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66 Years of Corticosteroids in Dentistry: And We Are Still at a Cross Road?

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Abstract

Most of the corticosteroids prescribed in dentistry are for topical applications or short-term usage, rarely for its systemic effects or for long-term consumption, as in the treatment of some medical conditions. Among the various specialties in dentistry, oral and maxillofacial surgery, oral medicine and endodontics are the more frequent users of corticosteroids. Corticosteroids are used in oral and maxillofacial procedures to reduce associated post-operative inflammation. The most researched outcome on the use of corticosteroids in oral and maxillofacial surgery revolves around their impact to reduce post-operative pain, swelling and trismus. Topical corticosteroids, on the other hand, are effective in treating various oral mucosal lesions including oral ulcerations and oral presentations of auto-immune diseases. Corticosteroids are also used as part of the treatment of temporomandibular joint disorders. Intracanal placement of corticosteroids is used in endodontic treatment. This chapter reviews the use of corticosteroids in the three specialties of dentistry as mentioned.

Keywords: corticosteroids, dentistry, oral and maxillofacial surgery, oral medicine, endodontology

1. Introduction

Corticosteroids is one well-known anti-inflammatory group of drugs that is listed in the Dental Practitioners' Formulary. Among the various specialties in dentistry, oral medicine, oral and maxillofacial surgery and endodontics are the more frequent users of corticosteroids. Most of the corticosteroids prescribed in dentistry are for topical applications or short-term usage, rarely for its systemic effects or for long-term consumption, as in the treatment of some medical conditions. Five years ago, a chapter entitled "The role of Corticosteroids in today's Oral and

Maxillofacial Surgery” [1] has been published in the book “Glucocorticoids—New Recognition of Our Familiar Friend”. The objective of this chapter is therefore to complement the previous publication as well as providing an update on the use of corticosteroids in dentistry, instead of merely oral and maxillofacial surgery.

Although corticosteroids were already used in the field of medicine since 1944, it was not until 1951 that they were introduced to dentistry. Then, Strean published a paper which represented the first scientific approach to the general use of corticosteroids in dentistry [2]. Strean and Horton [3] and Spies et al. [4] were the first to use (hydro)cortisone for the treatment of oral diseases related to local causes and oral manifestations of inflammatory systemic disease. Back then, corticosteroids were prescribed as topical medicament as well as systemic medication, depending on the oral manifestations of systemic diseases. Topical corticosteroids have proven to be effective in treating various oral mucosal lesions including oral ulcerations and oral presentations of auto-immune diseases. In oral medicine, injection of corticosteroids is part of the treatment of temporomandibular joint degeneration.

Corticosteroids are used in oral and maxillofacial surgical procedures to reduce associated post-operative inflammation. The suggestion of their use for managing post-operative sequelae of dentoalveolar surgery began as an editorial by Kenny in 1954 [5]. Following this, Ross and White performed a clinical trial comparing oral hydrocortisone against placebo in a double-blind study involving third molar surgeries that confirmed the former’s efficacy [6]. The most researched outcome on the use of corticosteroids in oral surgery revolves around their effect in reducing post-operative pain, swelling and trismus. Over the last 6 decades, the use of corticosteroids for third molar surgery had been studied extensively in different formulations, dosings, routes and sites of administration [7]. These corticosteroids include dexamethasone (per-oral/p.o.), dexamethasone acetate (intramuscular), dexamethasone sodium phosphate (intravenous and intramuscular), methylprednisolone (p.o.), methylprednisolone acetate and methylprednisolone sodium succinate (both intravenous and intramuscular) [8]. In recent years, a twin-mix combination of 2% lignocaine with 1:200,000 adrenaline and 4 mg dexamethasone was even given as an inferior alveolar nerve block [9]. A recent review concluded that there are benefits that can be derived from the short-term use of corticosteroids in reducing these inflammatory sequelae, with no side effects observed when given using the methods listed above [7]. However, the use of corticosteroids for periodontal and implant surgeries has not been investigated. The other use of corticosteroids in oral surgery is as medication for various cranial nerve disorders and application/injections for the treatment of facial scars [10]. It is a standard medication for Bell’s palsy [11], with prednisolone coupled with acyclovir being the most popular choice. The recommended dose is prednisolone 60–80 mg daily during first 5 days with dose tapering over next 5 days [12]. It is a drug within a cocktail with NSAIDs given to patients suffering from traumatic trigeminal nerve injuries [13]. One study even reported their beneficial effect on lingual and inferior alveolar nerve hypersensitivity following third molar surgery [14]. More controversial use of corticosteroids is related to their administration to patients with maxillofacial space infection. Low et al. recently reported that corticosteroids are useful as adjunct treatment for such cases [15]. Their patients experienced significant clinical improvement with reduction of pain, swelling and trismus, and shortening hospital stay to an average of 3.5 days, in addition to omission of surgical intervention in 50% of cases.

Lastly, corticosteroids are used as exposed pulp lining and intracanal medicament in endodontic therapy. This chapter reviews the use of corticosteroids in the three specialties of dentistry as mentioned. It shall answer the routinely asked impression: are dental surgeons and dental specialists still at a cross road in deciding whether corticosteroids should be routinely used in clinical dentistry?

