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Review

Management of postoperative pain in maxillofacial surgery

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Abstract

In this review we describe the evidence base for postoperative analgesia after maxillofacial surgery. We discuss the implications of poorly managed pain, risk factors for the development of severe pain, and pharmacological and non-pharmacological analgesic strategies to manage it.

Keywords: Postoperative pain; risk factors; acute pain; analgesia; surgery; postsurgical pain

Introduction

Clinicians have an ethical obligation to minimise pain,[1] which is defined as *"an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"*.[2] Roughly 80% of patients report moderate or severe pain after oromaxillofacial surgery.[3] We therefore present arguments for the optimisation of postoperative analgesia; we identify patients at high risk of developing severe postoperative pain, and discuss analgesic strategies.

Importance of optimising the management of postoperative pain

Patient-related outcomes

In the United Kingdom, 48% of patients experience moderate or severe postoperative pain, and they rate it as the second worst aspect of their operation after anxiety.[4] It impairs physical function, reduces quality of life and sleep[5] and, when severe, is predictive of dissatisfaction with anaesthesia services.

Pathophysiological consequences of acute pain

Severe, acute, postoperative pain increases the risk of the pain becoming chronic.[6,7] Continuous or repetitive nociceptive stimuli create a hyperexcitable state with exaggerated responses to stimuli and neuroplastic changes that magnify the transmission of pain (allodynia and hyperalgesia).[8] Evidence shows that up to 21% of orthognathic patients continue to feel pain one year after operation.[9]

Painful stimuli activate the surgical stress response. This initiates a cascade of pathophysiological changes that adversely affect many systems in the body and are detrimental to surgical outcomes.[10] Analgesia variably attenuates this response, and depends on the type of operation, drug, and mode of delivery. Regional analgesia with local anaesthetic drugs reduces it most, though much of this work has examined the effect in major abdominal or thoracic surgery.[11] The extraction of wisdom teeth under local anaesthesia, however, is associated with a reduction in the secretion of salivary cortisol when compared with general anaesthesia alone.[12]

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Table 1
Risk factors for severe postoperative pain.[4,17–20]

Patient factors	Surgical factors
Chronic pain/ pre-existing acute pain	Major operations
Preoperative use of opioid analgesics	Nature of operation (bony work > soft tissue)
Preoperative use of antineuropathic analgesics such as gabapentin	Duration of operation
Anxiety and depression	Cancer operations
Fear of surgery	Urgent operations
Catastrophisation of pain	
Age (18–65 years)	
Obesity	
Female sex	

Hospital-related outcomes

Postoperative pain lengthens the duration of hospital stay and associated costs.[13,14] In a study of day-case surgery, 38% of patients who returned to hospital reported that uncontrolled pain was the principle reason for doing so.[15]

Risk factors for severe postoperative pain (Table 1)

Preoperative recognition of patients who are "at risk" allows for timely multidisciplinary intervention, such as rationalisation and optimisation of pre-existing analgesic medication. A patient-centred, collaborative approach gives patients the time to develop realistic expectations, and to be educated about the treatment of severe pain[16] (Table 1[4,17–20]).

Strategies for the management of postoperative pain (Table 2)

Pharmacological

Simple analgesics
These include paracetamol, non-steroidal anti-inflammatory drugs (NSAID), and COX-2 inhibitors.

In a recent Cochrane review that re-examined the effect of single-dose oral analgesics on moderate or severe pain,[21] most of the data were derived from patients who had third molars extracted (Table 3). In broad terms, the number needed to treat (NNT) was lower (better) for increased dosage and for pairs of analgesics. For example, patients who were prescribed NSAID together with paracetamol reported a three-fold reduction in pain and need for analgesic supplementation when compared with either drug taken alone.[22] Unless contraindicated, this combination should be considered in all postoperative patients.[23]

Chronic NSAID-mediated inhibition of the COX-1 isozyme can adversely affect the upper or lower gastrointestinal, renal, and cardiovascular systems, and platelet aggregation. Gastric erosions occur in roughly half the patients who take NSAID regularly, and up to 30% of them

Table 2
Strategies for the management of postoperative pain.

Pharmacological:
Prevention of nociceptive input at the surgical site
Blockade of nociceptive impulse along peripheral nerves
Prevention of sensitisation
Multimodal analgesia
Psychological & physical:
Relaxation
Hilotherapy
Acupuncture
Organisational:
Acute pain pathways
Acute pain teams

Table 3
Number needed to treat (NNT) to achieve at least 50% reduction in maximal postoperative pain (moderate or severe) over 4–6 hours.[21] NNT of 2–5 is considered useful.

