Indispensable articaine

Peter Raftery[1]

Introduction

Dentistry is given a wide berth by Hollywood, and when it does feature it is generally related to ineffective local anaesthesia (LA). Painful dental treatment is so universally dreaded that the ability to deliver predictably successful dental LA can be the ultimate 'practice builder'. The benefits of being effective with a syringe do not end there; failing to achieve sufficiently profound LA can be dispiriting (for operator as well as patient) and expensive. It is therefore of the utmost importance to be technically sound and well-informed about LA. A busy GDP auditing his strike-rate reported that LA failures resulted in 10% of treatments being abandoned over a five day period.[1]

An informal assessment of my own LA performance confirmed to me that my struggles and prilocaine were related. "It works well in my hands" is a phrase I have often heard from colleagues when discussing prilocaine - just not in my hands then. Conversely, I very rarely miss with articaine and here at least I am in good company. Dentists looking for an evidence based product select articaine, shown to be a superior agent to lidocaine – itself previously labelled the 'gold-standard' agent.[2,3] The selection of prilocaine is generally associated with those (dreaded) "allergic to adrenaline" patients. Rather than true allergy, these patients will have had an unpleasant 'pounding heart' episode in the past that they do not wish to repeat. In all likelihood this would have been following a rare intravascular injection and probably involved a 'market-leading ' lidocaine 2% preparation containing as it does a generous 1:80,000 dose of adrenaline. For this reason I have found such patients are generally amenable to trying the reduced-concentration adrenaline preparations of articaine (1:100,000) which are available and so far all of these have gone off without incident. For anyone unwilling to try this strategy there is always plain mepivacaine (a 3% preparation that is adrenaline free) which I have had acceptable outcomes with.

Market share and evidence

Recent figures from Strategic Data Marketing show that lidocaine accounted for 57% of UK sales with articaine at 31% and mepivacaine and priolocaine accounting for much smaller shares (7% and 5% respectively).[28] Articaine also occupies second position in dental LA sales in the USA with 40% of the market share. In Canada and Denmark articaine is the clear number one, [4,5] whilst in Germany, the dominance is overwhelming with 4% articaine preparations accounting for 96.7% of the market.[6]

The striking sales figures are supported by an evidence base. Randomised controlled trials (RCTs) - accepted as being among the best forms of evidence - have shown that 4% articaine preparations perform every bit as well as 2% lidocaine preparations for the traditionally taught injections (maxillary infiltrations and mandibular blocks - whether the pulps are healthy or inflamed).[7-10] However, articaine is able to do what lidocaine *cannot* do in anesthetising mandibular teeth (incisors and molars)[12] via a simple buccal infiltration. Buccal articaine is as effective as the traditional lidocaine block at anesthetising mandibuilar teeth with healthy[13] and inflamed[14] pulps and - most

[1] Peter Raftery, BDentSc, MSc, MFDS, MClinDent, MRD, MEndo Specialist Endodontist, Hampshhire, UK

interestingly - it is the single best method for rescuing anaesthesia in cases of lower molars with 'hot pulps' where the lidocaine block has failed.[15]

Safety aspects

All amide dental local anaesthetics (lidocaine, articaine, mepivacaine and prilocaine) are very safe but like all drugs; harm is possible from overdose. Attaining toxic drug blood levels relates to interplay between the dose administered and the rate of clearance from the body. Toxic effects, which are difficult to achieve over the course of a normal dental treatment appointment, manifest mainly in the cardiovascular and central nervous systems.

Dose administered

The maximum recommended doses for lidocaine, articaine and prilocaine are similar, expressed here as maximum number of 2.2ml cartridges by bodyweight. The UK's preeminent local anaesthetic expert - John Meechan - advises the following;

- Lidocaine 2% preparations – the maximum dose is one cartridge per 7 kg bodyweight up to a maximum of 10 cartridges.
- Prilocaine 3% preparations – the maximum dose is 0.9 cartridges per 7 kg bodyweight up to a maximum of nine cartridges.
- Articaine 4% preparations – the maximum dose is 0.8 cartridges per 7kg bodyweight up to a maximum of eight cartridges.

A slow submucosal deposition makes for gradual drug release into the bloodstream whereas accidental IV administration rapidly elevates blood drug levels and so aspiration ought to be routine. Aspiration is easily done with Septodont's UltraSafety Plus system. If using an alternative armamentarium it is imperative to check for 'self-aspiration' capability.

It is worth remembering that amides readily cross the blood-brain barrier and are able to reach the foetal circulation in pregnant women (no adverse effects reported in dental literature). It is unclear whether LA is excreted in breast milk and so it may be prudent for nursing mothers to avoid breastfeeding in the hours after LA use.