2. Corticosteroids in oral and maxillofacial surgery

Corticosteroids are used mainly by oral and maxillofacial surgeons to reduce the post-operative sequelae (pain, swelling and trismus) of dentoalveolar surgery, orthognathic surgery, facial fractures and reconstructive surgery [16, 17]. Post-operative nausea and vomiting have been reported to be less in patients who were given corticosteroids when these surgeries were done under general anaesthesia [18]. In addition, corticosteroids have been proven to improve interpalpebral width as well as reducing post-operative pain after surgical repair of orbital blowout fractures [19, 20]. Local steroid injection of the tongue base had proven to reduce the incidence and severity of post-palatoplasty upper airway obstruction in children undergoing cleft palate surgery [21]. A questionnaire survey in North America reported that close to half of oral and maxillofacial surgeons stated that they use short-term, high-dose perioperative corticosteroids to control post-operative oedema [22]. Only 20% of oral and maxillofacial surgeons claimed that they never use it for dentoalveolar surgery [23]. In comparison, corticosteroids are less preferred for dentoalveolar surgeries by surgeons in at least one European country [16]. Their popularity for dentoalveolar surgeries elsewhere has not been established.

The group of corticosteroids of interest is the glucocorticoids (dexamethasone and betamethasone, and prednisolone and methylprednisolone), because of their anti-inflammatory activities with little or no effect on fluid and electrolyte balance [7]. Their effect has been well studied using the third molar surgery model over the past 6 decades (**Table 1**). In a study that reviewed the reported outcome of corticosteroids over the last 10 years (2006–2015), Ngeow and Lim [7] reviewed 34 studies that administered corticosteroids via different routes which included intravenous, intramuscular (masseter, deltoid or gluteus), submucosal, endoalveolar and oral administrations. They found that benefits could be derived from the short-term use of corticosteroids with regards to pain, swelling and trismus control following third molar surgery, with no side effects observed. However, there were two limitations to their study, namely restriction to studies performed only throughout the last decade, and exclusion of studies that compared corticosteroids with other drugs, intervention or treatment, except when the corticosteroid was administered with an adjuvant therapy related to third molar surgery, namely an antibiotic.

Some 10 years ago, a systematic review and meta-analysis by Markiewicz et al. [24] reported that perioperative administration of corticosteroids produced a mild to moderate reduction in swelling and improvement of trismus after third molar surgery. More recently, another three meta-analyses specifically reported on the effect of dexamethasone in third molar surgery. Two reviewed the effect of submucosal injection of dexamethasone [25, 26], while the third reviewed the preemptive effect of dexamethasone [27]. The findings of two meta-analyses on submucosal injection are different. Chen et al. reported that submucosal injection of dexamethasone

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
Ross and White (1958) [6]	Hydrocortisone 40 mg (multiple doses)	Reduced	No difference	Reduced	—
Ware et al. (1963) [51]	Dexamethasone 9 mg or 13.5 mg (multiple doses)	No difference	—	No difference	—
Lineberg (1965) [29]	Dexamethasone 9 mg (multiple doses)	Reduced	—	Reduced	—
Nathanson and Seifert (1964) [52]	Betamethasone 0.6 mg; multiple tablets (multiple doses)	Reduced	Reduced	Reduced	Reduced ecchymosis
Hooley and Francis (1969) [53]	Betamethasone 1.2 g (multiple doses)	Reduced	Reduced	Reduced	Increased dry socket (4%)
Messer and Keller (1975) [54]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—
Caci and Gluck (1976) [55]	Prednisolone 5 mg (multiple doses)	No difference	Reduced	Reduced	Comparison against papase; reduced ecchymosis
Huffman (1977) [56]	Methylprednisolone sodium succinate 40 mg or 125 mg (single dose)	Reduced	—	—	—
Edilby et al. (1982) [57]	Dexamethasone 4 mg and 8 mg (Two doses)	No difference	No difference	No difference	—
Skjelbred and Løkken (1982) [58]	Betamethasone 9 mg (single dose)	Reduced	Reduced	Reduced	Given preoperative
Skjelbred and Løkken (1982) [59]	Betamethasone 9 mg (single dose)	Reduced	Reduced	—	Give post-operative
Skjelbred and Løkken (1983) [60]	Methylprednisolone succinate 40 mg (single dose)	Reduced	—	—	—
Bystedt and Nordenram (1985) [61]	Methylprednisolone 12 mg followed by 4 mg (multiple doses)	No difference	No difference	No difference	—
ElHaq et al. (1985) [62]	Dexamethasone 10 mg (two doses)	Reduced	—	Reduced	Comparison against ultrasound, which is equally as effective
Pedersen (1985) [63]	Betamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
Sisk and Bonnington (1985) [64]	Methylprednisolone 125 mg (single dose)	No difference	Reduced	No difference	Comparison against flurbiprofen or placebo
Beirne and Hollander (1986) [65]	Methylprednisolone 125 mg (single dose)	Reduced	Reduced	No difference	—
Olstad and Skjelbred (1986) [66]	Methylprednisolone (multiple tapering doses)	Reduced	Reduced	—	—
Holland (1987) [67]	Methylprednisolone 40 mg (single dose)	Reduced	Reduced	—	—
Troullos et al. (1990) [68]	Methylprednisolone 125 mg (single dose)	Reduced	Reduced	Reduced	Less effective pain control than flurbiprofen or ibuprofen
Neupert et al. (1992) [69]	Dexamethasone 4 mg (single dose)	No difference	No difference	Reduced	—
Baxendale et al. (1993) [70]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	No difference	—
Hyrkäs et al. (1993) [71]	Methylprednisolone 40 mg (single dose)	—	Reduced	No difference	Increased efficacy in pain control in combination with diclofenac sodium
Milles and Desjardins (1993) [72]	Methylprednisolone 16 mg and 20 mg (two doses)	Reduced	—	No difference	—
Schmelzeisen and Frölich (1993) [73]	Dexamethasone 6 mg (two doses)	Reduced	Reduced	Reduced	—
Schultze-Mosgau et al. (1995) [74]	Methylprednisolone 32 mg (single dose)	Reduced	Reduced	—	Co-administered with ibuprofen
Esen et al. (1999) [75]	Methylprednisolone 125 mg (single dose)	Reduced	Reduced	Reduced	—
Dionne et al. (2003) [76]	Dexamethasone 4 mg (two doses)	—	Reduced	—	Synergistic pain relief with ketorolac
Üstün et al. (2003) [77]	Methylprednisolone 1.5 mg/kg or 3 mg/kg (single dose)	No difference	No difference	No difference	Comparison of two different doses of corticosteroids
Bamgbose et al. (2005) [78]	Dexamethasone 8 mg and 4 mg (two doses)	Reduced	Reduced	No difference	Co-administered with diclofenac sodium