Single dose analgesic		NNT (95% CI)
Ibuprofen 400 mg + Paracetamol 1000 mg	BEST	1.5 (1.4 to 1.7)
Ibuprofen 200 mg + Paracetamol 500 mg		1.6 (1.5 to 1.8)
Paracetamol 1000 mg + Oxycodone 10 mg		1.8 (1.6 to 2.2)
Diclofenac potassium 100 mg		1.9 (1.7 to 2.3)
Diclofenac potassium 50 mg		2.1 (1.9 to 2.5)
Ibuprofen 400 mg		2.1 (1.9 to 2.3)
Paracetamol 1000 mg + Codeine 60 mg		2.2 (1.8 to 2.9)
Ibuprofen 400 mg + Oxycodone 5 mg		2.3 (2.0 to 2.8)
Naproxen 500 mg		2.7 (2.3 to 3.3)
Paracetamol 1000 mg		3.6 (3.2 to 4.1)
Tramadol 100 mg		4.6 (3.6 to 6.4)
Tramadol 50 mg		9.1 (6.1 to 19)
Codeine 60 mg	WORST	12 (8.4 to 18)

have ulcers that are visible at endoscopy.[24] This risk can be reduced by concurrent use of proton pump inhibitors such as omeprazole, and the substitution of NSAID by COX-2 inhibitors such as celecoxib.[25] Upper gastrointestinal events occur in 3%–4.5% of patients, and are serious in about 1.5%. Predisposing factors include previous ulceration, increasing age (over 65 years), concurrent anticoagulation treatment, coexisting corticosteroids, and increasing doses of NSAID.[24,26]

Adverse renal effects develop in about 1%–5% of patients who take NSAID, and this accounts for roughly 15% of those with drug-induced acute renal failure.[27] As NSAID inhibit the synthesis of vasodilatory renal prostaglandins, which is normally increased to preserve renal perfusion in cases of hypotension or hypovolaemia, their use can lead to periop-

erative acute kidney injury, and may worsen the progression of chronic renal failure. Patients at risk include those with pre-existing renal impairment, hypovolaemia, heart failure, cirrhosis, multiple myeloma, and those who are taking ACE-inhibitors, angiotensin II receptor antagonists, or diuretics.[28]

Opioid analgesics

Opioids are required to treat moderate to severe postoperative pain and should be viewed as a course of treatment that will be reduced as appropriate.[29] Their acute side effects include nausea, constipation, itching, drowsiness, respiratory depression, and death from overdose. In the United Kingdom, the prescription of strong opioids for chronic non-cancer pain has increased considerably since the year 2000,[30] and Public Health England has funded the Opioids Aware resource,[31] which aims to help both patients and prescribers make informed decisions about their use.

Weak opioids

In UK practice, these include codeine phosphate and its analogue tramadol, both of which have a relative potency of 0.1 compared with morphine.[32] Neither is particularly useful as a sole oral analgesic (Table 3). Variable rates in the metabolism of codeine are problematic, with those who metabolise it slowly getting little relief, and those who metabolise it quickly experiencing severe adverse events such as respiratory depression. Codeine is contraindicated in any patient known to metabolise CYP2D6 ultra-rapidly, and in children under 12 years of age.[33] Tramadol is contraindicated in patients with poorly controlled epilepsy because of its excitatory serotonergic effects.

Strong opioids

Morphine, oxycodone, and fentanyl are commonly prescribed in the UK for postoperative analgesia. Oxycodone has a relative potency of 1.5–2 times that of morphine.[32] Fentanyl is 10 times more potent than morphine,[32] and has a substantial potential for respiratory depression when high doses are given.

Strong opioids are typically delivered intravenously as patient-controlled analgesia, or orally, as slow and immediate-release preparations (oxycodone and morphine). Transdermal delivery is not suitable for the relief of acute pain because of the slow onset of action and lack of rapid titratability. Patient-controlled opioids given intravenously confer little advantage over those taken orally, so should be used only when parenteral delivery is required.[34]

Chronic use of opioids

Chronic use of opioids gives rise to drug tolerance, physical dependence, and addiction.[35] These patients have higher pain scores both when active and when at rest, they require more postoperative analgesia, and also have a high risk of severe, acute, postoperative pain and of it becoming chronic.[6,7,36] They must be given their usual dose to meet their chronic need for analgesia, plus additional doses to treat their acute pain. A multidisciplinary approach to postoperative analgesia in these cases is essential, and should begin preoperatively.

It is important to assess the efficacy of the analgesic regimen so that it can be optimised preoperatively. The continuation of transdermal opioid patches perioperatively is controversial, as the rate at which the drug is delivered may be increased when the patient is warmed during surgery, but may be reduced if the patch is placed on poorly-perfused skin. Also, high doses of buprenorphine, a partial μ-opioid agonist, may antagonise full μ-opioid agonists such as morphine, and lead to analgesic failure and withdrawal. Current thinking is that buprenorphine delivered transdermally (less than 70 $\mu g/hour^{-1}$) is unlikely to interfere with full opioid agonists that are used to treat acute postoperative pain.

