INVITED REVIEW

Local anaesthesia

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Abstract

This article describes current concepts in the mechanism of action of local anaesthetic drugs and discusses recent advances in the equipment and drugs that may be used to provide intra-oral anaesthesia.

Introduction

Excellent pain control is an essential part of surgical practice. Local anaesthesia is the mainstay of pain control for outpatient oral surgery procedures. The anaesthetic effects of cocaine were discovered by Albert Niemann in the 1850s[1]. Since that time a number of advances have occurred in relation to local anaesthetic drugs and delivery systems.

This article will consider current concepts in the action of local anaesthetics and recent developments in drugs and the way they are delivered.

Current understanding of the mode of action of local anaesthetic drugs

There are two theories proposed for the action of local anaesthetics. These are the membrane expansion theory and the specific binding theory. The former is a non-specific mechanism that occurs by swelling of the nerve cell membrane as the lipophilic local anaesthetic is absorbed into the membrane. This perturbation influences the configuration of the sodium channel and inhibits entry of sodium into the cell, which prevents nerve cell depolarisation and thus firing. Although this mechanism may play some role in the action of local anaesthetic drugs, it is now accepted that the specific binding theory[2] is a more accurate explanation of the mechanism of action of local anaesthetics. The evidence to support this theory is strong. Different isomers of the same drug show different local anaesthetic activity[3] – a feature that cannot be readily explained by the non-specific membrane expansion theory. In order to understand the specific binding theory of local anaesthetic action, it is necessary to understand the structure of the voltage-gated sodium channel, which is the site of local anaesthetic action. The sodium channel has been well characterised and critical areas that affect local anaesthetic binding have been identified[4,5]. Indeed nine different types of sodium channels have so far been identified[6]. These different sodium channels are not all equally susceptible to the action of local anaesthetics and could explain why certain conditions such as inflammation, which might lead to the development of altered channels, can lead to failure of local anaesthesia[7]. The basic structure of the sodium channel consists of three subunits known as α, β_1 and β_2. The pore through which sodium enters the cell is contained in the α subunit; the β components are concerned with intercellular interactions and regulation of channel gating[4]. The α unit is composed of four very similar zones named domains I–IV. Each of these

