Pre- and post-operative management of dental implant placement. Part 1: management of post-operative pain

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VERIFIABLE CPD PAPER

IN BRIEF

- Provides dental practitioners with an overview of the mechanisms of post-operative pain following dental implant placement.
- Discusses the benefits and limitations of commonly employed pain medications for the control of post-operative dental implant pain.
- Provides practical recommendations for the prescription of pain medications post-dental implant placement.

PRACTICE

Although dental implant placements have high success rates and a low incidence of morbidity, post-operative pain and complications with the healing process have been reported. There is little guidance available regarding optimal pre- and post-operative management of dental implant placement. This first paper discusses the mechanisms of pain associated with dental implant placement and offers guidance to clinicians on optimal pre- and post-operative pain management regimes. The second paper aims to discuss pre- and post-operative means of reducing the risk of early healing complications.

INTRODUCTION

It is well recognised that high success rates¹ and levels of patient satisfaction² can be achieved with dental implants if sound pre-operative assessment/planning is adopted and an exacting surgical technique employed.³ Surprisingly, there is limited information available about the role that pre- and post-operative medication plays on treatment outcome and patient experience.

Certain aspects of patient management, generally relating to the prophylactic prescription of antibiotics as a preventative measure against infective endocarditis, have been reported on and feature within both Governmental (National Institute for Health and Care Excellence) and independent body (Royal College of Surgeons of England) guidelines. However, these bodies do not provide similar levels of evidence-based guidance for the use of pre- and post-operative management to improve outcome for patients receiving dental implant placement.

The aim of this two-part series is to update clinicians on current aspects of pre- and post-operative care associated with dental implant placement. In this first paper, the means of managing post-operative pain will be reviewed and recommendations made. Part two will aim to discuss aspects of pre- and post-operative patient management

that can be employed to optimise the healing process and reduce post-operative complications.

THE MECHANISM OF OROFACIAL PAIN

Post-operative pain is an unfortunate consequence of the unavoidable tissue damage that occurs following the surgical placement of dental implants. Pain has been defined as an 'unpleasant sensory and emotional experience associated with actual or potential tissue damage'.⁴ The sensation of pain may result from both the initial surgical insult and the subsequent inflammatory process. The surgical insult breaches the threshold of nociceptors located within both the periodontal and osseous tissues and mediates an acute pain sensation via fast signal-speed myelinated A-delta fibres (signal speed of 5–30 m/s). This signal is transmitted, via the dorsal horn of the spinal cord, to higher central nervous system (CNS) centres, where pain is perceived. Inflammatory pain is normally characterised as dull or throbbing in nature and is regulated by the activation of slower signal-speed unmyelinated C fibres (signal speed of 0.5–2 m/s). It is reported that inflammatory pain reaches its zenith at approximately 48–72 hours post-surgery⁵ and is guided by the release of inflammatory mediators. These inflammatory mediators can either act directly on peripheral nociceptors (for example, bradykinin ions [potassium, hydrogen], histamine and nitric oxide), resulting in spontaneous pain, or indirectly (growth factors, neuropeptides such as substance P and calcitonin gene-related peptide) by stimulating the release of pain-inducing

factors from recruited inflammatory cells. In addition, some factors, such as cytokines, leukotrienes and prostaglandins (via activation of the arachidonic acid pathway), are capable of both direct and indirect nociceptor stimulation (Fig. 1).

POST-IMPLANT PLACEMENT PAIN

Although it is accepted that the majority of patients will experience mild to moderate pain following dental implant placement,⁶ the exact role that general and specific factors play in this process is poorly understood. General patient factors such as gender, anxiety levels^{6,7} and smoking status⁵ have been implicated in exacerbating post-operative pain perception. Additional factors, specific to the surgical placement of implants, which are likely to increase post-operative pain include: grafting techniques,⁸ number of implants placed,⁸ posterior siting of implant (possibly due to greater extension of the surgical flap),⁸ excessive heat generation resulting from inadequate cooling of the surgical bur/osseous interface,⁹ extensive surgical flaps, poor flap management and over-torquing of the implant (Table 1).

Pain medications can reduce post-operative discomfort by depressing the nociceptive system, either within the central nervous system or on the peripheral nerve terminals. Those medications that can be used to manage pain subsequent to dental surgery, include:

1. Non-steroidal anti-inflammatories (NSAIDs) – non-specific and cyclooxygenase (COX)-specific
2. Paracetamol
3. Opioids
4. Corticosteroids.