In summary, the transdermal delivery of fentanyl and buprenorphine should be continued perioperatively, with the postoperative addition of opioids given orally or as patient-controlled analgesia.[36] If patches are stopped preoperatively, they must be replaced in a graded fashion by immediate-release opioids given orally, which can take up to 72 hours.

Opioid-induced hyperalgesia

Opioid-induced hyperalgesia presents as an increased response to a painful stimulus (hyperalgesia), or a painful response to a non-painful stimulus (allodynia), or both. In contrast to opioid tolerance, its onset may be abrupt, and increased doses will exacerbate pain.

Data suggest that only remifentanil is associated with opioid-induced hyperalgesia that can be measured postoperatively.[37] Specifically, its intraoperative use in high doses is associated with more intense pain at rest, and a moderate increase in the need for morphine during the first 24 hours postoperatively.[37] It is therefore sensible to reduce the dosage by using additional opioid-sparing techniques such as local anaesthetic or NSAID.

Local anaesthetic

Regional anaesthetic techniques are well established in maxillofacial practice, and many branches of the trigeminal nerves are amenable to peripheral blockade with local anaesthetics. These are recommended as part of a multimodal approach to postoperative analgesia, and are strongly recommended for techniques that are specific to the surgical site.[34] Continuous delivery through a catheter is preferable to a single-bolus dose if the duration of postoperative pain is likely to be longer than the duration of action of the drug used – for example, when harvesting rib grafts.[38] Table 4[39–56] summarises the techniques used in maxillofacial practice to provide or to supplement postoperative analgesia.

Intravenous infusion of lidocaine during operation has been used to reduce the requirement for perioperative opioids. A recent meta-analysis showed that when given perioperatively, pain scores improved after operation for up to 24 hours (open/laparoscopic abdominal surgery only), and there were reductions in the consumption of opioids, postoperative nausea and vomiting, and duration of stay.[57] Lidocaine given in

Table 4
Regional anaesthetic techniques used in maxillofacial practice for postoperative analgesia.[39–56]

Target or local anaesthetic (LA) technique, or both	Study	Outcome, findings, & comment
Inferior alveolar nerve block + buccal infiltration[39]	Split mouth, randomised Bilateral 3rd molar extraction under GA 2% lidocaine (1:80000 adrenaline) cf control (n = 52) 2% lidocaine (1:80000 adrenaline) cf 0.5% bupivacaine (n = 68)	2% lidocaine (1:80000 adrenaline) improves pain VAS compared with control. Pain VAS significantly lower for 0.5% bupivacaine at 3 – 8 hours postoperatively compared with 2% lidocaine (1:80000 adrenaline); no difference thereafter. Patients preferred bupivacaine over lidocaine
Dental LA:[40] Intraligamental injection Topical Infiltration	Cochrane review of use of dental LA in patients < 17 years (n = 1152)	Unable to establish effect because of clinical and methodological heterogeneity of studies
Anterior iliac crest donor site[41–46]	Triple blind RCT of 0.5% bupivacaine:[47] Single shot femoral nerve block Single shot subcutaneous injection Repeated bolus through subperiosteal catheter	Subperiosteal delivery of bupivacaine through catheter has considerable benefits with respect to dynamic analgesia, at-rest analgesia, and time to first mobilisation.
	RCT of 0.2% ropivacaine (n = 17) cf 0.25% bupivacaine (n = 17) infusions through periosteal catheter[48]	0.2% ropivacaine provides comparable analgesia to 0.25% bupivacaine
	Retrospective cohort study:[49] –Bupivacaine infiltration (n = 89) –Bupivacaine infiltration + bupivacaine-soaked absorbable sponge (BAS), (n = 118)	Compared with infiltration alone, BAS + infiltration offered considerable benefits in terms of acute pain, need for opioids, time to first mobilisation, and duration of stay No studies have compared catheter-based techniques with BAS.
Mandibular nerve block (MNB)	Blinded RCT of preinduction MNB (n = 21) cf control (n = 21) in patients having partial glossectomy or transmandibular lateral pharyngectomy.[50]	MNB reduced mean consumption of opioids by 56% and 45% at 12 hours and 24 hours, respectively, postoperatively. The incidence of severe pain was significantly lower in the MNB group on the first postoperative day (3 cf 10).
	Pilot study of preoperative MNB in patients with unilateral mandibular angle fracture (n = 6).[51]	Trismus relieved, and a 12-fold reduction in VAS pain scores after MNB block.
Maxillary nerve block	Double-blind RCT of bilateral suprazygomatic maxillary nerve block with 0.2% ropivacaine cf placebo for cleft palate repair in children (n = 60).[52]	The cumulative dose of intravenous morphine at 48 hours postoperatively was 50% less in the maxillary nerve block group.
Infraorbital nerve block	Cochrane review of infraorbital nerve block in cleft lip repair (n = 353).[53]	Low to very low quality evidence that infraorbital nerve block reduces postoperative pain more than placebo or intravenous analgesia.
	Retrospective study of infraorbital nerve block + subciliary infiltration to provide anaesthesia for isolated orbital floor fracture (n = 135).[54]	Able to assess globe movement during operation. Conversion to general anaesthesia in four patients. Mean VAS for pain and discomfort <20 at 1 hour and 24 hours postoperatively. Infraorbital nerve block may also provide analgesia for endoscopic sinus surgery, nasal septal surgery, and trans-sphenoidal hypophysectomy.[55]
Scalp nerve block:	Meta-analysis of 7 RCT (n = 320) of scalp nerve block for pain after craniotomy.[56]	Studies are of limited methodological quality. However, postoperative pain is consistently reduced by scalp nerve block. This is associated with a concomitant reduction in opioid use in the first 24 hours postoperatively.

