pain score (0–10), analgesic use, oral-health impact profile-14 (OHIP-14) and need for time away from work were collected. For 7 days post-operatively, participants recorded their NRS pain score, global rating of change score, medication use and their ability to work. Analysis used a mixed-effects model with post hoc Tukey's multiple comparisons test for continuous data and chi-squared or Fisher's exact test for categorical data. To test the effect of the corticosteroid/antibiotic paste, pulpectomy and pulpotomy groups were combined following Mantel–Haenszel stratified analysis or a weighted average of the difference between pulpotomy and pulpectomy with and without the use of corticosteroid/antibiotic paste. A binary composite score was constructed using pre- and post-operative data, whereby overall treatment success was defined as: (i) patients did not return for treatment due to pain by day seven; (ii) at day three, there was a 33% (or 2-points) reduction in NRS pain score; (iii) there was a change score of +3 in global rating; (iv) the patient was no longer using analgesia and able to return to work.

Results: Eighty-five participants were recruited, with 83 completing follow up. Overall treatment success was 57%, with 25% of participants returning for more treatment due to inadequate pain relief. Overall treatment success did not differ between the two groups ($p = .645$), although patients self-reported greater improvement with an antibiotic/corticosteroid dressing for global rating of change ($p = .015$).

Conclusions: This study identified limited evidence of improved outcomes using antibiotic/corticosteroid dressings in the management of symptomatic irreversible

pulpitis in the emergency setting. Further clinical research is needed to understand if these medications are beneficial in affording pain relief, above that of simple excision of irreversibly inflamed pulp tissue.

KEYWORDS

acute pain, pulpectomy, pulpitis, pulpotomy, root canal therapy

INTRODUCTION

In the United Kingdom (UK), acute dental pain is a significant problem, affecting 9% of the adult population per annum (Steele et al., 2011). Globally, the problem may be even more significant, with reports ranging from 12% to 24% per annum (McMillan et al., 2006; Peres et al., 2019). The most frequently encountered urgent dental condition is reported to be symptomatic irreversible pulpitis, contributing to up to one in three presentations (Currie et al., 2015; Edwards et al., 2023; Huang et al., 2019). Furthermore, symptomatic irreversible pulpitis has been found to have the biggest impact on oral health-related quality of life (OHRQoL) and to be the most painful of all urgent dental presentations (Cimilli et al., 2012; Currie et al., 2015; Edwards et al., 2023).

Despite the prevalence of this condition, and its significant impact on patients, there is no consensus on optimal emergency management. Two recent UK-based studies investigated the management of symptomatic irreversible pulpitis identified that 57%–62% and 77%–85% of practitioners aimed to undertake an emergency pulpotomy or pulpectomy respectively (Edwards et al., 2021; Gemmell et al., 2020). Both approaches have been shown to be equally effective for pain reduction (Eren et al., 2018). In multirooted teeth, an 'emergency' pulpotomy has been considered more appropriate and predictable than pulpectomy due to the challenges of complete pulp removal and root canal disinfection (Eren et al., 2018; Nyerere et al., 2006).

In endodontology, there is a current research focus on pulpotomy as a definitive treatment for symptomatic irreversible pulpitis (Clarkson et al., 2022), with a growing body of evidence on the effectiveness of calcium silicate cements (CSCs) as a definitive wound dressing (AAE, 2021; Asgary et al., 2017; Careddu & Duncan, 2021; Cushley et al., 2019; Li et al., 2019; Taha et al., 2017). Guidelines have emphasized the need for an 'enhanced' treatment protocol with magnification and stringent asepsis (Duncan et al., 2019). However, emergency pulpotomy conducted within the constraints of urgent dental care provision in primary dental care may not afford such refinement, particularly in systems such as the UK National Health Service (NHS) with its median urgent dental care appointment length of 20 min (Edwards et al., 2021). The challenges of delivering a definitive pulpotomy within the time constraints of an emergency appointment can be further compounded by anaesthetic difficulties, limited training of primary care clinicians in case selection and treatment procedures and access to materials and magnification (Edwards et al., 2021; Modaresi et al., 2005; Parirokh & Abbott, 2022). A single visit definitive pulpotomy may therefore be considered aspirational in many settings (Claffey et al., 2004; Edwards et al., 2021; Nusstein et al., 2010; Sampaio et al., 2012; Tortamano et al., 2009), reinforcing the need for effective approaches to emergency management in primary care.

Following an emergency pulpotomy or pulpectomy at an unscheduled or urgent dental care appointment, up to 74% of UK dentists report dressing the tooth with an antibiotic/corticosteroid paste (Edwards et al., 2021; Gemmell et al., 2020). Commonly used antibiotic/corticosteroid dressings include Ledermix (Haupt Pharma GmbH, Wolfratshausen, Germany) and Odontopaste (Australian Dental Manufacturing, Kenmore Hills, Qld, Australia). During the COVID-19 pandemic, the British Endodontic Society also recommended the use of antibiotic/corticosteroid dressings (ACD) for the management of symptomatic irreversible pulpitis in the emergency setting (BES, 2020).

The earliest report of corticosteroids and antimicrobials in the management of the inflamed pulp included 200 teeth and reported that pain disappeared in 2–3 h, the majority maintaining pulp vitality (Schroeder & Triadan, 1962). Later, Baume and Fiore-Donno (1970) investigated topical ACD for the treatment of painful pulp inflammation in 180 patients, noting pain relief within hours, though the majority of pulps became necrotic in the longer-term (Baume & Fiore-Donno, 1970).

Despite their popularity, there is little evidence of benefit from placing medicated dressings in the management of symptomatic irreversible pulpitis. Hasselgren and Reit (1989) investigated the use of a number of intrapulpal dressing materials (camphorated phenol, cresatin and eugenol) and found no additional benefit above caries removal, excision of irreversibly inflamed tissue and dressing with sterile cotton wool moistened with saline (Hasselgren & Reit, 1989). Another study found effective pain relief in posterior teeth using eugenol placed into the pulp chamber following pulpotomy, but there was no

comparator group (Nyerere et al., 2006). No studies have explored the benefit of using ACDs in the management of symptomatic irreversible pulpitis including a comparator group and detailed pain outcome measures.