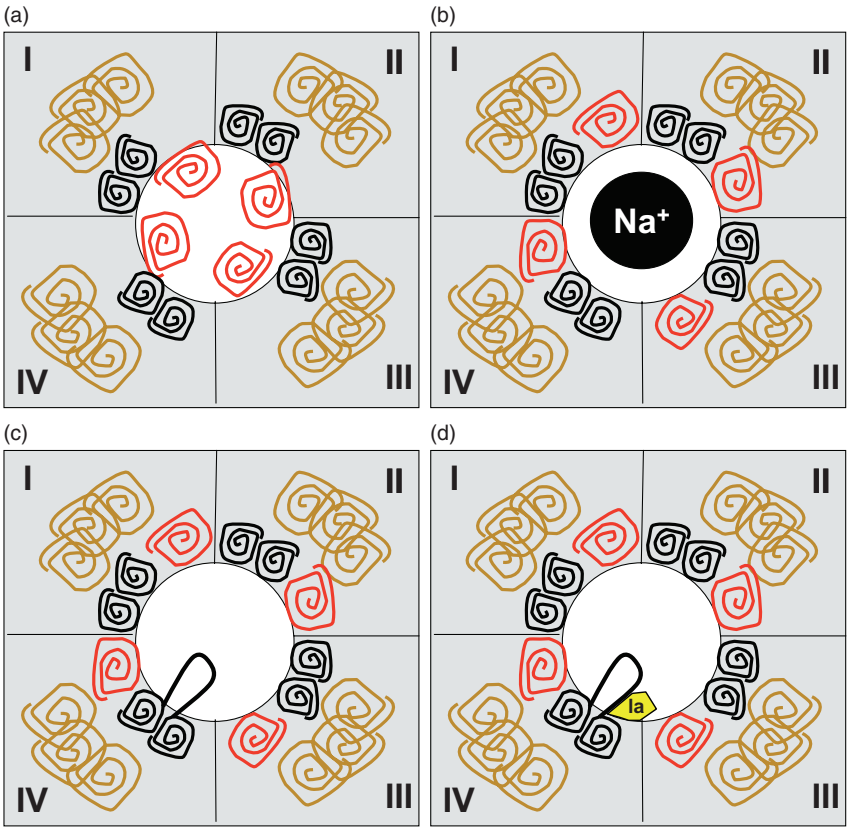

Figure 1 The α subunit of the sodium channel. The channel is comprised of four domains (I–IV), each of which contains six helical segments. Segments S1–S3 (brown) are negatively charged and segment S4 (red) is positively charged. (a) The nerve cell at rest with the segment S4 in the pore obstructing sodium entry. (b) The nerve during firing when the segments S4 slide into the body of the channel allowing entry of sodium. (c) The configuration during the refractory period when the nerve does not fire and a protein loop between domains III and IV acts as the obstruction to sodium entry. (d) The binding of the local anaesthetic (la) maintaining the channel in the refractory position.

domains contains six protein helical segments annotated S1–S6. These segments vary in their structure; segments S1, S2 and S3 are all negatively charged and S4 is positively charged[3]. Figure 1 is a diagrammatic representation of the alignment of the α unit at different stages of the nerve firing cycle and the effect of local anaesthetic binding. At rest the S4 segments are present in the channel of the pore and act as an obstruction to sodium entry (Fig. 1a). Depolarisation and entry of sodium into the cell is achieved by the S4 segments twisting into the body of the α unit (Fig. 1b) – an action known as the sliding helix. During the refractory period of the firing cycle a protein loop between domains III and IV extends into the channel preventing further entry of sodium[4] (Fig. 1c). Local anaesthetics block sodium entry by maintaining this loop in the position it occupies during the refractory period (Fig. 1d). Two amino acids have been identified on the S6 segment of domain IV (Phe 1764 and Tyr 1771) that are critical for local anaesthetic binding[4]. Access to the local anaesthetic binding site is most readily achieved when the nerve cell is in the inactivated conformation[3,7]. It has been claimed that local anaesthetic binding is 17 times lower for resting compared with inactivated channels[3]. The more frequently a nerve fires the more times it enters the inactivated configuration. This means that rapidly firing neurones are the most susceptible to the effects of local anaesthetics, which explains the phenomenon known as use- (or frequency-) dependent block. The fact that specific drug binding sites are now being identified[8] is exciting as this means that local anaesthetic agents with greater specificity for specific sodium channels could be developed. This could lead to the development of agents that are less cardiotoxic as well as those that may perform better in the presence of inflammation. In addition, there is a greater understanding of the heterogeneity of adrenergic receptors[9,10]; this could lead to the development of site-specific vasoconstrictors, which might further reduce the unwanted effects of local anaesthetics.

Recent advances in intra-oral local anaesthesia

A number of developments have occurred over the last decade both in relation to the drugs used for local anaesthesia and in relation to the equipment used to deliver these drugs. Changes in delivery systems have

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led to the development of different techniques of intra-oral anaesthesia.

Local anaesthetic drugs

Developments in relation to local anaesthetic drugs will be discussed in relation to three areas: first, the introduction of articaine to a larger market; second, the development of new longer-acting agents; and finally the development of drugs to reverse the effects of local anaesthesia.

Articaine

Articaine is not a new drug. It has been used extensively in Europe and Canada for over 20 years; however, it has only been available in the UK and the USA for a few years. Articaine has been shown to be a safe and effective local anaesthetic in clinical trials in both adults and children[11–15].

Articaine contains a sulphur molecule and this must be remembered in patients allergic to sulphur-containing drugs. It is unique among the amide group of local anaesthetics in that it is initially metabolised in the plasma[16]. The other amides are metabolised in the liver although prilocaine does undergo some degradation in the lungs. This means that articaine has a much shorter plasma half-life (around 20 min) compared with lidocaine (about 90 min). Therefore, articaine is systemically less toxic than lidocaine[16] and is safer should 'top-up' anaesthesia be required during longer procedures. It is important to point out that it is the plasma half-life that is reduced, which does not affect the duration of activity of articaine.