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
López-Carriches et al. (2005) [79]	Methylprednisolone 40 mg (single dose)	—	No difference	—	Comparison with diclofenac
Moore et al. (2005) [80]	Dexamethasone 10 mg (single dose)	—	Reduced	Reduced	Synergistic effect with rofecoxib
Tiwana et al. (2005) [81]	Dexamethasone 8 mg or methylprednisolone 40 mg (single dose)	No difference	No difference	No difference	Improved sleep and decreased nausea
Buyukkurt et al. (2006) [82]	Prednisolone 25 mg (single dose)	Reduced	Reduced	Reduced	Synergistic effect with diclofenac
Graziani et al. (2006) [83]	Dexamethasone 4 mg or 10 mg (single dose)	Reduced	Reduced	Reduced	—
López-Carriches et al. (2006) [84]	Methylprednisolone 40 mg (single dose)	Reduced	—	No difference	Comparison with diclofenac
Mico Llorens et al. 2006 [85]	Methylprednisolone 40 mg (single dose)	Reduced	No difference	Reduced	
Ordulu et al. (2006) [86]	Methylprednisolone 1.5 mg/kg (single dose)	No difference	No difference	Reduced	Comparison with tube drainage
Grossi et al. (2007) [87]	Dexamethasone 4 mg or 8 mg (single dose)				
Filho et al. (2008) [88]	Dexamethasone 4 mg or 8 mg (single dose)	Reduced	No difference	Reduced	No difference between two dosages
Zandi et al. (2008) [89]	Dexamethasone 8 mg (single dose) followed by methylprednisolone 5 mg (multiple doses)	Reduced	Reduced	Reduced	Comparison against rubber drain, which reduced pain and trismus
Vegas-Bustamante et al. (2008) [90]	Methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	
Chopra et al. (2009) [91]	Betamethasone 0.5 mg (single dose)	Reduced	Reduced	Reduced	Comparison against paracetamol, serratiopeptidase, ibuprofen
Gataa and Nemat (2009) [92]	Methylprednisolone 10 mg (single dose)	Reduced	Reduced	Reduced	Oral route more effective than submucosal route in controlling pain and trismus
Tiigimae-Saar et al. (2010) [93]	Prednisolone 30 mg (single dose)	Reduced	Reduced	Reduced	

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
Kang et al. (2010) [94]	Prednisolone 10 mg or 20 mg (single dose)				No difference between the two dosages. Dose need to be more than 20 mg to be effective
Majid and Mahmood (2011) [95]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	No difference between intramuscular and submucosal routes
Majid (2011) [96]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	No difference between intramuscular and submucosal routes. Improved QoL
Deo and Shetty (2011) [97]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	Reduced	—
Antunes et al. (2011) [98]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	Reduced	No difference between submucosal and intramuscular (masseter) routes
Kaur et al. (2011) [99]	Methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	—
Mushtaq et al. (2011) [100]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—
Boonsiriseth et al. (2012) [101]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	Reduced	No difference between oral and intramuscular (deltoid) routes
Klongnoi et al. (2012) [102]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	No difference	
Loganathan and Srinivasan (2012) [103]	Methylprednisolone 40 mg (single dose) or dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	No difference between the two drugs
Murugesan et al. (2012) [104]	Dexamethasone 1 mg (multiple doses)	Reduced	Reduced	No difference	Comparison with serratiopeptidase
Panwar (2012) [105]	Prednisolone 5 mg (single dose)	Reduced	Reduced	Reduced	—
Acham et al. (2013) [106]	Methylprednisolone 60–80 mg based on body weight (single dose)	Reduced	Reduced	Reduced	—
Arakeri et al. (2013) [107]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	—	Comparison with aprotinin (a serine protease inhibitor)
Bauer et al. (2013) [108]	Dexamethasone 8 mg (single dose)	—	Reduced	—	Synergistic effect with ibuprofen

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
Bortoluzzi et al. (2013) [109]	Dexamethasone 8 mg (single dose)	No difference	No difference	No difference	Dexamethasone was combined with amoxicillin or placebo
Channar et al. (2013) [110]	Dexamethasone 8 mg (two doses)	No difference	—	No difference	—
Chaurand-Lara and Facio-Umaña (2013) [111]	Methylprednisolone 20 mg (single dose)	Reduced	Reduced	—	—
Christensen et al. (2013) [112]	Methylprednisolone 16 mg (two doses)	Reduced	Reduced	—	Co-administered with bupivacaine or lignocaine
Flores et al. (2013) [113]	Betamethasone 11.4 mg (single dose)	Reduced	—	Reduced	Comparison with oral deflazacort
Majid and Mahmood (2013) [114]	Dexamethasone 4 mg (single dose) IM deltoid, IV, submucosal, endoalveolar, divided doses of 4× 1 mg)	Reduced	Reduced	Reduced	Improved quality of life
Mehra et al. (2013) [115]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	Reduced	Synergistic effect with ibuprofen
Nair et al. (2013) [116]	Dexamethasone 4 mg (single dose)	Reduced	No difference	No difference	—
Warraich et al. (2013) [117]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—
Agostinho et al. (2014) [118]	Dexamethasone 4 mg or 12 mg (single dose)	Reduced	Reduced	Reduced	No difference between two dosages
Bhargava et al. (2014) [9]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—
Ehsan (2014) [119]	Dexamethasone 4 mg (single dose)	Reduced	—	Reduced	—
Kaur et al. (2014) [120]	Methylprednisolone (single dose)	Reduced	Reduced	Reduced	Studied the synergistic effects with ibuprofen
Marques et al. (2014) [121]	Betamethasone 12 mg (single dose)	No difference	No difference	No difference	—
Noboa et al. (2014) [122]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	Submucosal injection is as effective as oral intake
Shaikh et al. (2014) [123]	Dexamethasone 8 mg (two doses)	Reduced	—	Reduced	—