Rate of clearance

Amide local anaesthetics are primarily metabolised (detoxified) in the liver and excreted via the kidneys in urine although articaine undergoes some additional early metabolism in the bloodstream because of some molecular characteristics unique to it. This is a factor in making articaine's half-life (measure of time for 50% reduction in blood level of the drug) the shortest by far. Liver and kidney function therefore play a significant role in drug elimination. Patients with hypotension, or cirrhosis may struggle to metabolise amides giving rise to higher blood levels of drug and increased risks of toxicity. Likewise patients with renal impairment may risk toxicity through an inability to eliminate metabolites - some of them active - from the bloodstream.

Cardiovascular system

Excessive blood concentration of LA depresses normal electrical excitability of the myocardium. The resultant decrease in myocardial contractility and decreased cardiac output both contribute to circulatory collapse. Methemglobinaemia is a condition of respiratory depression in which circulating red blood cells no longer give up their oxygen to the tissues. Administration of excessive amounts of prilocaine can - in theory - predispose red blood cells to this non-functional state. Patients reaching such a state of respiratory distress, which do not respond to 100% oxygen therapy, are thought to have methemglobinaemia and require urgent hospital admission.

Central nervous system

As blood concentrations of LA rise beyond the therapeutic range the effect on the CNS manifests as an initial drowsiness giving way to seizures. Circumoral tingling is said to be a precursor symptom.

Controversies

Every dentist performing the traditional (Halstead) block technique will, irrespective of LA agent selected, unavoidably be risking a paraesthesia.[16] Paraesthesia is altered sensation, often tingling, sometimes temporary but sometimes permanent, in an area supplied by the nerves[16] (inferior alveolar or lingual) which run close to the target area for the needle tip required by the Halstead technique. Lingual nerve paraesthesias tends to be permanent and so seems to be the type reported more frequently.[17] Paraesthesia is thankfully rare (estimated at one such incident per career of a full-time dentist[16] or described elsewhere as one in every 785,000 blocks)[18] so that at present (in the UK) these iatrogenic injuries are not considered to be negligent and warning of patients is not considered necessary.

Suspicion regarding paraesthesia and articaine were raised not long after its introduction to USA following early usage reports from Canada[18] and later Denmark.[18] It is

interesting however to note that no solution is implicated more frequently in studies on paraesthesia than 2% lidocaine preparations.[19-23]

Failure to specifically implicate articaine with paraesthesia extends to the UK literature – most of which comes from the well-respected King's College London professor Tara Renton. Her studies[19, 23-24] as well as others with UK involvement[21] did not show any increased association for articaine. Professor Brian Millar (also from King's College London) co-authored a recent review paper on articaine which concluded that: "Articaine-induced paraesthesia after inferior alveolar nerve block is no longer a controversial issue and is no greater than for other local anaesthetics in use in the dental clinic."[25] This view was shared by the Pharmacovigilance Working Party of the European Union when in 2006 they reviewed the safety of articaine following publication of the concerning Denmark reports on paraesthesia. This review, described as the "most careful scientific analysis of the perceived 'problem' of articaine-related paraesthesia to date", determined that no medical evidence exists to prohibit the use of articaine according to the current guidelines.[26] For final clarity on this subject it is worth mentioning explicitly that ever since articaine's introduction to the UK market 1999 the MRHA has licensed it for 'any and all' dental injections including inferior dental nerve blocks. UK dental indemnity firms 'do not advise against' articaine's use for IDN blocks.[27]

If an association of paraesthesia with any one specific agent does not seem to hold then what is becoming apparent is that instances of permanent lingual nerve paraesthesia are associated with repeat IDN injections.[23] An explanation for this may be deformation of the thin, bevelled leading edge of the LA needle point once it has struck the bony landmarks during the first IDN block. It is thought that reinsertion of this, now deformed, needle can predispose to tearing of the lingual nerve during the second injection. In any event, in light of the excellent results from buccal articaine[13,15] it would seem that repeat IDN block injections ought to be strictly avoided.

Conclusion

Because of its incredible clinical performance and safety profile I predict that the popularity of articaine 4% preparations in the UK is soon to soar to a Teutonic state of near complete market dominance. I have noted in recent times that the literature and mood from the profession is becoming less frantic about the issue of articaine and paraesthesia.

References

1 . Kaufman E, Weinstein P, Milgrom P. Difficulties in achieving local anaesthesia. J Am Dent Assoc. 1984 Feb;108(2):205-8.

2 . Katyal V. The efficacy and safety of articaine versus lignocaine in dental treatments: a meta-analysis. J Dent. 2010 Apr;38(4):307-17

3. Brandt RG, Anderson PF, McDonald NJ, Sohn W, Peters MC. The pulpal anesthetic efficacy of articaine versus lidocaine in dentistry: a meta-analysis. J Am Dent Assoc. 2011 May;142(5):493-504.