The use of ACDs for emergency pain relief has theoretical benefits in suppressing the 'inflammatory soup' and reducing the sensitization of peripheral nociceptors (Allison et al., 2020). This may include suppression of vasodilation, polymorphonuclear leukocyte migration and phagocytosis, and through blocking the cyclooxygenase and lipoxygenase pathways by inhibiting the formation of arachidonic acid. Tetracycline (a constituent of the proprietary product Ledermix®) may also have the potential to modify the host response by the inhibition of matrix metalloproteinases (MMPs) (Golub et al., 1998).

ACDs are commonly placed in contact with highly vascularized inflamed tissues, and have been reported to be frequently placed without the use of dental dam, both of which may promote systemic uptake (Edwards et al., 2021; Gemmell et al., 2020). It is also known that local and systemic effects are likely due to leaching of dressings through dentinal tubules (Abbott et al., 1988). This may theoretically contribute to the expression of antibiotic resistant genes both in the oral microbiome and within the root canal itself (Al-Ahmad et al., 2014; Almeida et al., 2020; Andersson & Hughes, 2014; Rôças & Siqueira, 2013). The systemic administration of antimicrobials for the management of symptomatic irreversible pulpitis is ineffective, and therefore their topical application must also be justified (Agnihotry et al., 2019).

The present study therefore aimed to investigate treatment outcomes in adult patients diagnosed with symptomatic irreversible pulpitis following a pulpotomy or pulpectomy with and without the application of an ACD in primary dental care.

MATERIALS AND METHODS

All patients attending for urgent dental care at an out-of-hours (OOH) clinic, a dental emergency clinic (DEC) and five primary care practices in the North East of England were invited to participate in the study between February 2021 and October 2021. Patients were provided with a participant information sheet (PIS) and a questionnaire to collect information on demographics, presenting pain and oral health-related quality of life impact (OHRQoL) (Appendix S1). Participants completed questionnaires pre-operatively, after which they entered the dental surgery and handed the questionnaire to the treating dentist or a researcher. The dentist/researcher then obtained consent for participation, assigned a unique identifier to the participant and recorded a diagnosis following examination. Patients diagnosed with symptomatic irreversible pulpitis and electing for a pulpotomy or pulpectomy (not extraction) were offered the opportunity to complete an electronic daily post-operative questionnaire for 7 days, detailing their pain and other symptoms. All participants received a £30 gift voucher after 7 days of completion. Responses were monitored daily by a researcher (DE or SR) and participants were sent a reminder email if they had not completed the questionnaire daily.

Inclusion criteria included age 16 years, capacity to consent, diagnosis of symptomatic irreversible pulpitis affecting 1 tooth, treatment by pulpotomy or pulpectomy with or without the use of an ACD. Additional data collected from participants included dental pulp sensibility, the clinical appearance of the exposed pulp, radiographic appearance of the tooth and any anaesthetic problems. The treatment provided was recorded and post-operative instructions provided (Appendix S2). Patients who did not align with a diagnosis of symptomatic irreversible pulpits by clinical signs and symptoms or direct visualization of the pulp were excluded from participation (AAE, 2013). This included: comprehensive history; response to EPT; response to cold testing; mechanical allodynia; periapical radiograph; appearance of pulp (bleeding).

This study is reported following STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines (STROBE, 2023).

Site recruitment/questionnaire design

Five primary care practices were recruited from the Northern Dental Practice Based Research Network following a research event held on 06 February 2020 (NDPBRN, 2022). Both DEC and OOH clinics were hosted by Newcastle Dental Hospital, Newcastle upon Tyne, UK. Primary care practitioners were involved in study and questionnaire design through several meetings held remotely (Zoom Video Communications, California, USA). Patients and members of the public were also involved in study design through several patient and public involvement and engagement (PPIE) events. These included interviews with patients diagnosed with symptomatic irreversible pulpitis attending DEC, the Newcastle Dental Hospital Patient and Public Involvement Group (Newcastle University, 2022) and VOICE Global (VOICE, 2023).

Questions involving demographics included age, salary, occupation and index of multiple deprivation (IMD). The participants' home address was used to calculate their IMD, a quantitative measure of deprivation in the UK,

using the 2019 English indices of deprivation tool (GOV.UK, 2019).

Questions in the initial questionnaire exploring the pain and impact of the patients' urgent dental condition on OHRQoL included the Oral Health Impact Profile 14 (OHIP-14) and interference domain from the modified Graded Chronic Pain Scale (GCPS) (Appendix S1). Within the modified GCPS, three questions explore pain, three questions explore the impact on normal daily activities and one question asks the number of days the disability has been experiences. For pain, a composite pain score was calculated based on an 11-point Likert scale for 'pain now', 'worst pain' and 'average pain' in the last 30-days. The post-operative questionnaire used a 15-point global ratings of change scale, an 11-point numerical rating scale (NRS), the use of medication, ability to return to work/normal activities and the need to return for more treatment due to pain (Appendix S3).

All dentists involved in data collection received face-to-face training in study design and to align to agreed diagnostic terms (AAE, 2013). Dentists were instructed not to alter their usual approach to treatment, providing either a pulpotomy or pulpectomy followed by the placement of either an ACD or non-setting calcium hydroxide (CH) or simply cotton wool.

Sample size and recruitment period

No previously published data exist which would enable a power calculation, and no pilot study was undertaken. Participants were recruited for a wider study exploring the impact of urgent dental conditions on quality of life ($n = 713$), of which participants in the present study represent a cohort of patients diagnosed with symptomatic irreversible pulpitis who received operative intervention in the form of a pulpotomy or pulpectomy (Edwards et al., 2023). Once the power calculation of the wider study was satisfied, the recruitment for the present study was stopped. Data were collected over an 8-month period between February and October 2021. Potential bias between groups were identified through presentation of pre-operative symptoms and clinical signs.