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Little research has been applied to the investigation of the efficacy of oral analgesics in the management of post-implant placement pain. In contrast, the greater proportion of studies has investigated the effectiveness of different analgesics in the management of post-operative pain, using an established third-molar extraction model.¹⁰ Although there are obvious differences between the extraction of a tooth and the placement of a dental implant, the mucosal and alveolar tissues are traumatised in both procedures, resulting in similar mechanisms of inflammatory pain. By examining the existing literature on the use of analgesics in the management of post-extraction pain, tentative conclusions can be drawn regarding their efficacy as post-operative analgesics for implant procedures.

NSAIDS

Given the known role that prostaglandins play in both the inflammatory and pain pathways, it is unsurprising that NSAIDs hold prominent standing within dentists' post-operative prescription armamentarium. This class of drug exerts an analgesic effect by inhibiting the action of one or both isoenzymes of the cyclooxygenase enzymes, COX-1 and COX-2, resulting in decreased production of pain-mediating prostaglandins and thromboxane. However, while the inhibition of COX-2 is paramount to pain reduction, COX-1 plays an important role within homeostatic function and its inhibition can produce unwanted side-effects such as alterations in the functions of the stomach mucosal lining and decreased platelet coaggregation. These drugs can also significantly affect the action of other medication such as the anticoagulant, warfarin.

Although there are approximately 20 different types of NSAIDs available for prescription in the British National Formulary (and many more outside the formulary), the most extensively evaluated have been the non-selective COX inhibitors: aspirin, ibuprofen and diclofenac.

A meta-analysis assessing the efficacy of commonly provided analgesics found that 800 mg ibuprofen prescribed 6-8 hourly offered the most effective pain relief.¹¹ However, the dose-effectiveness relationship that relates to the prescription of ibuprofen also incurs the increased risks of adverse side effects. In general, effective analgesia is achieved with 400-600 mg of ibuprofen administered every 4-6 hours, but not exceeding 2,400 mg in a 24 hour period.¹¹ The analgesic efficacy of diclofenac is similar to that of ibuprofen and effective pain relief is reported with 50 and 100 mg of diclofenac taken every 4-6 hours.¹² There is evidence to

Fig. 1 An overview diagram, simplifying the mechanism of inflammatory pain

Table 1 Post-operative pain related to general and site-specific factors

General factors	Site specific
Gender (increased pain reported by females)	Increased numbers of implants
High anxiety levels	Placement within posterior regions
Smoking habits	Use of grafting techniques
	Extent of flap
	Operator technique
	Heat generation at surgical site

suggest that longer-term dosing of ibuprofen is associated with reduced gastric side effects than diclofenac¹³ and may also lead to severe complications within asthmatic patients.¹⁴ Both ibuprofen and diclofenac have been reported to offer more effective pain relief than aspirin.

To combat some of the unwanted effects of non-selective COX inhibition, selective (for example, rofecoxib and NS-389) and preferential COX-2 inhibitors (for example, etodolac, meloxicam, nimesulide, celecoxib) have been developed. Selective COX-2 inhibitors have also been shown to have minimal impact on platelet coaggregation or the anticoagulant effect of warfarin, in contrast to their non-selective counterparts.¹⁵ However, there has been controversy regarding selective COX-2 inhibitors and their use has been implicated with the increased risk of myocardial infarction. It is also worth considering that selective COX-2 inhibitors have not been shown to have greater pain-relieving efficacy than their non-selective counterparts and their gastric-protective advantages are likely to be limited, given the short

dosing-duration that could be expected in the management of post-implant placement pain. Given the aforementioned limitations and the considerable increased cost associated with their prescription, the use of COX-selective inhibitors is probably not justified for routine post-operative implant treatment and should be reserved for those where other medications are contra-indicated, such as patients suffering from chronic gastric conditions or asthma.