Table 4 (*Continued*)

Target or local anaesthetic (LA) technique, or both	Study	Outcome, findings, & comment
Supratrochlear nerve		
Supraorbital nerve		
Auriculotemporal nerve		
Great auricular nerve		
Greater, lesser & 3rd occipital nerves		
Other blocks:[55]		
Palatine nerves – analgesia for cleft palate repair		
Mental nerve – analgesia for surgery on lower lip, skin of chin		
Superficial cervical plexus – anaesthesia of external pinna, post-auricular, & temporoparietal areas of scalp, anterior neck & supraclavicular region		

cf = compared with; LA = local anaesthetic; GA = general anaesthetic; RCT = randomised controlled trial; VAS = visual analogue scale.

this way during bimaxillary osteotomy reduced postoperative pain scores for eight hours, and also the need for rescue analgesia.[58]

Local anaesthetic toxicity is associated with neurological and cardiac side effects that progress from circumoral tingling to tonic-clonic convulsions, and then to cardiac arrhythmia and cardiac arrest. The risk can be reduced considerably if doses are within advised limits [59] and susceptible patients are identified (those with reduced α-1 antitrypsin concentrations, the elderly, children, and women who are pregnant).

Ketamine

Ketamine antagonises the N-methyl D-aspartate (NMDA) receptor that mediates central sensitisation because of nociceptive stimuli. As such, it reduces the intensity of pain, the requirement for rescue analgesia, consumption of patient-controlled opioids, and postoperative nausea and vomiting; and its effects last beyond its pharmacological duration of action.[60,61] The risk of psychomimetic effects is minimised if doses are less than 0.5 mg/kg.[62] Ketamine therefore is increasingly used in anaesthetic practice (particularly for painful operations) and may be particularly helpful in opioid-tolerant patients because it can lessen their requirement for these drugs, and can have a beneficial effect on opioid-induced hyperalgesia.[63,64] In dental practice, ketamine 0.5 mg/kg considerably reduces postoperative pain after the extraction of third molars whether it is given topically, submucosally, or intravenously.[65–67]

Gabapentinoids

Gabapentin and pregabalin are known to have antineuropathic analgesic effects, and are purported to have analgesic benefit to patients at risk of severe acute postoperative pain.[68,69] However, two meta-analyses of the perioperative use of gabapentin and pregabalin showed only marginal improvements in postoperative analgesia that was associated with an increased risk of serious adverse events – for example, oversedation.[70,71] Two studies of patients who had bimaxillary surgery (n = 60 patients) reported a reduction in postoperative pain scores and requirements for opioids with pre-emptive pregabalin.[72,73] Nevertheless, there is little robust evidence to support the routine postoperative use of gabapentinoids, although they may be considered when benefit is felt to outweigh risk.

Corticosteroids

Corticosteroids, such as dexamethasone and methylprednisolone, given perioperatively, have been shown to reduce postoperative pain and swelling in orthognathic and third molar surgery, with minimal risk of adverse sequelae.[74–76]

α2 adrenoceptor agonists

Two commonly used α2 adrenoceptor agonists are dexmedetomidine and clonidine. Their activation of α2 adrenoceptors in the central and peripheral nervous systems inhibits the transmission of pain and sympathetic activity. Pharmacologically, they produce anxiolysis, analgesia, sympatholysis, sedation, and hypnosis. A meta-analysis of 30 randomised controlled trials (n = 1792) in 2012 found that both these drugs, when given orally or intravenously, reduced the postoperative consumption of morphine for the first 24 hours by 25% and 30%, respectively.[77] In turn, visual analogue scores for acute pain were considerably reduced by both drugs, but this benefit was lost by 48 hours postoperatively. The meta-analysis, however, could not establish optimal dosing regimens for either drug because of the heterogeneity of the studies included.