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
Ashraf et al. (2014) [124]	Methylprednisolone 125 mg (single dose)	Reduced	Reduced	Reduced	No difference between submucosal and intramuscular (gluteus) routes
Kocer et al. (2014) [125]	Methylprednisolone 20 mg (single dose)	Reduced	Not studied	Reduced	No difference in reducing trismus. IM masseter better in reducing swelling
Selvaraj et al. (2014) [126]	Methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	No difference between the masseter and gluteus intramuscular routes
Vyas et al. (2014) [127]	Methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	IM masseter more effective
Alcantara et al. (2014) [128]	Dexamethasone 8 mg (single dose) or Methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	Dexamethasone better in reducing swelling and trismus but no difference in reducing pain
Darawade et al. (2014) [129]	Dexamethasone 8 mg (single dose) or methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	Dexamethasone better in reducing swelling and trismus but no difference in reducing pain
Chappi et al. (2015) [130]	Methylprednisolone 5 m (multiple doses)	No difference	Reduced	No difference	Comparison against serratiopeptidase
Chaudhary et al. (2015) [131]	Dexamethasone 4 mg or 8 mg (single dose)	Reduced	Reduced	Reduced	—
Gopalakrishnan et al. (2015) [132]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	Submucosal more effective than intramuscular (deltoid) route
Sabhlok et al. (2015) [133]	Dexamethasone 4 mg (multiple dose) or dexamethasone 4 mg (single dose)	No difference	No difference	Reduced	Continuous oral medication is more effective than single IM
Zerener et al. (2015) [134]	Dexamethasone 4 mg (single dose) or triamcinolone acetonide 4 mg (single dose)	Reduced	Reduced	Reduced	No difference between the two drugs
Dereci et al. (2016) [135]	Dexamethasone 8 mg (single dose)	Reduced	—	—	—
Paiva-Oliveira et al. (2016) [136]	Dexamethasone 8 mg (single dose)	No difference	No difference	Reduced	Comparison with ketorolac tromethamine
Quadri et al. (2016) [137]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—
Saravanan et al. (2016) [138]	Dexamethasone 4 mg/2 ml (single dose)	Reduced	Reduced	Reduced	SC is more effective than IM

Authors (year)	Corticosteroids studied	Summary outcomes			
		Swelling	Pain	Trismus	Others
Al-Dajani et al. (2017) [139]	Dexamethasone 0.1 mg/kg (single dose)	Reduced	Reduced	Reduced	
Al-Shamiri et al. (2017) [140]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	Reduced	
Barbalho et al. (2017) [141]	Dexamethasone 8 mg (single dose)	Reduced	No difference	No difference	Co-administered with nimesulide 100 mg
Chugh et al. (2017) [142]	Dexamethasone 8 mg (single dose) or methylprednisolone 40 mg (single dose)	No difference	Reduced	Reduced	Dexamethasone more efficacious than methylprednisolone
Gozali et al. (2017) [143]	Dexamethasone 8 mg (single dose)	—	Reduced	—	—
Khalida et al. (2017) [144]	Dexamethasone 4 mg (single dose)	Reduced	—	Reduced	—
Lim and Ngeow (2017) [145]	Dexamethasone 4 mg or methylprednisolone 40 mg (single dose)	Reduced	Reduced	Reduced	—
Lima et al. (2017) [146]	Dexamethasone	Reduced	Reduced	Reduced	Comparison with diclofenac sodium
Lima et al. (2017) [147]	Dexamethasone 8 mg (single dose)	Reduced	Reduced	No difference	Comparison with diclofenac sodium
Mojsa et al. (2017) [148]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	Post-operative superior to preoperative in pain control
Rocha-Neto et al. (2017) [149]	Dexamethasone 8 mg (single dose)	No difference	Reduced	Reduced	Preoperative superior to post-operative in swelling reduction
Selimović et al. (2017) [150]	Methylprednisolone 32 mg (single dose)	—	—	Reduced	Co-administered with meloxicam
Syed et al. (2017) [151]	Dexamethasone 4 mg (single dose)	Reduced	Reduced	Reduced	—

Table 1. Summary of outcome of various researches related to the use of corticosteroids in oral and maxillofacial surgery, using impacted third molar surgery model.

reduced not only early and late oedema but also early trismus [25], while Moraschini et al. reported that submucosal dexamethasone was effective in reducing pain and swelling, but not trismus [26]. The last meta-analysis looking solely on preemptive dexamethasone against other oral anti-inflammatories found that it is more effective than methylprednisolone for reducing swelling and trismus. However, the authors found insufficient evidence to conclude that dexamethasone is better than other nonsteroidal anti-inflammatories or methylprednisolone as a preemptive analgesic [27]. In term of mode of administration, it has been suggested that systemic administration of corticosteroids is more effective [8].