It is important to recognise that, although appropriate analgesia is crucial, management of post-operative pain should not be at the expense of either healing- or osseointegration- processes. While the inhibition of prostaglandins by NSAIDs may have useful anti-inflammatory effects, such as reducing swelling, it also poses a potentially detrimental effect on bone metabolism by impairing angiogenesis and osteoblast/osteoclast pre-cursor differentiation. Presently, there is still uncertainty regarding the extent to which NSAIDs interfere with the osseointegration process and this warrants consideration, if such drugs are

to be prescribed following dental implant placement. The interpretation of results from animal-based studies are inconclusive with some studies indicating that the use of selective and non-selective NSAIDs may affect osseointegration, particularly within the 21–28 day healing period,^{16–19} while other studies found no difference in longer-term healing outcomes.²⁰ The use of flubiprofen, a non-selective COX inhibitor, has been demonstrated to improve peri-implant bone deposition^{21,22} but these findings are unsupported by longer term clinical trials. Despite ongoing research within this field, it is still unclear whether short courses of NSAIDs, required for post-operative management, have a clinically relevant detrimental impact on implant osseointegration. Subsequently, no direct contraindicating advice can be given for the short-term prescription of such medications for the management of post-operative pain.

PARACETAMOL

Paracetamol exerts only a weak anti-inflammatory effect and is not considered to be a member of the NSAID family. The exact mechanism of action of paracetamol is poorly understood but it is believed to act both peripherally, via inhibition of the COX-2 enzyme, and also centrally, by inhibiting the reuptake of endogenous cannabinoid anandamide within sensory neurons. As regards the latter process, inhibited anandamide reuptake results in lower synaptic levels and reduced nociceptor activation. Either of these inhibitions by themselves has been shown to reduce pain but it has been demonstrated that paracetamol's analgesic effects are inhibited following the blocking of cannabinoid receptors with synthetic antagonists, suggesting that this is the drug's primary mode of action.

Although ibuprofen is generally regarded as a more effective analgesic,²³ paracetamol still has good pain-relieving properties and also fewer reported side effects. It is relevant that paracetamol has reduced impact on prostaglandin production and, therefore, poses less risk to the osseointegration process. The therapeutic dose of paracetamol has been established at approximately 1,000 mg to be taken every four hours with the maximum dose not to exceed 4,000 mg in a 24-hour period.²⁴ Patients should also be warned about the risk of hepatic failure in cases of overdose.

The combined use of NSAIDs and paracetamol has been demonstrated to have a synergistic effect on the management of post-operative dental pain²⁵ and combined regimes of these drugs should be considered if severe post-implant pain is anticipated.

There is no evidence to suggest that combining NSAIDs and paracetamol has an antagonistic action on osseointegration.

OPIOIDS

Painful stimuli are transmitted to the medullary region of the central nervous system via A-delta and C fibres within the trigeminal nerve. Subsequent regulation of this painful response is via a family of endogenous opioid peptides (met-enkephalin, dynorphin, beta-endorphin) that act on opiate receptors to suppress pain. Four types of opiate receptor have been categorised: mu, kappa, sigma and delta. The activation of mu and kappa receptors results in analgesia but can also cause euphoria and respiratory depression. Other unwanted side-effects such as constipation (sigma receptor activation) and altered behaviour (delta receptor activation) can also result from the administration of opioids. Although unlikely to be a factor within the shorter term management of post-implant pain, prolonged use of opiates is associated with increased risk of dependence and desensitisation of opioid receptors that can, in turn, reduce the pain-relieving effectiveness of these drugs.

Codeine (3-methylmorphine) is a member of the opiate family and its potency is one sixth of that of morphine. Codeine's mechanism of action is via the activation of opioid receptors. Codeine, as a sole drug, can be prescribed at strengths of 8, 15, 30 or 60 mg four times daily with a maximum dose of 360 mg in a 24-hour period. However, its pain-relieving effectiveness, when prescribed as a sole analgesic, is disputed with studies showing only minimal benefit for post-operative pain.²⁶ The side effects associated with codeine are dose related and include nausea, constipation and drowsiness.²³ It is advised that the prescription of Codeine is combined with either paracetamol (in ratios of 8/500, 12/500 or 30/500 mg) or ibuprofen (in ratios of 12/400) where it has a synergistic impact on relieving post-operative pain.^{23,27,28}

Tramadol is a synthetic analogue of codeine but has a reduced affinity for μ -opioid receptors while also having an action on 5-hydroxytryptamine–noradrenaline reuptake inhibitors (SNRIs).²⁹ Like codeine, its analgesic efficacy is improved when prescribed in combination with paracetamol.¹⁵ However, greater side effects associated with its use are reported and include: constipation, anxiety, seizure, tolerance and dependence. Although its use for post-operative dental pain is common within the United States, the drug courts controversy regarding the severity of its side effects. In the UK tramadol is not commonly prescribed for dental pain.