More recently, the POISE-2 trial (n = 10010) showed that clonidine was associated with clinically significant hypotension and bradycardia.[78] In a planned subanalysis, the authors found that clonidine 0.2 mg given orally was not associated with improved pain scores or consumption of morphine; higher doses may provide an analgesic benefit, but this would probably be associated with unwanted hypotension and bradycardia.[79] When the data were added to the previous meta-analysis, no analgesic benefit was associated with

clonidine perioperatively, so this use could not be justified. In contrast, a 2013 meta-analysis of 28 randomised controlled trials (n = 1420) reaffirmed that intraoperative dexmedetomidine reduced postoperative pain and consumption of opioids, though there was an association with bradycardia.[80]

Psychological and physical

Relaxation
Further studies are necessary to establish whether relaxation techniques have a role in the management of postoperative pain.[81–83]

Hilotherapy
Hilotherapy, which is the application of cold compression through a facemask at a regulated temperature of 15 °C, significantly reduces pain and swelling at 48–72 hours postoperatively.[84,85] Clinical trials are required to establish its efficacy for specific procedures and the optimal duration of treatment.

Acupuncture
In a meta-analysis of 15 studies, acupuncture significantly reduced postoperative pain scores and consumption of opioids (29% reduction in morphine consumption at 72 hours);[86] three of these studies were of patients treated by oral and maxillofacial surgery.

Organisational

The availability and engagement of well-resourced acute pain services has the greatest potential to benefit patients who have moderate or severe pain.[87] Acute pain teams should target those most at risk, as this has the greatest potential to alleviate distress.[88]

Summary

Acute postoperative pain is a problem that has a considerable impact on the patient and the wider healthcare system.[89] Overall, the evidence favours a multimodal approach to analgesia, which is defined as the use of two or more analgesics with different modes of action through the same or different mode of delivery.[34] The early identification of patients at risk, coordinated multidisciplinary intervention, and multimodal analgesia, can considerably reduce the burden of postoperative pain, and could lead to a reduction in postoperative complications, distress, duration of stay, and the risk of developing chronic postsurgical pain.[90,91]

Conflict of interest

SWE: I have no conflicts of interest.

RAM: Received bench models for surgical airway training and an honorarium from AMBU UK Ltd in exchange for consultation work on the AMBU aScope 3 & 4.

Ethics statement/confirmation of patients' permission

Not applicable.

References

1. Domain 1: Knowledge, skills and performance. In: *Good Medical Practice.* London: General Medical Council; 2013, p.8. Available from URL: https://www.gmc-uk.org/-/media/documents/good-medical-practice—english-1215_pdf-51527435.pdf (last accessed 7 November 2018).
2. Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *Pain* 1979;**6**:249–52.
3. Coulthard P, Haywood D, Tai MA, et al. Treatment of postoperative pain in oral and maxillofacial surgery. *Br J Oral Maxillofac Surg* 2000;**38**:588–92.
4. Walker EM, Bell M, Cook TM, et al. Patient reported outcome of adult perioperative anaesthesia in the United Kingdom: a cross-sectional observational study. *Br J Anaesth* 2016;**117**:758–66.
5. Sinatra R. Causes and consequences of inadequate management of acute pain. *Pain Med* 2010;**11**:1859–71.
6. Pluijms WA, Steegers MA, Verhagen AF, et al. Chronic post-thoracotomy pain: a retrospective study. *Acta Anaesthesiol Scand* 2006;**50**:804–8.
7. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. *Anesthesiology* 2000;**93**:1123–33.
8. Feizerfan A, Sheh G. Transition from acute to chronic pain. *Contin Educ Anaesth Crit Care Pain* 2015;**15**:98–102.
9. Luo Y, Svensson P, Jensen JD, et al. Quantitative sensory testing in patients with or without ongoing pain one year after orthognathic surgery. *J Oral Facial Pain Headache* 2014;**28**:306–16.
10. Desborough JP. The stress response to trauma and surgery. *Br J Anaesth* 2000;**85**:109–17.
11. Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. *Br J Anaesth* 2001;**87**:62–72.
12. Hill CM, Walker RV. Salivary cortisol determinations and self-rating scales in the assessment of stress in patients undergoing the extraction of wisdom teeth. *Br Dent J* 2001;**191**:513–5.
13. Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiol Clin North Am* 2005;**23**:21–36.
14. Stephens J, Laskin B, Pashos C, et al. The burden of acute postoperative pain and the potential role of the COX-2-specific inhibitors. *Rheumatology* 2003;**42**(Suppl. 3):iii40–52, http://dx.doi.org/10.1093/rheumatology/keg497.
15. Coley KC, Williams BA, DaPos SV, et al. Retrospective evaluation of unanticipated admissions and readmissions after same day surgery and associated costs. *J Clin Anesth* 2002;**14**:349–53.
16. Dykstra KM. Perioperative pain management in the opioid-tolerant patient with chronic pain: an evidence-based practice project. *J Perianesth Nurs* 2012;**27**:385–92.
17. Sommer M, de Rijke JM, van Kleef M, et al. Predictors of acute postoperative pain after elective surgery. *Clin J Pain* 2010;**26**:87–94.
18. Dahmani S, Dupont H, Mantz J, et al. Predictive factors of early morphine requirements in the post-anaesthesia care unit (PACU). *Br J Anaesth* 2001;**87**:385–9.
19. Ip HY, Abrishami A, Peng PW, et al. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology* 2009;**111**:657–77.