Table 1 summarises all relevant studies on the use of corticosteroids using the third molar surgical model throughout the last 61 years. It shows a change in the trend of corticosteroid prescription, with low-dose single dose being favoured in the last two decades instead of the multiple or high-doses popular in the 1970s till 1990s. However, not many studies have look into the effect of corticosteroids in other oral surgical procedures. One reason for this limitation is the lack of opportunity to perform standardisation that is needed with other oral surgery/dentoalveolar surgical procedures. Mead et al. and Linenburg were among the few researchers who were able to conduct tests on patients undergoing different types of oral surgical procedure, including third molar surgery [28, 29]. Mead et al. administered oral triamcinolone post-operatively to 96 patients who had undergone varied oral surgical procedures and reported that it was superior to placebo in reducing oedema, pain and trismus [28].

In contrast, Linenburg studied the effect of dexamethasone on patients undergoing treatment of cellulitis and trismus due to an infectious process [29]. He reported a higher percentage of patients treated with corticosteroids being cured of cellulitis and trismus after 4 days than conventional treatment of hospitalisation, antibiotics, drainage and heat application. Linenburg also conducted a trial on 12 patients undergoing a full-mouth or a maxillary alveoloplasty and found that oedema and trismus last longer in patients without dexamethasone. A double-blinded comparison was performed on 50 patients undergoing both removal of bilaterally impacted third molars and full-mouth or maxillary alveoloplasty, and again he found that oedema and trismus last longer in patients without dexamethasone [29].

Not many randomised trials have been undertaken to study the effects of corticosteroids in oral and maxillofacial surgery. With regards to pain and swelling, its effect in traumatology has been studied once only in two separate RCTs; one on patients with blow out fracture [20] and the other on those with mandibular fracture [30]. In the observer-blinded study on the effect of dexamethasone 30 mg in blowout fracture surgery, Kormi et al. concluded that dexamethasone decreased post-operative pain and recommended it as a preemptive analgesic. In comparison, Dongol et al. reported that submucosal administration of dexamethasone after open reduction and internal fixation for mandibular fractures was effective in reducing post-operative swelling and pain. However, they did not observe any significant difference in mouth opening or difficulty in mandibular function [30].

Systemic corticosteroids are used to prevent post-surgical facial oedema, enhance patient comfort and prevent potential upper airway compromise in orthognathic surgery. Several trials even hinted a neuroregenerative effect on inferior alveolar nerve affected by orthognathic surgery [31]. Seo et al. reported that corticosteroids have the potential to accelerate the recovery

of sensory impairment and it is desirable to start treatment later than 1 week post-operatively. For the record, the first recommendation for using corticosteroids in orthognathic surgery was made by Guernsey and DeChamplain [32] who reviewed complications affecting 22 patients who underwent sagittal ramisection. They suggested that post-operative swelling could be controlled by a regimen of dexamethasone used perioperatively. They described the diminution of post-operative oedema empirically but did not explain how they arrived at their recommended regime of corticosteroids. A study undertaken by Munro et al. [33] 2 years later however, failed to support this recommendation. There are, however, several trials that later confirmed the reduction of swelling in orthognathic patients [17, 34]. Most of them have been meta-analysed and/or underwent systematic review by several authors throughout the last 7 years [35]. Among others, Schaberg et al. reported that perioperative methylprednisolone (1 mg/kg) was effective in patients who underwent either a Le Fort I osteotomy or a transoral vertical osteotomy, as compared to control patients who were not given this medication [36]. Similarly, Weber and Griffin reported a reduction of swelling when dexamethasone was given perioperatively in patients undergoing bilateral sagittal split osteotomy (BSSO) [37]. This finding has been confirmed by other authors [34] who recently reported that the most effective dose of dexamethasone for bilateral sagittal split osteotomy was 16 mg given preoperatively.

Widar et al. although reported that betamethasone (single dose or multiple repeated dose up to 16 mg) reduces swelling, it does not reduce neurosensory disturbances over time in patients undergoing bilateral sagittal split osteotomy [17]. Similar findings have been reported by Mensink et al. and Pourdanesh et al. [38, 39]. Similar impact on the neurosensory disturbances after zygomatic complex fracture has been reported recently by Haapanen et al. [40]. Because of the limited number of studies that listed the benefit of administration of corticosteroids in orthognathic surgery, there is still a need for more robust evidence to support their use [41].

Although many studies and systematic reviews found that corticosteroids are beneficial in controlling various post-operative sequelae, there are some who discouraged their use because of the fear of several potential adverse side effects [42]. A most recent systemic review and meta-analysis on the perioperative use of corticosteroids in orthognathic surgery although confirmed that they reduced facial oedema, found that adverse effects were inconsistently screened and reported [37]. The least severe adverse effect is the development of steroid induced acne in some female orthognathic surgery patients [43]. Other more severe complications include adrenal suppression [44], acute psychiatric reactions such as psychosis or inappropriate euphoria [42], a higher infection rate and decreased healing potential.

There are several recent studies that reported conflicting adverse effects with regards to disturbance in surgical wound healing, especially in major oral and maxillofacial surgeries. Thorén et al. in a retrospective study reported that the rate of disturbance in surgical wound healing for patients who had received perioperative steroids was more than twice (6.0%) the corresponding rate for patients who did not receive steroids (2.8%), although this difference was not statistically significant. They reported that intraoral surgical approach was a significant predictor to this adverse effect [45]. Snäll et al. in contrast, did not observe similar problem in operative treatment of mandibular fractures, although they found that older age was a significant predictor of impaired healing [46]. However, in another study on open reduction and fixation

of zygomatic complex fractures, Snäll et al. reported increased disturbance in surgical wound healing and did not recommend the administration of corticosteroids for such surgery [47].