CORTICOSTEROIDS

Synthetic glucocorticosteroids are the primary type of corticosteroids that can be used to inhibit both immune and inflammatory responses. Glucocorticosteroids inhibit inflammatory pathways at multiple levels and their full mechanism of action is out with the realms of this paper. To summarise, the scope of glucocorticoid action is far less selective than that of NSAIDs and they inhibit the vascular and cellular inflammatory responses at multiple levels, in addition to impacting on the immune system (via inhibition of cytokine production). The analgesic effects exerted by the use of corticosteroids result from the inhibition of prostaglandins,³⁰ in a manner that is similar to that of NSAIDs. Corticosteroids such as cortisol, prednisolone and dexamethasone³¹ can be effectively used in the management of post-operative pain in fields such as endodontics and oral surgery. However, glucocorticosteroids have a profound action on osteoblast precursor cells^{22,32} and their use has been shown to reduce osteoblast adhesion to the implant surface,³³ therefore potentially compromising osseointegration. It can therefore not be recommended for post-operative implant pain management.

ADJUNCTS TO POST-OPERATIVE ANALGESIA

The use of prophylactic or single-dose analgesics, before the surgical procedure, to manage post-operative pain has been investigated but with inconclusive results. Ibuprofen, paracetamol (with or without codeine) and diclofenac taken prophylactically can reduce perceived pain in the immediate post-operative aftermath.³⁴ Similarly, post-operative single doses of ibuprofen or diclofenac have achieved 50% pain relief in one third of patients. However, single dose analgesics are rarely successful in achieving complete post-operative pain control and many patients will ultimately seek 'rescue' analgesics to mediate discomfort. The provision of single dose prophylactic- or post-operative analgesic does not serve as a predictable method of managing post-operative pain^{35,36} and it is advised that this form of medication should be seen as an adjunct to a more comprehensive post-operative analgesic regime.

Long acting local anaesthetics, such as bupivacaine, have also been recommended as a useful adjunct for the management of immediate post-operative pain.³⁷ They can provide up to eight hours of analgesia, affording the patient with ample time to commence their post-operative analgesic regime. However, prolonged anaesthesia of the oral tissues can interfere with function and may

also increase the risk of soft tissue trauma through accidental cheek or lip biting. These factors should be taken into consideration, if a long-acting local anaesthetic is to be used.

The use of alternative therapies for management of post-operative pain has been studied with techniques such as acupuncture,³⁸ electro-acupuncture,³⁹ traditional Chinese medicines, homeopathy (such as arnica) and herbal remedies, having been investigated. Much of the available evidence is of low quality and care should be taken if adopting such an approach for management of post-operative pain subsequent to implant placement.

CONCLUSION

A degree of post-operative pain can be expected following dental implant surgery and it is crucial that the clinician provides effective analgesia without compromising either healing or osseointegration of the dental implant. Table 2 summarises the advantages and disadvantages of each group of analgesics. Despite the undisputed analgesic efficacy of NSAIDs for managing post-surgical dental pain, there lies potential for these drugs to interfere with the healing/osseointegration process. Given this risk, it would therefore seem sensible to consider alternatives to the prescription of NSAIDs. The prescription of 1 g paracetamol four times daily has been shown to be effective when compared to NSAIDs, while incurring less risk to the osseointegration process. Paracetamol should therefore be considered as a first line post-operative analgesic. Enhanced analgesia can be obtained with the addition of codeine although, due to variable individual tolerances, codeine dosage should be assessed on a case-by-case basis. While 60 mg codeine combined with paracetamol four times daily offers optimal pain relief, this regime must be weighed against the potential for increased side effects. If in doubt, a reduced dosage of codeine should be adopted. Finally, further research is needed to evaluate the risk to the osseointegration process posed by commonly prescribed analgesics.

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Table 2 Summary of advantages/disadvantages associated with commonly employed analgesics in dental implant placement

Medication	Advantages	Disadvantages
NSAIDs Non-selective COX selective	Excellent pain relief Beneficial anti-inflammatory effects Cheap Excellent pain relief	Uncertain impact on osseointegration process Drug interactions Limited use in patients' suffering gastric conditions and asthmatics Expensive Concerns over side-effects
Paracetamol	Excellent pain relief Minimal impact on osseointegration process Inexpensive	No anti-inflammatory effects
Opioids	Good pain relief	Addiction No anti-inflammatory effects
Corticosteroids	Anti-inflammatory action	Non-selective inhibition of inflammatory response Reduction of osteoblast adhesion with potential compromise of osseointegration process

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