Analysis

A binary composite score was produced using five outcome measures collected in the post-operative questionnaire: Need to return for treatment due to pain; global ratings of change; pain relieving medication use; pain score and ability to return to work/normal activities (Table 1). This enabled an overall assessment of success vs failure for different treatment approaches. For several measures, day 3 was selected as a pragmatic timepoint that patients may expect to have a clinically important difference. This decision was supported through individual analyses undertaken at day 2 and day 4 for the five outcome measures (Table S1). The outcome measures chosen to construct a binary score are all considered important pain outcome measures to indicate treatment success (Doğramacı & Rossi-Fedele, 2023; Dworkin et al., 2005; Farrar et al., 2000). An improvement of 33% (or 2 points) in a 0–10 NRS may be considered the minimally clinically important difference (Farrar et al., 2000, 2001, 2003; Ogura et al., 2020; Stjernberg-Salmela et al., 2022). An increase of 2–3 points is considered a detectable change for a 15-point global ratings of change scale, whereas no change is considered for changes of 0–1 points (Masood et al., 2014). As a result, a change of +3 was chosen (somewhat better) for a successful outcome.

Where participants reported the need for further treatment due to insufficient pain relief, it was considered that outcomes were not valid after the secondary procedure, which could have been a different approach, including tooth extraction. It was therefore assumed that medication use, the ability to work and pain scores remained at pre-operative levels for the duration of the study following

TABLE 1 Composite score calculation for treatment success or failure.

Outcome measure	Criteria for treatment 'success'
Need to return for more treatment	Not returned for more treatment over the 7-day follow-up period
Global ratings of change	Score of +3 (somewhat better) or greater by day 3
Use of medication	Pain relieving medication not being used by day 3
Pain score	Improvement of ≥33% (or 2 points) by day 3
Ability to return to work[a]	Able to return by day 3

Note: Treatment success was considered where all criteria were met.

[a]Includes ability to return to 'normal activities' where participants did not work.

re-intervention. For global ratings of change, it was assumed that participants received a score of 0 ('No change'). Secondary analysis of data without these assumptions did not affect the results.

Four different treatment approaches were investigated: Pulpotomy with ACD; pulpotomy without ACD, pulpectomy with ACD; pulpectomy without ACD. Due to the size of these groups, inferential statistics were not calculated. Instead, pulpotomy and pulpectomy groups were combined, adjusting for the use of ACD using Mantel–Haenszel analysis for categorical variables. For continuous variables the adjustment was achieved by using a summary measure obtained as the weighted average of the difference between pulpotomy and pulpectomy with and without the use of an ACD. Operative approach using pulpotomy vs pulpectomy did not affect outcome when adjusted for the use of ACD, enabling the formation of two-groups: pulpectomy or pulpotomy with ACD; pulpectomy or pulpotomy without ACD. These groups were analysed using a mixed-effects model with post hoc Tukey's multiple comparisons test for continuous data and chi-squared test or Fisher's exact test for categorical variables.

RESULTS

In total, 83 participants were included in the analysis, with an overall response rate of 85.6% (Figure 1). Patient demographics are shown in Table 2, with pre-operative signs and symptoms and intra-operative details shown in Table 3.

All dentists that used an ACD reported using Ledermix® (Haupt Pharma GmbH, Wolfratshausen, Germany). Where no ACD was used, the majority (23/32; 71.9%) used non-setting CH, with 9/32 (28.1%) overlaid with dry or damp cotton wool, with no significant difference between pulpotomy and pulpectomy groups ($p = .400$). Some dentists reported problems achieving anaesthesia and required supplemental techniques (17/83; 20.5%), with no significant difference between the two groups ($p = .419$).

Overall success measured as a composite score (Table 1) was 43/76 (56.6%), with seven participants excluded due to missing data in at least one of the five outcome measures. There was no significant difference between the two groups ($p = .645$) (Table 4). In the present study, 21/83 (25.3%) of participants reported returning for further treatment due to insufficient pain relief, with no significant difference between the two groups ($p = .960$) (Table 4).