20. Macintyre PE, Jarvis DA. Age is the best predictor of postoperative morphine requirements. *Pain* 1996;**64**:357–64.
21. Moore RA, Derry S, Aldington D, et al. Single dose oral analgesics for acute postoperative pain in adults – an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2015;(9):CD008659, http://dx.doi.org/10.1002/14651858.CD008659.pub3.
22. Ong CK, Seymour RA, Lirk P, et al. Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: a qualitative systematic review of analgesic efficacy for acute postoperative pain. *Anesth Analg* 2010;**110**:1170–9.
23. Gupta A, Bah M. NSAIDs in the treatment of postoperative pain. *Curr Pain Headache Rep* 2016;**20**:62.
24. Laine L. Approaches to nonsteroidal anti-inflammatory drug use in the high-risk patient. *Gastroenterology* 2001;**120**:594–606.
25. Momeni M, Katz JD. Mitigating GI risks associated with the use of NSAIDs. *Pain Med* 2013;**14**:S18–22.
26. Laine L, Curtis SP, Cryer B, et al. Risk factors for NSAID-associated upper GI clinical events in a long-term prospective study of 34701 arthritis patients. *Aliment Pharmacol Ther* 2010;**32**:1240–8.
27. Whelton A. Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications. *Am J Med* 1999;**106**:13S–24S.
28. *Non-steroidal anti-inflammatory drugs (NSAIDS): reminder on renal failure and impairment*. Medications and Healthcare Products Regulatory Agency; 2009. Available from URL: https://www.gov.uk/drug-safety-update/non-steroidal-anti-inflammatory-drugs-nsaids-reminder-on-renal-failure-and-impairment (last accessed 7 November 2018).
29. Hermanowski J, Levy N, Mills P, et al. Deprescribing: implications for the anaesthetist. *Anaesthesia* 2017;**72**:565–9.
30. Zin CS, Chen LC, Knaggs RD. Changes in trends and pattern of strong opioid prescribing in primary care. *Eur J Pain* 2014;**18**:1343–51.
31. Opioids aware: a resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. Royal College of Anaesthetists Faculty of Pain Medcine. London: The Royal College of Anaesthetists, 2015. Available from URL: https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware. (last accessed 7 November 2018).
32. Medicines guidance. Prescribing in palliative care. In: British National Formulary. National Institute for Health and Care Excellence. Available from URL: https://bnf.nice.org.uk/guidance/prescribing-in-palliative-care.html. (last accessed 7 November 2018).
33. Drugs – codeine phosphate. In: British National Formulary. National Institute for Health and Care Excellence. Available from URL: https://bnf.nice.org.uk/drug/codeine-phosphate.html. (last accessed 7 November 2018).
34. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016;**17**:131–57.
35. Coluzzi F, Bifulco F, Cuomo A, et al. The challenge of perioperative pain management in opioid-tolerant patients. *Ther Clin Risk Manag* 2017;**13**:1163–73.
36. Simpson GK, Jackson M. Perioperative management of opioid-tolerant patients. *BJA Educucation* 2017;**17**:124–8.
37. Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. *Br J Anaesth* 2014;**112**:991–1004.
38. Anantanarayanan P, Raja DK, Kumar JN, et al. Catheter-based donor site analgesia after rib grafting: a prospective, randomized, double-blinded clinical trial comparing ropivacaine and bupivacaine. *J Oral Maxillofac Surg* 2013;**71**:29–34.
39. McCarthy C, Warren E, Sleeman D. Comparison of anaesthetic regime in patients undergoing third molar extraction. *Oral Surg* 2018;**11**:33–40.
40. Parekh S, Gardener C, Ashley PF, et al. Intraoperative local anaesthesia for reduction of postoperative pain following general anaesthesia for dental treatment in children and adolescents. *Cochrane Database Syst Rev* 2014;**12**:CD009742.