4. Malamed SF. Handbook of Local Anaesthesia 6th Edition. Elsevier 2014 .Chapter 4, p66

5. Hillerup S1, Jensen RH, Ersbøll BK. Trigeminal nerve injury associated with injection of local anesthetics: needle lesion or neurotoxicity? J Am Dent Assoc. 2011 May;142(5):531-9.

6 . Market data, GlaxoSmithKline, Germany.

7 Evans G, Nusstein J, Drum M, Reader A, Beck M. A prospective, randomized, double-blind comparison of articaine and lidocaine for maxillary infiltrations. J Endod. 2008 Apr;34(4):389-93.

8. Kanaa MD, Whitworth JM, Meechan JG. A comparison of the efficacy of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:80,000 epinephrine in achieving pulpal anesthesia in maxillary teeth with irreversible pulpitis. J Endod. 2012 Mar;38(3):279-82.

9. Mikesell P, Nusstein J, Reader A, Beck M, Weaver J. A comparison of articaine and lidocaine for inferior alveolar nerve blocks. J Endod. 2005 Apr;31(4):265-70

10. Claffey E1, Reader A, Nusstein J, Beck M, Weaver J. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. J Endod. 2004 Aug;30(8):568-71.

11. Jaber A, Whitworth JM, Corbett IP, Al-Baqshi B, Kanaa MD, Meechan JG. The efficacy of infiltration anaesthesia for adult mandibular incisors: a randomised double-blind cross-over trial comparing articaine and lidocaine buccal and buccal plus lingual infiltrations. Br Dent J. 2010 Nov;209(9):E16.

12. Kanaa MD, Whitworth JM, Corbett IP, Meechan JG. Articaine and lidocaine mandibular buccal infiltration anesthesia: a prospective randomized double-blind cross-over study. J Endod. 2006 Apr;32(4):296-8

13. Corbett I P, Kanaa MD, Whitworth JM, Meechan JG. Articaine infiltration for anesthesia of mandibular first molars. J Endod. 2008 May;34(5):514-8

14. Poorni S, Veniashok B, Senthilkumar AD, Indira R,

Ramachandran S. Anesthetic Efficacy of Four Percent Articaine for pulpal anesthesia by using inferior alveolar nerve block and buccal infiltration techniques in patients with irreversible pulpitis: A prospective randomized double-blind clinical trial. J Endod. 2011 Dec;37(12):1603-7

15. Kanaa MD, Whitworth JM, Meechan JG. A prospective randomized trial of different supplementary local anesthetic techniques after failure of inferior alveolar nerve block in patients with irreversible pulpitis in mandibular teeth. J Endod. 2012 Apr;38(4):421-5

16. Pogrel MA, Thamby S. Permanent nerve involvement resulting from inferior alveolar nerve blocks. J Am Dent Assoc. 2000 Jul;131(7):901-7.

17. Hillerup S, Jensen R. Nerve injury caused by mandibular block analgesia. Int J Oral Maxillofac Surg. 2006 May;35(5):437-43.

18. Haas DA, Lennon D. A 21 year retrospective study of reports of paresthesia following local anesthetic administration. J Can Dent Assoc. 1995 Apr;61(4):319-20, 323-6, 329-30.

19. Renton T, Janjua H, Gallagher JE, Dalgleish M, Yilmaz Z. UK dentists' experience of iatrogenic trigeminal nerve injuries in relation to routine dental procedures: why, when and how often? Br Dent J. 2013 Jun;214(12):633-42.

20. Pogrel MA, Bryan J, Regezi J. Nerve damage associated with inferior alveolar nerve blocks. J Am Dent Assoc. 1995 Aug;126(8):1150-5.

21. Malamed SF, Gagnon S, Leblanc D. Articaine hydrochloride: a study of the safety of a new amide local anaesthetic. J Am Dent Assoc. 2001 Feb;132(2):177-85.

22. Pogrel MA. Permanent nerve damage from inferior alveolar nerve blocks–an update to include articaine. J Calif Dent Assoc. 2007 Apr;35(4):271-3.

23. Renton T, Adey-Viscuso D, Meechan JG, Yilmaz Z. Trigeminal nerve injuries in relation to the local anaesthesia in mandibular injections. Br Dent J. 2010 Nov;209(9):E15.

24. Renton T. Prevention of iatrogenic inferior alveolar nerve Injuries in relation to dental procedures. Dent Update. 2010 Jul-Aug;37(6):350-2, 354-6, 358-60

25. Kakroudi SH, Mehta S, Millar BJ. Articaine Hydrochloride: is it the Solution? Dent Update. 2015 Jan-Feb;42(1):88-90, 92-3.

26. Malamed SF. Articaine versus lidocaine: the author responds. J Calif Dent Assoc. 2007 Jun;35(6):383-5.

27. Personal communication, (N Torlot), Dental Defence Union, 2015

28. SDM Data: UK Anaesthetics Market Q4 2014

Dr Peter Raftery is a keynote speaker at the Nomads Congress, Gauteng, November 2017.