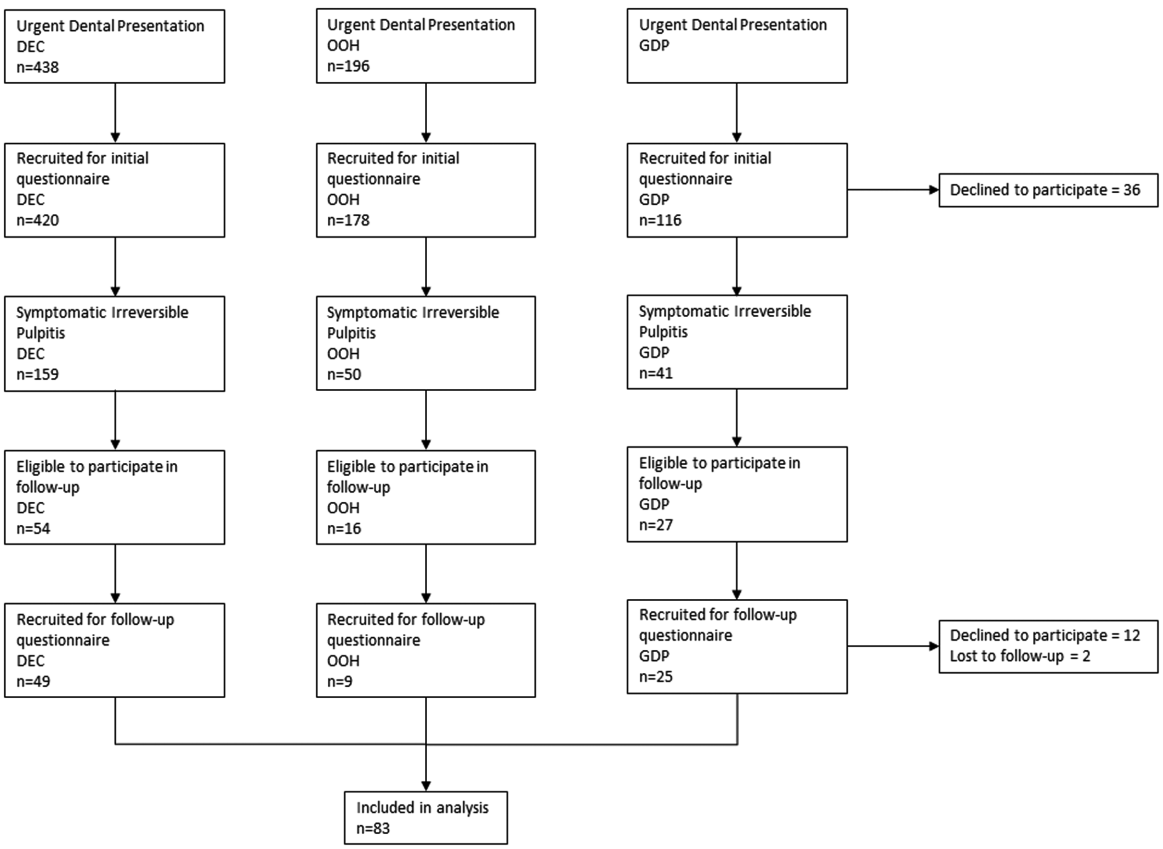

FIGURE 1 Flow diagram showing participant recruitment. DEC, dental emergency clinic; GDP, general dental practice; OOH, out of hours clinic. The number of participants presenting with an urgent dental condition could not be calculated for primary care.

TABLE 2 Participant demographics.

	No ACD ($n=32$)	ACD ($n=51$)	All patients ($n=83$)
Age – mean (SD)	36.1 (12.9)	33.5 (11.5)	34.5 (12.0)
Gender – *n* (%)			
Female	17 (53.1)	26 (51.0)	43 (51.8)
Male	14 (43.8)	24 (47.1)	38 (45.8)
Missing data	1 (3.1)	1 (2.0)	2 (2.4%)
IMD – *n* (%)			
1	6 (18.8)	15 (29.4)	21 (25.3)
2	8 (25.0)	14 (27.5)	22 (26.5)
3	6 (18.8)	6 (11.8)	12 (14.5)
4	4 (12.5)	8 (15.7)	12 (14.5)
5	2 (6.3)	4 (7.8)	6 (7.2)
Missing data	6 (18.8)	4 (7.8)	10 (12.0)
Employment status – *n* (%)			
Employed	26 (81.3)	30 (58.8)	56 (67.5)
Self-employed	3 (9.4)	9 (17.6)	12 (14.5)
Retired	1 (3.1)	2 (3.9)	3 (3.6)
Unemployed	1 (3.1)	10 (19.6)	11 (13.3)
Missing data	1 (3.1)	0 (0.0)	1 (1.2)

Note: Divided into quintiles, with 5 representing the lowest social deprivation.

Abbreviations: ACD, antibiotic/corticosteroid dressing; IMD, index of multiple deprivation.

Post-operative mean pain scores all reduced following treatment, with the greatest improvement seen the day following treatment (Figure 2). There was no significant difference between the two groups ($p=.515$) through mixed effects modelling. The use of an ACD appeared to offer more self-reported improvement through global ratings of change assessment, with the association found to be significant through mixed effects modelling ($p=.015$). The use of pain-relieving medication or the ability to work did not significantly differ between treatment approaches (Table 4).

DISCUSSION

This pragmatic prospective cohort study is the first to investigate the pain relieving benefits of placing ACDs following an emergency pulpotomy, which is the most common approach to managing symptomatic irreversible pulpitis in the UK, and popular worldwide. ACDs appear to offer little benefit over the simple excision of irreversibly inflamed tissue and placement of either cotton wool or non-setting CH. Although patients receiving an ACD reported feeling better than those receiving no dressing when assessed by global ratings of change—pain scores, medication use, the ability to work and success measured as a binary outcome did not differ between groups. Irrespective of the placement of an ACD, more than 25% of participants returned for further treatment because they were still in pain, suggesting that overall, the management of this common and impactful condition in primary care may be less effective than previously reported by studies in secondary care environments.

Demographics

Of the eligible participants for this study, 85/97 (87.6%) agreed to participate, with 2/85 (2.4%) lost to follow up (Figure 1). Participants were representative of residents in the North East of England in terms of gender, age, IMD and employment status (GOV.UK, 2019; NCC, 2021). The majority (86.8%) of procedures in all groups were undertaken on posterior teeth. Pre-operative OHIP scores, medication use and time away from work were similar in all groups. When arranged as two groups (ACD v no ACD), NRS scores were almost identical pre-operatively. In terms of time to presentation, it is notable that the pulpectomy with ACD group had symptoms for a mean of 14.8 days before presenting for treatment, compared to a mean of 10.8 for all participants (Table 3). All pulps exposed in the study were bleeding, with the majority (81.9%) considered hyperaemic across all groups. The main cause of symptomatic irreversible pulpitis was caries (63.9%), followed by a historic deep restoration (20.5%), which did not differ significantly across groups. Rubber dam use was reported by 57.8% of dentists, which was similar across groups. Periapical radiolucencies were also identified with similar frequency in all groups (41.0%). The main irrigant used for disinfection and haemorrhage control was chlorhexidine 0.2%, which was the case in both groups. Finally, 20.5% of cases were difficult to anaesthetize, a more common finding in the 'without ACD' group than the ACD group (31.3% vs. 13.7%) (Table 3). Other pre-operative data appeared to be similar across all groups (Table 2).

Current emergency approaches to managing symptomatic irreversible pulpitis are not effective for all patients

Mean pain scores and medication use reduced following treatment, with global ratings of change scores suggesting significant improvement and most patients being able to return to work within 7-days. However, a binary measure of success (Table 1) suggests treatment was only successful in 56.6% of participants, and over

TABLE 3 Pre-operative impact on oral health-related quality of life, pain score and related pain measures and signs/symptoms.