Other serious complications associated with the administration of corticosteroids are acute gastrointestinal reactions (abdominal pain, haematemesis, and/or maelena), hyperglycemia, superinfection and septicaemia [48] and avascular necrosis of the femoral head [49]. It has been reported that common regimes used in orthognathic surgery involve a total dose of 1830 mg of methylprednisolone over a 30-hour period, a dosage similar to some short-term, high-dose regimens described in orthopaedic case reports of avascular necrosis of the femoral head [49]. Hence, there is a potential risk for this group for patients to develop avascular necrosis. Fortunately, Precious et al., found no evidence that this has occurred in the only study that reviewed the need of total hip replacement in 1276 orthognathic patients. They concluded that the use of systemic corticosteroids for short duration in orthognathic surgery is unlikely related to AVN of the femoral head and the attendant need for total hip replacement [50].

3. Corticosteroids in oral medicine

3.1. Recurrent aphthous ulcer

Recurrent aphthous ulcers top the list of the commonest oral mucosal lesions encountered by any dental practitioners. Generally, this condition is self-limiting and resolves within 2–3 weeks with the exception of major recurrent aphthous ulcer [162]. Despite it being self-limiting, the pain and the frequency of recurrence can be very devastating to the patients. Corticosteroid is one of the available treatment options for recurrent aphthous ulcers.

The use of topical corticosteroids can be advocated when topical anesthetic, antiseptics and anti-inflammatory agents are no longer effective in relieving the discomfort caused by these ulcers. It was suggested to begin with less potent drug such as triamcinolone and moving gradually to more potent corticosteroids like clobetasol [163]. These corticosteroids come in the form of mouthwashes, ointments, creams and adhesive pastes.

Triamcinolone acetonide 0.1% is the commonly used concentration although it can actually be used at concentration ranging from 0.05 to 0.5%, and is usually applied 3–4 times a day [164]. For maximum effect of the drug, it should be in contact with the ulcer for as long as possible. Therefore, it is advisable to refrain from any oral intake within 20 minutes after application or touching the affected area [164]. Fluocinolone acetonide and clobetasol require lower concentrations of 0.025–0.05% since they are potent corticosteroid. These drugs are usually applied 4–5 times a day [164]. Al-Na'amah et al. in 2009 studied the use of dexamethasone 0.1% by comparing it to triamcinolone acetonide 0.1% and found that both drugs are effective in the treatment of recurrent aphthous ulcers [159].

On the other hand, systemic corticosteroids are rarely required in the treatment of recurrent aphthous ulcers except for cases that are not responsive to topical medications [165]. Oral prednisone with starting dose of 25 mg/day is recommended [165]. This is then followed by tapering

of the dosage during a period of 2 months. The tapering regime as reported by Femiano et al. in 2003 and 2010 (**Table 2**) had been shown to be effective in the treatment and prevention of recurrence of aphthous ulcer [161].

3.2. Oral lichen planus

Table 3 shows that topical corticosteroids are reasonably effective in the treatment of oral lichen planus. The use of more potent corticosteroids was associated with more improvement following therapy. However, incidence of oral candidiasis also increased in proportion

Authors (year)	Corticosteroids	Outcomes			
		Pain reduction	Ulcer size reduction	Duration of ulcer	Recurrence
Topical					
Yeoman (1978) [152]	Betamethasone valerate 1 puff QID (max 16 puff/24 hours)	Reduced	—	Reduced	—
Pimlott (1983) [153]	0.05% fluocinonide ointment + orabase	Reduced	—	Reduced	Less
Lo Muzio et al. (2001) [154]	0.05% clobetasol ointment	Reduced	—	—	—
Rhodus and Bereuter (1998) [155]	Kenalog-in-Orabase, TDS	Reduced	—	Reduced	—
Teixeira et al. (1999) [156]	0.1% mometasone furoate lotion QID	Reduced	—	Reduced	—
Rodriguez (2007) [157]	0.05% clobetasol propionate oral paste QID × 5 days	Reduced	Faster	—	—
Al-Na'amah et al. (2009) [158]	Dexamucobase; 0.1% dexamethasone QID	Reduced	Faster	Reduced	—
Al-Na'amah et al. (2009) [158]	Kenalog; 0.1% triamcinolone acetonide QID	Reduced	Fast	Reduced	—
Fani et al. (2012) [159]	0.1% triamcinolone acetonide ointment TDS	Significantly better therapeutic effect in triamcinolone group			
Systemic					
Femiano et al. (2003) [160]	Prednisone 25 mg OD × 1 week, 20 mg OD × 2 weeks, 15 mg OD × 2 weeks, 10 mg OD × 2 weeks, 5 mg OD × 1 week	Reduced	—	Reduced	Less
Femiano et al. (2010) [161]	Prednisone 25 mg OD × 15 days, 12.5 mg OD × 15 days, 6.25 mg OD × 15 days, 6.25 mg EOD × 15 days	Reduced.	—	Reduced	Less

Table 2. Topical and systemic corticosteroids used in the treatment of recurrent aphthous ulcer.