41. Barkhuysen R, Meijer GJ, Soehardi A, et al. The effect of a single dose of bupivacaine on donor site pain after anterior iliac crest bone harvesting. *Int J Oral Maxillofac Surg* 2010;**39**:260–5.
42. Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technic of lumbar plexus anesthesia: the "3-in-1 block". *Anesth Analg* 1973;**52**:989–96.
43. Cook AC, Valchanov KP, Oosthuysen SA. Psoas sheath block for providing analgesia for iliac crest donor site pain. *Acute Pain* 2004;**6**:79–81.
44. Liu SS, Richman JM, Thirlby RC, et al. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: a quantitative and qualitative systematic review of randomized controlled trials. *J Am Coll Surg* 2006;**203**:914–32.
45. Wilson PA. Pain relief following iliac crest bone harvesting. *Br J Oral Maxillofac Surg* 1995;**33**:242–3.
46. Kennedy BD, Hiranaka DK. Use of a modified epidural catheter for analgesia after iliac crest bone procurement. *J Oral Maxillofac Surg* 1995;**53**:342–3.
47. Kumar Raja D, Anantanarayanan P, Christabel A, et al. Donor site analgesia after anterior iliac bone grafting in paediatric population: a prospective, triple-blind, randomized clinical trial. *Int J Oral Maxillofac Surg* 2014;**43**:422–7.
48. Kukidome H, Matsuura N, Kasahara M, et al. Continuous postoperative pain control using a multiple-hole catheter after iliac bone grafting: comparison between ropivacaine and levobupivacaine. *Int J Oral Maxillofac Surg* 2016;**45**:454–9.
49. Dashow JE, Lewis CW, Hopper RA, et al. Bupivacaine administration and postoperative pain following anterior iliac crest bone graft for alveolar cleft repair. *Cleft Palate Craniofac J* 2009;**46**:173–8.
50. Plantevin F, Pascal J, Morel J, et al. Effect of mandibular nerve block on postoperative analgesia in patients undergoing oropharyngeal carcinoma surgery under general anaesthesia. *Br J Anaesth* 2007;**99**:708–12.
51. Heard AM, Green RJ, Lacquiere DA, et al. The use of mandibular nerve block to predict safe anaesthetic induction in patients with acute trismus. *Anaesthesia* 2009;**64**:1196–8.
52. Chiono J, Raux O, Bringuier S, et al. Bilateral suprazygomatic maxillary nerve block for cleft palate repair in children: a prospective, randomized, double-blind study versus placebo. *Anesthesiology* 2014;**120**:1362–9.
53. Feriani G, Hatanaka E, Torloni MR, et al. Infraorbital nerve block for postoperative pain following cleft lip repair in children. *Cochrane Database Syst Rev* 2016;**4**:CD011131.
54. Spinelli G, Rocchetta D, Carnevali G, et al. Infraorbital nerve block for isolated orbital floor fractures repair: review of 135 consecutuve cases. *Plast Reconstr Surg Glob Open* 2014;**2**:e97.
55. Suresh S, Voronov P. Head and neck blocks in children: an anatomical and procedural review. *Pediatr Anesth* 2006;**16**:910–8.
56. Guilfoyle MR, Helmy A, Duane D, et al. Regional scalp block for postcraniotomy analgesia: a systematic review and meta-analysis. *Anesth Analg* 2013;**116**:1093–102.
57. Kranke P, Jokinen J, Pace NL, et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane Database Syst Rev* 2015;(7):CD009642.
58. Lee U, Choi YJ, Choi GJ, et al. Intravenous lidocaine for effective pain relief after bimaxillary surgery. *Clin Oral Investig* 2017;**21**:2645–52.
59. Christie LE, Picard J, Weinberg GL. Local anaesthetic systemic toxicity. *BJA Educ* 2015;**15**:136–42.
60. Wu CL, Raja SN. Treatment of acute postoperative pain. *Lancet* 2011;**377**:2215–25.
61. Bell RF, Dahl JB, Moore RA, et al. Perioperative ketamine for acute postoperative pain. *Cochrane Database Syst Rev* 2006;**1**:CD004603.
62. Gorlin AW, Rosenfeld DM, Ramakrishna H. Intravenous sub-anesthetic ketamine for perioperative analgesia. *J Anaesthesiol Clin Pharmacol* 2016;**32**:160–7.