	No ACD ($n=32$)	ACD ($n=51$)	All patients ($n=83$)
Tooth – *n* (%)			
Incisor/canine	4 (12.9)	6 (11.8)	10 (12.0)
Premolar	11 (34.4)	8 (15.7)	19 (22.9)
Molar	16 (50.0)	37 (72.5)	53 (63.9)
Missing data	1 (3.1)	0 (0.0)	1 (1.2)
OHIP-14 score – mean (SD)	26.4 (10.6)	26.9 (11.2)	26.7 (10.9)
NRS pain score – mean (SD)	6.4 (2.3)	6.6 (2.7)	6.5 (2.5)
Medication use – *n* (%)			
Yes	32 (100.0)	45 (88.2)	77 (92.8)
No	0 (0.0)	4 (7.8)	4 (4.8)
Missing data	0 (0.0)	2 (3.9)	2 (2.4)
Days away from work[a] – mean (SD)	1.5 (3.9)	0.9 (1.9)	1.1 (2.8)
Days of symptoms – mean (SD)	7.7 (7.8)	12.8 (13.4)	10.8 (11.8)
Appearance of pulp – *n* (%)			
Normal bleeding	9 (28.1)	6 (11.8)	15 (18.1)
Hyperaemic	23 (71.9)	45 (88.2)	68 (81.9)
Haemorrhage control			
Chlorhexidine (0.2%)	9 (28.1)	22 (43.1)	31 (37.3)
Sodium hypochlorite (2%)	7 (21.9)	10 (19.6)	17 (20.5)
Missing data	16 (50.0)	19 (37.3)	35 (42.2)
Periapical appearance – *n* (%)			
Normal	20 (62.5)	24 (47.1)	44 (53.0)
Radiolucency	11 (34.4)	23 (45.1)	34 (41.0)
Missing data	1 (3.1)	4 (7.8)	5 (6.0)
Problems achieving anaesthesia – *n* (%)			
Yes	8 (25.0)	9 (17.6)	17 (20.5)
No	23 (71.9)	42 (82.4)	65 (78.3)
Missing data	1 (3.1)	0 (0)	1 (1.2)
Use of rubber dam – *n* (%)			
Yes	22 (68.8)	26 (51.0)	48 (57.8)
No	10 (31.3)	25 (49.0)	35 (42.2)
Primary aetiology – *n* (%)			
Caries	22 (68.8)	31 (60.8)	53 (63.9)
Recent deep restoration (<3 months)	3 (9.3)	5 (9.8)	8 (9.6)
Historic deep restoration (≥3 months)	5 (15.6)	12 (23.5)	17 (20.5)
Recent trauma (<3 months)	0 (0.0)	2 (3.9)	2 (2.4)
Historic trauma (≥3 months)	1 (3.1)	0 (0.0)	1 (1.2)
Other	1 (3.1)	1 (2.0)	2 (2.4)

Abbreviations: ACD, antibiotic/corticosteroid dressing; NRS, numerical rating scale; OHIP-14, oral health impact profile 14.

[a]Includes days away from normal daily activities for participants who do not work.

one-quarter of participants had to return for more treatment because they were in pain, irrespective of ACD use. This contrasts with other studies investigating the emergency management of symptomatic irreversible through pulpotomy. In the study of Eren et al. (2018), 66 patients received a pulpectomy or pulpotomy procedure without the use of ACDs and found that no patients returned for further treatment within 7 days (Eren

TABLE 4 Treatment success, need to return for further treatment due to pain, the ability to return to work and the use of medication arranged as four or two groups.

	Pulpotomy + no ACD, *n* (%)	Pulpotomy + ACD, *n* (%)	Pulpectomy + no ACD, *n* (%)	Pulpectomy + ACD, *n* (%)	No ACD, *n* (%)	ACD, *n* (%)	All patients (%)
Treatment success	6/13 (46.2)	8/13 (61.5)	10/17 (58.8)	19/33 (57.6)	14/30 (53.3)	27/46 (58.7)	56.6
Return for treatment	4/14 (28.6)	4/14 (28.6)	4/18 (22.2)	9/37 (24.3)	8/32 (25.0)	13/51 (25.5)	25.3
Unable to work[a]							
Pre-op	9/13 (69.2)	8/14 (57.1)	9/17 (52.9)	26/36 (72.2)	18/30 (60.0)	34/50 (68.0)	65.0
Day 1	4/13 (30.8)	2/10 (20.0)	4/17 (23.5)	5/31 (16.1)	8/30 (26.7)	7/41 (17.1)	21.1
Day 2	3/13 (23.1)	2/12 (16.7)	2/16 (12.5)	5/32 (15.6)	5/29 (17.2)	7/44 (15.9)	16.4
Day 3	3/13 (23.1)	2/13 (15.4)	1/16 (6.3)	5/33 (15.2)	4/29 (13.8)	7/46 (15.2)	14.7
Day 4	5/13 (38.5)	3/13 (23.1)	2/17 (11.8)	7/31 (22.6)	7/30 (23.3)	10/44 (22.7)	23.0
Day 5	4/13 (30.8)	4/14 (28.6)	3/16 (18.8)	7/32 (21.9)	7/29 (24.1)	11/46 (23.9)	24.0
Day 6	4/12 (33.3)	2/13 (15.4)	3/17 (17.6)	6/32 (18.8)	7/29 (24.1)	8/45 (17.8)	20.3
Day 7	4/11 (36.4)	2/14 (14.3)	3/17 (17.6)	6/32 (18.8)	7/28 (25.0)	8/46 (17.4)	20.3
Use of pain-relieving medication							
Pre-op	13/14 (92.9)	13/14 (92.9)	18/18 (100)	33/36 (91.7)	31/32 (96.9)	46/50 (92.0)	93.9
Day 1	7/13 (53.8)	6/10 (60.0)	10/17 (58.8)	17/31 (54.8)	17/30 (56.1)	23/41 (56.1)	56.3
Day 2	6/13 (46.2)	8/12 (66.7)	8/16 (50.0)	14/32 (43.8)	14/29 (48.3)	22/44 (50.0)	49.3
Day 3	5/13 (38.5)	5/13 (38.5)	6/16 (37.5)	12/33 (36.4)	11/29 (37.9)	17/46 (37.0)	37.3
Day 4	6/13 (46.2)	5/13 (38.5)	2/17 (11.8)	13/31 (41.9)	8/30 (26.7)	18/44 (40.9)	35.1
Day 5	6/13 (46.2)	3/14 (21.4)	4/16 (25.0)	12/32 (37.5)	10/29 (34.5)	15/46 (32.6)	33.3
Day 6	6/12 (50.0)	3/13 (23.1)	3/17 (17.6)	11/32 (34.4)	9/29 (31.0)	14/45 (31.1)	31.1
Day 7	5/11 (45.5)	2/14 (14.3)	3/17 (17.6)	9/32 (28.1)	8/28 (28.6)	11/46 (23.9)	25.7