There are a number of issues relating to articaine that merit discussion. There is a feeling among general practitioners that articaine with adrenaline is an extremely effective solution and appears better than lidocaine with adrenaline. It has been suggested that it is able to diffuse more widely than other local anaesthetics[16] although this has not been supported in some clinical trials[17]. One study has suggested that palatal injections are not required after buccal anaesthesia with 4% articaine for maxillary dental extractions[18]. Most studies that have compared articaine with adrenaline to lidocaine with adrenaline have shown the drugs to have comparable efficacy[11,19,20]. There are data suggesting that articaine has a shorter onset time and longer duration of action compared with lidocaine after infiltration anaesthesia in the maxilla[21]. One study[22] showed that mandibular buccal infiltration with 4% articaine with 1:100 000 adrenaline was more effective in obtaining molar pulpal anaesthesia than a similar injection of 2% lidocaine with 1:100 000 adrenaline. This may be the result of the increased concentration of local anaesthetic drug as an earlier investigation showed no difference in efficacy following mandibular buccal infiltration between 4% articaine and 4% prilocaine[23]. A point of interest is that, as far as anaesthesia of the lower first molar is concerned, the infiltration of 4% articaine produced equivalent success to inferior alveolar nerve block with 2% lidocaine in a similar study population[24]. This is an interesting finding that merits further investigation as the avoidance of regional block anaesthesia could be an advantage, for example, the reduction of traumatic and chemical injuries to nerve trunks.

An area of controversy concerning the use of 4% articaine is the suggestion that the production of long-lasting paraesthesia is more likely, compared with other local anaesthetic solutions, when this drug is administered as a regional block. A greater prevalence of long-lasting paraesthesia, especially of the lingual nerve, has been reported in North America and Europe after the use of 4% articaine compared with lower concentrations of mepivacaine and lidocaine[25,26]. These findings have been questioned by some workers[27] as large-scale studies have shown no difference in the production of paraesthesias following the intra-oral injection of lidocaine and articaine[11]. Those who argue that articaine does not produce a greater incidence of paraesthesia claim that, as it is chiefly the lingual nerve that suffers[27], this might be due to direct trauma from the needle and that over-reporting of problems is natural when a new drug is introduced to practice. Nevertheless, nerve damage increases with increasing local anaesthetic concentration[28] and both 4% articaine and 4% prilocaine have been implicated in a greater incidence of paraesthesias than 2% lidocaine[25].

Long-acting local anaesthetics

Long-acting local anaesthetics have been used in oral surgery for a number of years. They are not available in dental cartridges in all countries, including the UK. Drugs such as bupivacaine have been shown to be useful in reducing postoperative discomfort[29] and decreasing the need for postoperative analgesia. The most recently developed drugs are ropivacaine and levobupivacaine. Ropivacaine has a shorter elimination half-life compared with bupivacaine[30]. One useful property attributed to ropivacaine is an inherent vasoconstrictive property[31]. There is evidence that ropivacaine is as effective with and without additional vasoconstrictor[32]. This is potentially useful in oral surgery as it might reduce the unwanted effects of local

anaesthesia. Ropivacaine has been shown to be effective in obtaining dental anaesthesia after intra-oral injection[33,34]; however, when tested during intraligamentary anaesthesia, a technique that requires good vasoconstriction for acceptable efficacy, ropivacaine was not as effective as lidocaine with adrenaline in obtaining pulpal anaesthesia[35].

Levobupivacaine is a single isomer of bupivacaine. A number of studies have demonstrated similar efficacies of levobupivacaine and bupivacaine[36,37]. The advantage of the former drug is that it is less toxic compared with the latter[38,39]. They appear equally effective in obtaining pulpal anaesthesia after inferior alveolar nerve blocks[40] and levobupivacaine has been shown to reduce analgesic consumption and decrease postoperative pain compared with placebo and injection of lidocaine with adrenaline following oral surgery[41].

Reversal of local anaesthesia

Recently there has been a renewed interest in reversal of local anaesthesia.