63. Farrington M, Hanson A, Laffoon T, et al. Low-dose ketamine infusions for postoperative pain in opioid-tolerant orthopaedic spine patients. *J Perianesth Nurs* 2015;**30**:338–45.
64. Barreveld AM, Correll DJ, Liu X, et al. Ketamine decreases postoperative pain scores in patients taking opioids for chronic pain: results of a prospective, randomized, double-blind study. *Pain Med* 2013;**14**:925–34.
65. Landari E, Hustveit O, Trumpy IG, et al. Ketamine as single dose analgesics on acute postoperative pain in both genders following surgical removals of third molars. *J Oral Maxillofac Surg* 2013;**71**:e38.
66. Gönül O, Satilmiş T, Ciftci A, et al. Comparison of the effects of topical ketamine and tramadol on postoperative pain after mandibular molar extraction. *J Oral Maxillofac Surg* 2015;**73**:2103–7.
67. Hadhimane A, Shankariah M, Neswi KV. Pre-emptive analgesia with ketamine for relief of postoperative pain after surgical removal of impacted mandibular third molars. *J Maxillofac Oral Surg* 2016;**15**:156–63.
68. Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. *Br J Anaesth* 2011;**106**:454–62.
69. Ramaswamy S, Wilson JA, Colvin L. Non-opioid-based adjuvant analgesia in perioperative care. *Contin Educ Anaesth Crit Care Pain* 2013;**13**:152–7.
70. Fabritius ML, Geisler A, Petersen PL, et al. Gabapentin for post-operative pain management – a systematic review with meta-analyses and trial sequential analyses. *Acta Anaesthesiol Scand* 2016;**60**:1188–208.
71. Fabritius ML, Strøm C, Koyuncu S, et al. Benefit and harm of pregabalin in acute pain treatment: a systematic review with meta-analyses and trial sequential analyses. *Br J Anaesth* 2017;**119**:775–91.
72. Cillo Jr JE, Dattilo DJ. Pre-emptive analgesia with pregabalin and celecoxib decreases postsurgical pain following maxillomandibular advancement surgery: a randomized controlled clinical trial. *J Oral Maxillofac Surg* 2014;**72**:1909–14.
73. Ahiskalioglu A, Ince I, Aksoy M, et al. Effects of a single-dose of preemptive pregabalin on postoperative pain and opioid consumption after double-jaw surgery: a randomized controlled trial. *J Oral Maxillofac Surg* 2016;**74**:53, e1-7.
74. Lima CA, Favarini VT, Torres AM, et al. Oral dexamethasone decreases postoperative pain, swelling, and trismus more than diclofenac following third molar removal: a randomized controlled clinical trial. *Oral Maxillofac Surg* 2017;**21**:321–6.
75. Dan AE, Thygesen TH, Pinholt EM. Corticosteroid administration in oral and orthognathic surgery: a systematic review of the literature and meta-analysis. *J Oral Maxillofac Surg* 2010;**68**:2207–20.
76. Ngeow WC, Lim D. Do corticosteroids still have a role in the management of third molar surgery? *Adv Ther* 2016;**33**:1105–39.
77. Blaudszun G, Lysakowski C, Elia N, et al. Effect of perioperative systemic α2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2012;**116**:1312–22.
78. Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. *N Engl J Med* 2014;**370**:1504–13.
79. Turan A, Babazade R, Kurz A, et al. Clonidine does not reduce pain or opioid consumption after noncardiac surgery. *Anesth Analg* 2016;**123**:749–57.
80. Schnabel A, Meyer-Frießem CH, Reichl SU, et al. Is intraoperative dexmedetomidine a new option for postoperative pain treatment? A meta-analysis of randomized controlled trials. *Pain* 2013;**154**:1140–9.
81. Seers K, Carroll D. Relaxation techniques for acute pain management: a systematic review. *J Adv Nurs* 1998;**27**:466–75.
82. Kwekkeboom KL, Gretarsdottir E. Systematic review of relaxation interventions for pain. *J Nurs Scholarsh* 2006;**38**:269–77.
83. de Jong AE, Gamel C. Use of a simple relaxation technique in burn care: literature review. *J Adv Nurs* 2006;**54**:710–21.
84. Glass GE, Waterhouse N, Shakib K. Hilotherapy for the management of perioperative pain and swelling in facial surgery: a systematic review and meta-analysis. *Br J Oral Maxillofac Surg* 2016;**54**:851–6.
85. Bates AS, Knepil GJ. Systematic review and meta-analysis of the efficacy of hilotherapy following oral and maxillofacial surgery. *Int J Oral Maxillofac Surg* 2016;**45**:110–7.
86. Sun Y, Gan TJ, Dubose JW, et al. Acupuncture and related techniques for postoperative pain: a systematic review of randomized controlled trials. *Br J Anaesth* 2008;**101**:151–60.
87. Sussman M, Goodier E, Fabri I, et al. Clinical benefits, referral practice and cost implications of an in-hospital pain service: results of a service evaluation in a London teaching hospital. *Br J Pain* 2017;**11**:36–45.
88. Lee A, Chan SK, Chen PP, et al. The costs and benefits of extending the role of the acute pain service on clinical outcomes after major elective surgery. *Anesth Analg* 2010;**111**:1042–50.
89. Smith BH, Torrance N, Bennett MI, et al. Health and quality of life associated with chronic pain of predominantly neuropathic origin in the community. *Clin J Pain* 2007;**23**:143–9.
90. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006;**367**:1618–25.
91. Pozek JP, Beausang D, Baratta JL, et al. The acute to chronic pain transition: can chronic pain be prevented? *Med Clin North Am* 2016;**100**:17–30.