Note: No results were significant at the $p = .05$ level when analysed as four or two groups using chi-squared test or Fishers Exact test. Data were tested for normality using histogram and Shapiro–Wilk test.

Abbreviation: ACD, antibiotic/corticosteroid dressing.

[a]For participants who were unemployed/retired, the ability to perform normal daily activities is reported.

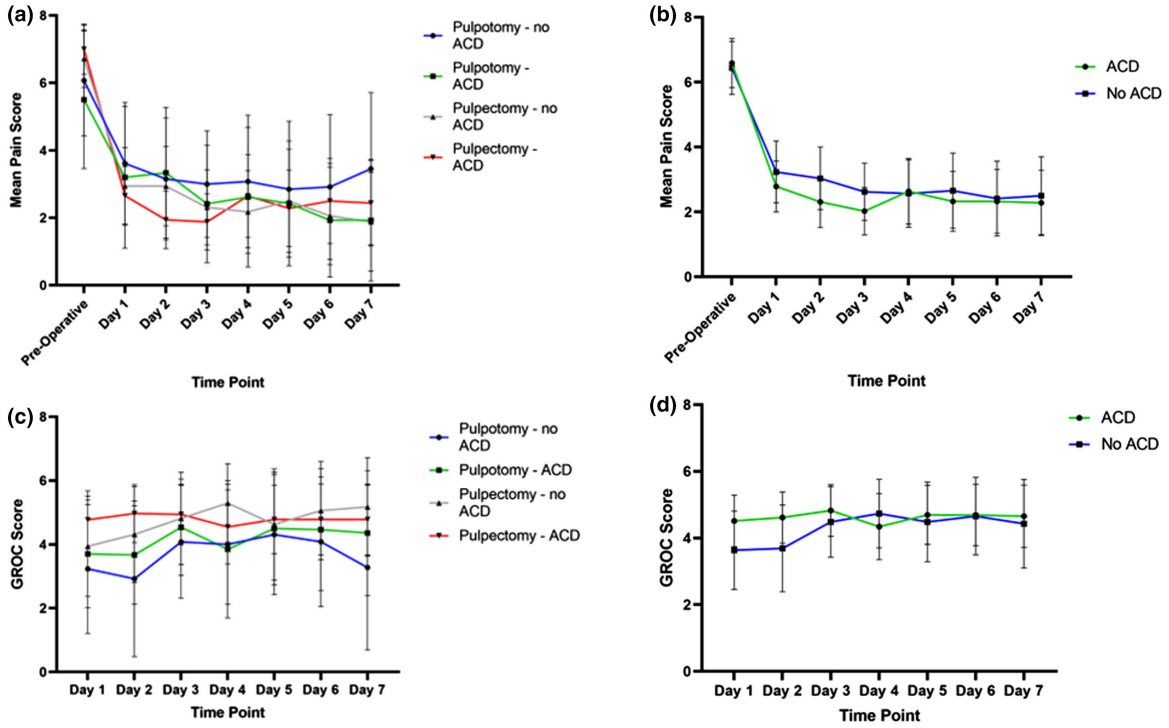

FIGURE 2 Pre-operative and post-operative daily mean pain scores (a, b) and post-operative daily mean global ratings of change scores (c, d) organized as two or four groups, with 95% confidence intervals. ABC, antibiotic/corticosteroid dressing; GROC, global ratings of change.

et al., 2018). However, it is worth noting that similar to the present study, Eren 2018 found that despite reductions in mean pain score and medication use, some patients reported an increase in pain score at day 3 and day 7 following treatment, so not all procedures can be considered successful (Eren et al., 2018). Similarly, Hasselgren and Reit (1989) reported 100% pain relief 1-day following an emergency pulpotomy, although three participants (4%) were excluded from the analysis who returned for more treatment because they were still in pain (Hasselgren & Reit, 1989). Oguntebi et al. (1992) undertook a pulpotomy or pulpectomy in patients with symptomatic irreversible pulpitis and found that 8%–13% returned within 24 h because they were still in pain, although no further follow up was undertaken (Oguntebi et al., 1992). The studies of Hasselgren and Reit (1989), Oguntebi et al. (1992) and Eren et al. (2018) were all undertaken in a controlled secondary care environment, in contrast to the present study which was conducted in primary care settings. The increased incidence of patients returning for more treatment in the present study may offer more translatable outcomes from current approaches due to its pragmatic design in a primary care setting. Furthermore, the present study considered more outcome measures with more frequent follow up.