This is achieved by injecting the alpha-adrenergic antagonist phentolamine mesylate at the end of treatment to oppose the effects of the vasoconstrictor (adrenaline) in the original local anaesthetic. The local injection of phentolamine has been shown to significantly shorten the time taken for return to normal sensation of the lip and tongue after dental anaesthesia. In one double-blind, placebo-controlled trial phentolamine reduced return to normal sensation in the upper lip by 78 min and by 56 min in the lower lip[42]. In another report the duration of soft tissue anaesthesia in the lower lip was reduced by 55% and in the upper lip by 62% when phentolamine was injected compared with a sham-injection control group[43]. It is anticipated that a suitable formulation for clinical use will be introduced into the USA in 2008. Although reversal of local anaesthesia may be welcomed in some of the dental specialties there will be few indications in oral surgery where postoperative pain control relies to a degree on local anaesthetic action; thus the value of the long-acting agents mentioned earlier.

Delivery systems

The changes in delivery systems relate to the types of syringes used. Modifications have been made to increase safety and comfort. Two will be discussed here, namely safety syringes and electronic (or computer-controlled) delivery systems.

Safety syringes have been developed to decrease the incidence of accidental needle-stick injury. This can be reduced if needle resheathing is avoided. The importance of the avoidance of accidental needle-stick injury has been recognised in the USA. President Clinton signed the Needle-Stick Safety and Prevention Act in November 2000[44]. Prior to this federal act some 17 states in the USA had passed state legislation in this regard. The Federal act states that 'the use of safer medical devices, such as needleless systems and sharps with engineered sharps injury protections, when they are used as part of an overall blood-borne pathogens risk-reduction program, can be extremely effective in reducing accidental sharps' injuries'[44]. The act does not ban the use of traditional needles, but requires that new systems must be considered for implementation on an annual basis. Thus, advances that reduce the risk of needle stick are to be welcomed. In safety syringe systems the needle and its protective sheath are supplied and disposed of as part of the syringe (Fig. 2). The entire assembly is disposed of as a unit, thus needle removal is not required. The introduction of such syringes has been shown to reduce the incidence of

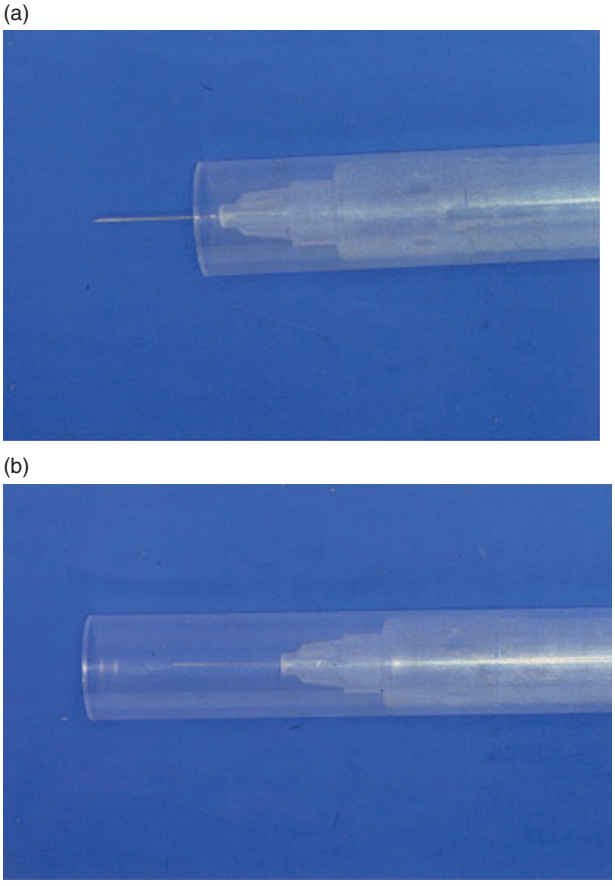

Figure 2 A safety syringe showing the protective sheath that guards the needle: (a) sheath partly covering needle; (b) sheath protecting needle.