Corticosteroid	Author (year)	Results (%)		
		Complete response	Partial response	No response
Hydrocortisone hemisuccinate	Holbrook et al. (1988) [165]	48	37	15
Betamethasone sodium phosphate	Hegarty et al. (2002) [166]	0	73	27
Betamethasone valerate 0.1 mg	Cawson (1968) [167]	43	23	34
Triamcinolone acetonide 0.1%	Thongprasom et al. (1992) [168]	42	Not mentioned	Not mentioned
Fluocinolone acetonide 0.1%	Thongprasom et al. (1992) [168]	68	Not mentioned	Not mentioned
Fluocinonide 0.05%	Lozada and Silverman (1980) [169]	52	48	0
	Voute et al. (1993) [170]	20	60	20
	Carbone et al. (1999) [171]	25	65	10
Fluticasone propionate 0.05%	Hegarty et al. (2002) [166]	0	80	20
Clobetasol propionate 0.05%	Lozada-Nur et al. (1991) [172]	56	22	22
	Sardella et al. (1988) [173]	57	21.5	21.5
	Carbone et al. (1999) [170]	75	25	0
	Gonzales-Moles et al. (2002) [174]	93	0	7

Table 3. Topical corticosteroids used in the treatment of oral lichen planus.

to the potency of corticosteroids used [169, 171]. Carbone et al. in 2003 reported that the use of topical corticosteroid can be as effective or even more effective than systemic corticosteroids in the treatment of oral lichen planus [175]. On the other hand, the use of systemic corticosteroids should be restricted to acute exacerbations or multiple lesions. Topical regime can be prescribed in combination of systemic regime to reduce side effects of systemic corticosteroids [176]. The commonly used systemic corticosteroid is prednisone which is usually prescribed within the range of 40–80 mg/day to achieve clinical response. To avoid adverse effects of this drug, it is best to prescribe the lowest dose for the shortest duration possible. To achieve this, prednisone can either be given for a brief period of 5–7 days and stop abruptly or the dose can be tapered down by 5–10 mg/day gradually over a period of 2–4 weeks [177].

Intralesional injection is another alternative for administrating corticosteroids in the treatment of oral lichen planus. Hydrocortisone, dexamethasone, betamethasone, triamcinolone acetonide and methylprednisolone have been used for intralesion injection. This method is however, painful and causes localised mucosal atrophy. Intralesional injection is also not feasible in cases of multiple widespread lesions [176, 178].

3.3. Pemphigus vulgaris and mucous membrane pemphigoid

Corticosteroids have become the mainstay of treatment for pemphigus ever since the first case series reported by Ryan in 1971 [179]. Despite being the gold standard in the treatment of pemphigus, the use of corticosteroids is still mulled by many physicians due to the adverse effects of long-term treatment and difficulty in ascertaining the best regimen [180]. Due to the high mortality rate of this condition, studies conducted were just comparing various groups of drugs used, different dosages and modes of administration rather than purely investigating the efficacy of a particular drug. Most of the articles published were mainly case reports and case series [181].

More than three-quarter of the patients with pemphigus vulgaris presented with oral lesions. And these lesions are the presenting signs of half of the patients diagnosed with pemphigus vulgaris [182]. As in the treatment of oral lesions in pemphigus vulgaris, oral lesions secondary to mucous membrane pemphigoid are also treated with moderate to high potency topical corticosteroids (fluocinonide 0.05%, clobetasol 0.05%), applied 2–3 times per day. The frequency of application can be tapered gradually with improvement of symptoms [182]. Bear in mind that as a result of prolonged topical corticosteroids use, infection such as candidiasis and reactivation herpes simplex virus can occur. Combination of other drugs such as dapsone, tetracycline and nicotinamide is recommended.

As for systemic corticosteroids, an initial dose of 0.5–1 mg/kg/day of prednisone plus adjuvant immunosuppressants is recommended. This dose is continued until all existing lesions have healed and no development of new lesions is noticed clinically. Once this is achieved, tapering of the dose can be performed [182]. The ultimate aim in the treatment strategy is to minimise the dose of systemic corticosteroids while controlling the disease with immunosuppressants.

In patient with severe pemphigus vulgaris, corticosteroid pulse therapy can be administered to induce remission. In this therapy, a very high-dose of corticosteroid (500–1000 mg methylprednisolone or 100–200 mg dexamethasone given in divided dose on 3 consecutive days) is given in a short period of time in combination immunosuppressants and maintenance dose of corticosteroids [183].

3.4. Bell's palsy

With an unclear knowledge of the aetiology of Bell's palsy, it poses a great challenge in coming up with an optimal treatment of the condition. To achieve a good outcome, corticosteroid needs to be given within 72 hours of onset of facial palsy. Berg et al. in 2012 found that prednisolone given within 72 hours of onset of palsy significantly improve outcome in mild to moderate palsy but not in severe palsy. The regime used was prednisolone 60 mg/day for 5 days, followed by 10 mg/day for another 5 days [184]. Using the same regimen, another study found that prednisolone significantly achieve complete recovery in mild to severe palsy and less synkinesis observed in mild and moderate palsy. However, no significant reduction of synkinesis in severe cases was reported [185]. Murthy and Saxena in 2011 suggested two corticosteroid regimens for the treatment of Bell's palsy which were either prednisolone 60 mg/day for 5 days followed by 10 mg/day for another 5 days or prednisolone 25 mg twice a day for 10 days [186]. The American Academy of Otolaryngology-Head and Neck Surgery recommended a 10-day course of oral

steroids with at least 5 days at a high-dose (either prednisolone 50 mg for 10 days or prednisone 60 mg for 5 days with a 5-day taper) initiated within 72 hours of symptom onset [187].

Conflicting results were reported in different studies on the benefit of combining anti viral therapy with corticosteroid to achieve better outcome. Minnerop et al. reported that combination of famciclovir and prednisone was superior to prednisone alone in cases of severe Bell's palsy [188]. Combining antiviral therapy with prednisone increase the recovery rate slightly but not significantly compared to prednisone monotherapy [189]. On the other hand, valacyclovir was found to have no additional effect to prednisolone in sequelae of Bell's palsy [869] and the addition of acyclovir to prednisolone did not significantly improve recovery from Bell's palsy [190]. Despite conflicting results from various studies, Madhok et al. in their Cochrane review in 2016 concurred with current evidences that corticosteroids showed significant benefit in the treatment of Bell's palsy [191].