Taken in isolation, individual outcome measures in the present study did not show a significant benefit of ACDs. However, they offer further insight to the impact that symptomatic irreversible pulpitis can have on our patients. The present study represents a cohort of participants from a wider study investigating the impact of urgent dental conditions on patients (Edwards et al., 2023). This highlighted that symptomatic irreversible pulpitis is one of the most painful and impactful urgent dental conditions. This included medication use (92.3%) and inability to work (38.8), which remained high in the present study, even 5-day post-operatively (33.3% and 24.0% respectively). This, in addition to the need for further treatment increases the financial burden of urgent dental conditions on both the individual and society where care is accessed through state funded healthcare systems (Edwards et al., 2023). Other studies have also highlighted the challenges of attending dental appointments due to work commitments (Currie, 2022; Harris et al., 2017; van der Zande et al., 2021).

Antibiotic/corticosteroid dressings appear to offer minimal benefit in the management of symptomatic irreversible pulpitis

Early studies exploring ACDs presented limited clinical outcome data, often with no comparator groups (Baume & Fiore-Donno, 1970; Lawson & Mitchell, 1964;

Schroeder & Triadan, 1962). In the present study, most pain outcome measures were unaffected by the use of ACDs compared to simple excision of inflamed pulp with or without the application of non-setting CH. There was little difference in overall success, with the number needed to treat (NNT) being 19 to avoid an unsuccessful outcome. Considering individual outcome measures, there were no significant differences in the ability to return to work/normal activities, medication use, NRS pain score and the need to return for more treatment. The exception was global ratings of change for which the patients reported feeling better in the first 2 days following treatment where they received ACDs compared to simple pulp excision and non-medicated wound dressing.

If ACDs confer limited benefit in their current formulation, their use in the management of symptomatic irreversible pulpitis should be reviewed. In the present study, dentists reported using Ledermix® which contains 1% triamcinolone acetonide, a mid-strength corticosteroid (but at a relatively high concentration) and 3% demeclocycline calcium. Antibiotic and corticosteroid components have the potential for local and systemic involvement as unintended consequences of their use, as they are able to exit the tooth into the periapical tissues (Abbott et al., 1988, 1989). Recently, almost three quarters of patients were found to have antibiotic resistant genes expressed in the oral microbiome (Almeida et al., 2020), which have also been isolated from root canals following symptomatic irreversible pulpitis (Al-Ahmad et al., 2014; Rôças & Siqueira, 2013). Even subtherapeutic doses of antibiotics may impact microbial evolution, acting as cell signalling molecules which induce host or microbial gene expression (Andersson & Hughes, 2014). Further evidence of systemic involvement of topically applied ACDs comes from reports of a Type 1 allergic reaction to the antibiotic component following their placement (Kaufman et al., 2014). In addition, non-metabolized tetracyclines are released into the environment during dressing placement, removal and excretion (Halling-Sørensen, 2000; Jjemba, 2006), potentially contributing to global antibiotic resistance and ecological damage (Baquero et al., 2008; Batt et al., 2006; Daghrir & Drogui, 2013; Jeong et al., 2010; Kemper et al., 2008; Liu et al., 2009; Rivera-Utrilla et al., 2013; Sarmah et al., 2006).

The problem of antibiotic resistance is increasingly a global concern. The world health organization considers it to be one of the biggest threats to global health (WHO, 2022) and several antibiotic stewardship campaigns are currently ongoing, aimed at reducing antibiotic usage (Palmer, 2020; Segura-Egea et al., 2018). Although the focus is commonly on systemic administration, the frequency of local application of antibiotics in dentistry demands consideration.

Drug delivery or central pain mechanisms may explain why pain relief does not occur for all patients with symptomatic irreversible pulpitis

It may be expected that corticosteroids may reduce pain through general suppression of the 'inflammatory soup', reducing the sensitization of peripheral nociceptors. Their local effects may include suppression of vasodilation, polymorphonuclear leukocyte migration and phagocytosis and by blocking cyclo-oxygenase and lipoxygenase pathways by inhibiting the formation of arachidonic acid. Furthermore, tetracyclines are potent inhibitors of matrix metalloproteinases (Golub et al., 1998), although they may actually increase pain when applied directly to the pulp (Baume & Fiore-Donno, 1970).

The findings of the present study are therefore surprising. Given that a quarter of participants returned for further pain-relieving treatment and that just over half of procedures may be considered successful, it is possible that pain and inflammatory mechanisms in symptomatic pulpitis are more complex than classically interpreted. Topical corticosteroids may have limited effect on peripheral and central sensitization. At the peripheral level, nerve sprouting, the presence of inflammatory mediators and phenotypic changes (e.g. upregulation of sodium channels) result in both reduced threshold and spontaneous depolarization of neurons (Byers, 1990; Byers et al., 1992; Kimberly & Byers, 1988; Luo et al., 2008; Zhang et al., 2008). Although these changes are initially driven by inflammation, it is possible that antibiotic/corticosteroid medications will not have a significant impact on these mechanisms once established, particularly in the 'late' presentation of pulpitis managed in urgent dental care settings.

The trigeminal ganglion (TG) further contributes to peripheral sensitization through the release of inflammatory cytokines and chemokines such as IL-1β, IL 6 and TNFα by satellite cells, which become 'activated' in the pulpitic tooth (Dubový et al., 2010; Li et al., 2015; Lin et al., 2015; Liu et al., 2018; Zhang et al., 2007). In addition, N-methyl-D-aspartate (NMDA) receptors are upregulated, and neuropeptides are released, further reducing the threshold for neuronal depolarization (Benoliel et al., 2001; Chudler & Byers, 2005; Lee & Ro, 2007). More centrally, similar mechanisms have been identified in the trigeminal nucleus (located in the brainstem), with the activation of astroglia and microglia thought to play a key role in the maintenance of neuropathic pain and the transition to persistent pain (Lee et al., 2017; Mika et al., 2009; Raghavendra et al., 2004;

Romero-Sandoval et al., 2008; Tsuboi et al., 2011). It is unlikely that topically applied ACDs will have any significant impact on pain mechanisms at the level of the TG or the brainstem and this may explain why some patients continue to experience significant pain despite operative intervention. This was highlighted by the study of Nixdorf et al. (2016) who found that up to 10% of patients continue to feel pain beyond 6-months following endodontic intervention (Nixdorf et al., 2016).