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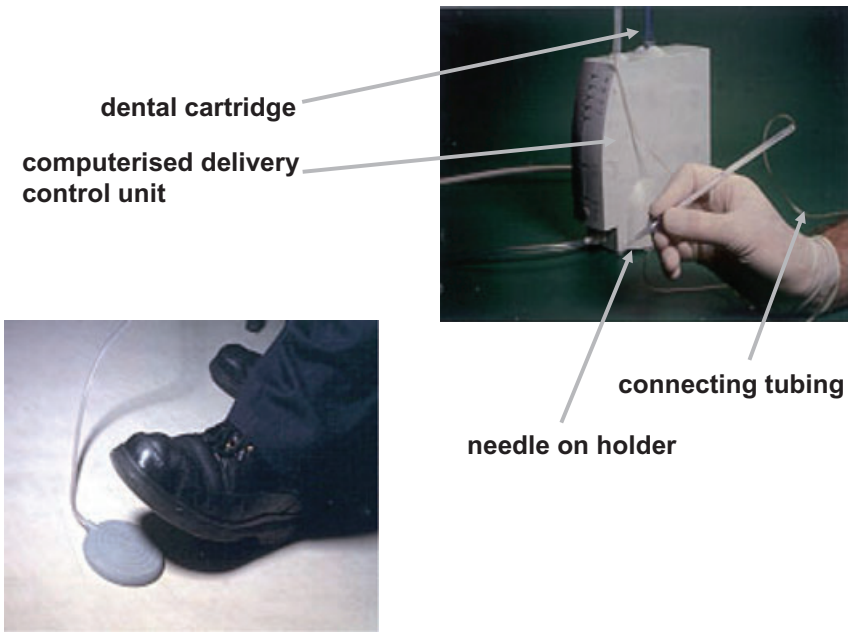

Figure 3 An example of an electronic local anaesthetic delivery device showing the console, connecting tubing and needle holder. The unit is activated by a foot control.

needle-stick injury[45] and the system has been shown to aspirate effectively with standard dental cartridges[46,47].

The most radical change in the way that local anaesthetics are delivered has been the introduction of electronic delivery systems. Many different types are available such as the Compudent (previously known as 'The Wand'), the comfort control syringe, Anaeject and Ora star. A brief description of an electronic system (Fig. 3) illustrates the differences between electronic and conventional cartridge syringes[48]. The Compudent consists of a free-standing control unit that contains a microprocessor, which controls the flow rate during injection. By dictating the flow rate the pressure created during anaesthetic delivery is controlled. This, in theory, should aid patient comfort. The control unit contains a holder for a standard dental local anaesthetic cartridge[46], which is connected via a cannula to the handpiece that holds the needle. This system uses standard medical needles rather than those designed to fit dental cartridge syringes. The latest version includes safe needle guards as described earlier in relation to safety syringes. The signal to inject and aspirate is governed by a foot control. In addition to a controlled injection pressure, another revolutionary aspect of this design is the method of holding the working end. The handpiece is held like a pen, which makes it comfortable to use. In addition, the ability to rotate the handpiece between the fingers during injection may overcome needle deflection produced by the bevel of the needle, which is apparent during deep penetration when using a conventional syringe.

The electronic systems deliver local anaesthetic slowly. Speed of injection is related to injection discomfort; the faster the injection the greater the discomfort. This is apparent in both children and adults[24,49]. As computerised systems deliver the solution slowly, it would be anticipated that they provide comfortable injections. When the Compudent system is compared at different rates of injection into palatal mucosa, it is apparent that the slower rate produces less discomfort[50]. Other studies have shown no statistical difference in injection discomfort between computerised and traditional syringes in adults[51,52]; however, in children the computerised system does seem to produce less disruptive behaviour than the traditional system[53,54].

There is another potential advantage of the slower delivery that is afforded by electronic syringes. There is evidence that, as well as being safer and more comfortable, some techniques of intra-oral local anaesthesia are more successful when the solution is deposited slowly. This has been shown to be the case after inferior alveolar nerve blocks[24] and maxillary infiltration[55]. The incisive/mental block injection does not seem to be influenced by the rate of injection, although as with other methods it is more comfortable when administered slowly[56].