3.5. Temporomandibular joint

In year 1953, Horten reported the use of intraarticular injection of steroids into the temporomandibular joint (TMJ) space. Being the first to perform this procedure in the TMJ, he was then inspired by Hollander and colleagues' work where they injected hydrocortisone into other arthritic joints [192]. Kopp et al. in 1985 injected betamethasone into the TMJ space in a group of patients with TMJ pain and dysfunction, showed that betamethasone was effective in reducing joint pain up to 4 weeks [193]. About 6 years later, Kopp and colleagues performed intraarticular injection using methylprednisolone which showed similar promising results up to 4 weeks [194]. Bjørnland et al. injected betamethasone into the TMJ space of patients with osteoarthritis and myofascial pain 10 years ago. Although betamethasone managed to reduce joint pain, sodium hyaluronate which was given in the other study group was found to be more effective [195]. Another promising use of corticosteroids is for the management of disc displacement without reduction. Samiee et al. found that combined intraarticular injection of local anaesthetic and corticosteroids improved mouth opening [196].

Using computed tomography (CT) scan, Møystad et al. evaluated the bony changes in osteoarthritic TMJ following intraarticular injection of sodium hyaluronate and corticosteroid (betamethasone). The number of cases that showed disease progression, regression and no changes were almost equal [197]. This finding raised the question on the effectiveness of corticosteroids as intraarticular injection. Another study by Bouloux et al. recently again showed no added effect of using corticosteroids or another agent, hyaluronic acid in arthrocentesis [198]. In cases of juvenile idiopathic arthritis, a study by Resnick et al. showed that although intraarticular corticosteroid (triamcinolone hexacetonide) injection did reduce TMJ sinovitis pain, its efficacy for long-term inflammation and joint destruction control needs further studies.

4. Corticosteroids in endodontology

The first intracanal medication using corticosteroids was reported by Wolfsohn in 1954. In that study, he showed that hydrocortisone was effective in reducing severe secondary

inflammatory reactions in the apical periodontal tissue following endodontic treatment [208]. Other authors who also used corticosteroids as intracanal medication, as listed in **Table 4**, reported beneficial outcome in the post-operative or post-instrumentation pain. Besides reducing pain, Thong et al. reported that the use of corticosteroid-antibiotic and calcium hydroxide significantly inhibited periodontal ligament inflammation and inflammatory root resorption [209]. A well-known intracanal medication, Ledermix[®], is corticosteroid-antibiotic compound which consists of 1% triamcinolone acetonide and 3.2% demeclocycline hydrochloride in a polyethylene glycol base. The function of antibiotic in that paste is to compensate for the possible corticosteroid-induced immunosuppressing effect [210]. Despite being an effective intracanal medication, Ledermix[®] was found to cause discolouration of the teeth especially when it is placed above the cemento-enamel junction. Therefore, to avoid this Ledermix[®] should be placed below the gingival margin [211].

Similar to the use of corticosteroids in third molar surgery, local injection of corticosteroids have been found to reduce post treatment pain. Kaufman et al. evaluated the effect of intraligamental injection of corticosteroids on post treatment pain. They found that intraligamental injection of methylprednisolone significantly decreased post treatment pain [202]. Nobuhara et al. in their histological study found that local infiltration of dexamethasone significantly reduced inflammation of the periapical tissue [212].

Author (year)	Corticosteroids	Outcome
		Post treatment pain
Intracanal		
Rogers et al. (1999) [199]	Dexamethasone 0.4 mg (intracanal) and ketorolac tromethamine 3 mg (intracanal)	Reduced
Negm (2001) [200]	Kenacomb (antibiotics and triamcinolone acetonide 0.1%)	Reduced
Ehrmann et al. (2003) [201]	Ledermix (1% triamcinolone acetonide, 3.2% demeclocycline)	Reduced
Local (injection)		
Kaufman et al. (1994) [202]	4–8 mg methylprednisolone (intraligamental injection)	Reduced
Systemic		
Stewart and Chilton (1958) [203]	Metreton (2.5 mg prednisone, 2 mg chlorpheniramine) TDS × 2 days, penicillin 250 mg TDS × 3 days	Reduced
Stewart (1962) [204]	Dexamethasone 0.75 mg BD × 2 days	Reduced
Krasner and Jackson (1986) [205]	Dexamethasone 0.75 mg × 7 tablets, 3 tablets immediately after procedure, one tablet every 3 hours	Reduced
Glassman et al. (1989) [206]	Dexamethasone 4 mg × 3 tablets, one tablet taken immediately after procedure, one tablet every 4 hours	Reduced
Liesinger et al. (1993) [207]	Dexamethasone 0.07–0.09 mg/kg (intramuscular injection)	Reduced

Table 4. Studies on usage of corticosteroids via various routes of administration.

From the studies shown in **Table 4**, it is obvious that they confirmed the favourable result of systemic administration of corticosteroids in alleviating post treatment pain. In all the studies, corticosteroids were only given for a very short period. Therefore, the possibility of adverse effects arising from short-term corticosteroids is very unlikely [7].

5. Conclusion

The uses of corticosteroids are very well established in the field of oral medicine and endodontology. On the other hand, in the field of oral and maxillofacial surgery, despite being consistently effective in controlling post-surgical oedema, corticosteroids provide rather less consistent outcome in pain control as well as trismus reduction. Its impact on wound healing is varied.

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