Histologically, the direct application of corticosteroids to inflamed pulp tissue is associated with a reduction in the number of inflammatory cells (Barker & Lockett, 1972; Baume & Fiore-Donno, 1970; Bloch & Austin, 1976; de Freitas Oliveira et al., 2009; Schroeder & Triadan, 1962). This appears not to have translated into clinical outcomes in the present study, and therefore, another possible reason for the lack of difference between groups is that the antibiotic/corticosteroid preparation in its present formulation does not affect the disease process for a sustained period. Similar to the study of Eren et al. (2018), some of the current patients reported initial pain relief followed by an increase in pain over a 7-day period (Eren et al., 2018). It is therefore possible that both the corticosteroid and antibiotic components of topical dressings fall below their therapeutic range relatively quickly.

It has been known for some time that the antibiotic component of Ledermix® is likely to fall below is minimum inhibitory concentration (MIC) within 24 h following application, and due to a diffusion gradient may never reach MIC in apical and periapical parts of the root canal system (Abbott et al., 1988, 1989; Heling & Pecht, 1991). Similarly, the corticosteroid component rapidly drops within the first 24 h, and is considered to drop below therapeutic levels within 6 weeks (Abbott et al., 1989). Interestingly, these studies measured release through dentine tubules into a surrounding solution and found a more rapid loss in younger teeth. Importantly, this in vitro model does not account for the hyperaemic pulp and it is therefore likely that therapeutic levels within the tooth will drop much more rapidly for both the antibiotic and corticosteroid components.

Limitations and future directions

Although the present exploratory study presents 'real-world' outcomes of current management strategies for symptomatic irreversible pulpitis in primary care dentistry, no formal power calculation was possible and therefore the results must be interpreted with caution. Given the findings of the present study, and the limited histological and clinical data currently available surrounding a common treatment modality for an impactful and common dental emergency, further research is needed. With the global drive to reduce antibiotic use, a non-inferiority trial may be appropriate to demonstrate a significant clinical advantage of using such medications. Given the wide confidence intervals and similar post-operative pain measures of the present data (Table S1), a large sample size may be needed for any future clinical studies. Furthermore, studies to investigate inflammatory and pain mechanisms in symptomatic irreversible pulpitis are needed to understand the apparent lack of clinical benefit of local ACDs.

Although this study had a good response rate with low rate of attrition, data were incomplete at all time points for some participants. This meant multiple imputation would have been required to enable repeated measures ANOVA, and it was decided that a mixed-effects model would be more appropriate. All efforts were made to monitor responses and contact participants for reminders, but a more extensive discussion about the aims of the study with the principal investigator (DE) rather than the treating dentist may have improved the follow up, especially given the limitations of the emergency dental appointment.

All participants in the antibiotic/corticosteroid group received a Ledermix® dressing, whereas the comparator group received either no dressing (28%) or non-setting CH (72%). A sub-analysis comparing pain outcomes from these groups showed a statistically significant relationship between time and group, suggesting better initial pain relief without CH, and a benefit in CH demonstrated after several days (Figure S1). Future research could further explore these findings, as well as limit the comparator group to a single treatment approach.

As an observational study, dentists' approach to managing symptomatic irreversible pulpitis was not allocated to a specific treatment approach. This may have introduced bias through the selection of one approach over another depending on the patient's symptoms or appearance of the pulp. One such example would be performing a pulpotomy instead of pulpectomy due to inadequate anaesthesia. There was no significant difference between anaesthetic failure rates between the two groups, and other pre- and peri-operative parameters reported in the present study were similar across the groups.

The criteria for success (Table 1) encompassed five post-operative measures, which could be considered a high threshold. A sensitivity analysis encompassing only three post-operative measures (NRS pain, global ratings of change and the need to return to treatment) did not significantly improve overall outcome, with no significant difference between groups (Table S2).

Finally, COVID-19 presented significant challenges to the study. Data collection was deferred due to the closure of primary care practices, and once care resumed, several limitations were in place which may have altered dental practitioners' usual approach to treatment (Thompson et al., 2022).

Ultimately, the power calculation for the wider study investigating the impact of urgent dental conditions on patients was achieved through an extended period of recruitment. It is possible that more patients elected for extraction during this period which ultimately will have reduced the number of endodontic interventions for symptomatic irreversible pulpitis, impacting recruitment for the present study.

CONCLUSION

This study identified limited evidence of improved outcomes using antibiotic/corticosteroid dressings in the management of symptomatic irreversible pulpitis in the emergency setting. Further clinical research is needed to understand if these medications are beneficial in affording pain relief, above that of simple excision of irreversibly inflamed pulp tissue.

AUTHOR CONTRIBUTIONS

David Edwards: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Validation, Writing—Original Draft Preparation, Writing—Review and Editing. Sabrina Rasaiah: Data Curation, Formal Analysis, Investigation, Methodology, Writing—Original Draft Preparation. Lise-Lotte Kirkevang: Formal Analysis, Supervision, Validation, Visualization, Writing—Original Draft Preparation, Writing—Review and Editing. Michael Vaeth: Formal Analysis, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing—Review and Editing. Simon J Stone: Conceptualization, Funding Acquisition, Methodology, Supervision, Writing – Original Draft Preparation, Writing—Review and Editing. Ilona Obara: Supervision, Visualization, Writing—Review and Editing. Justin Durham: Conceptualization, Funding Acquisition, Methodology, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing—Review and Editing. John Whitworth: Conceptualization, Funding Acquisition, Methodology, Supervision, Visualization, Writing—Original Draft Preparation, Writing—Review and Editing. Have made substantial contributions to conception and design, or acquisition of data or analysis and interpretation of data. Been involved in drafting the manuscript or revising it critically for important intellectual content. Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL STATEMENT

A favourable ethical review was confirmed by the Sheffield Research Ethics Committee, UK (IRAS ID: 283867; REC reference: 20/YH/0282).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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