One consequence of the development of computerised systems is a renewed interest in different methods of intra-oral anaesthesia. Two block techniques for use in the maxilla have been investigated. These are the anterior middle superior alveolar nerve block

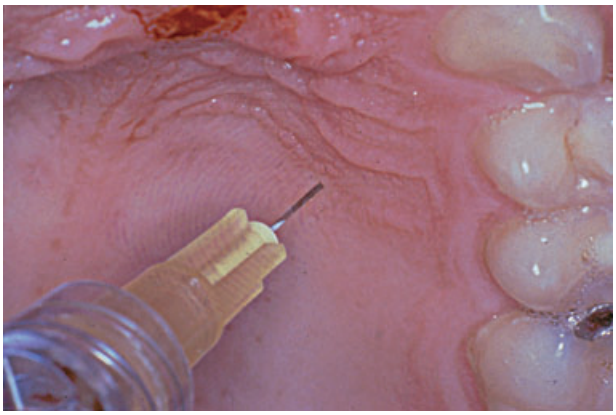

Figure 4 The position of the needle during the anterior middle superior alveolar nerve block.

Table 1 Reported success rates of the AMSA and PASA injections in adults using a computerised delivery system[59,61]

Maxillary tooth	Success (%) with AMSA	Success (%) with PASA
Central incisor	35	55–58
Lateral incisor	58	48–58
Canine	52	32–55
First premolar	42	
Second premolar	55	

AMSA, anterior middle superior alveolar nerve block; PASA, palatal anterior superior alveolar nerve block.

(AMSA)[57] and the palatal anterior superior alveolar nerve block (PASA)[58].

These techniques are novel in that they are advocated as means of obtaining pulpal anaesthesia via a palatal approach.

The AMSA technique relies on the presence of multiple small foramina in the palatal surface of the maxilla. Solution deposited slowly in the palatal mucosa midway between the midline and mid-premolar gingival margin (Fig. 4) diffuses through these foramina to enter the cancellous space and then the pulpal supply. It has been proposed that this technique can anaesthetise the pulps of the premolar and anterior maxillary teeth. Although this has been shown to occur, the success reported for the technique is limited and varies between the teeth[59] (Table 1).

The PASA achieves its effect by injecting solution into the nasopalatine duct (Fig. 5). This has been claimed to produce anaesthesia of the maxillary incisor and canine teeth bilaterally from one injection. The technique has been shown to provide pulpal anaesthesia. One study in children claimed that clinical effectiveness did not differ between PASA injections and buccal infiltrations[60]; however, the success is limited in adults[61] (Table 1).

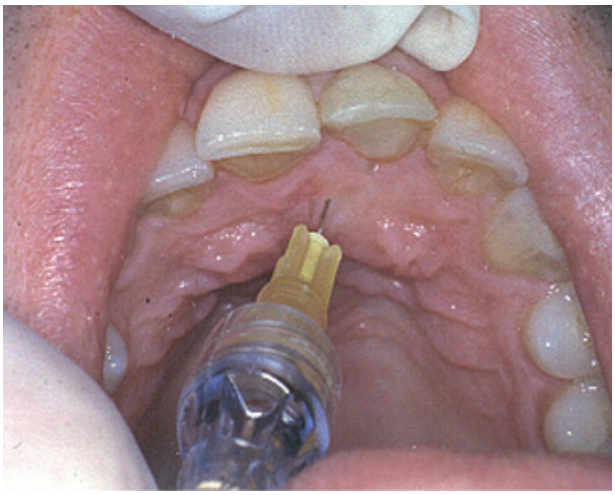

Figure 5 The position of the needle during the palatal anterior superior alveolar nerve block.

Overall, these techniques show some promise and might be useful as supplementary techniques in oral surgery; however, at present they are not preferable to standard primary methods of local anaesthesia.

Conclusions

Local anaesthesia has been used intra-orally for over 100 years and continues to develop. New drugs, delivery methods and techniques have increased the pain control armamentarium. Developments continue to improve the comfort and safety of local anaesthetics in dentistry.

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