



Review Article

Local anesthesia in oral and maxillofacial surgery: A review of current opinion



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Abstract Local anesthesia (LA) is the most important pain management process in oral and maxillofacial surgery. Safe and effective LA not only enable patients to obtain high-quality treatment, but also relieve the anxiety of patients when they come to the clinic. The choices of local anesthetic and injection methods determine the success of LA to a great extent. At present, in most countries or regions, common local anesthetics used in oral and maxillofacial surgery belong to amides and they are injected into patients' body mainly through block or infiltration anesthesia. In addition, the operators' technique level, patient's subjective psychology and anatomical variation of maxillofacial structure also have a strong influence on LA in dental clinic. Due to the existence of above factors, the worldwide success rates of LA in oral and maxillofacial surgery is very different. There are no specific LA methods that ensure 100% successful LA rates. Fortunately, the development of new local anesthetic and injection technology are providing us with new ideas to solve this problem. This review mainly report the new research progress on LA in oral and maxillofacial surgery in recent decades and help clinicians with dental LA operation.

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Introduction

Oral and maxillofacial surgery is a subject that mainly focuses on surgical treatment in stomatology department. It studies on oral organs, facial soft and maxillofacial bone tissues, temporomandibular joint, salivary glands and some related diseases of neck. Doctors from maxillofacial surgery need to master different kinds of operations, such as tooth extraction, tissue biopsy and alveolar bone repair. Among them, extracting impacted wisdom teeth is the most common in the clinic.¹ Impacted mandibular third molars are often extracted due to the existence of caries and acute pericoronitis, and they also easily destroy neighbor crowns and roots if no treatment is done. Patients with impacted mandibular third molars have to go to hospital when acute inflammation occurs, otherwise, their daily life will be seriously affected.²

Perfect pain management not only eliminates patients' anxiety effectively after they come to clinic, but also makes the operation process undisturbed, both of which are positive to the treatment outcome.³ In addition, most patients feel pain for a long time after receiving maxillofacial surgery.^{4–6} It has been reported that the pain of patients undergoing tooth extraction usually reach its peak within 6–8 h after surgery.^{7,8} Pain in dental treatment is the root cause of dental phobia, especially in children, although the proportion of patients suffering from dental phobia gradually decreases with age.⁹ According to the data from Raducanu's study, about 21% of Romanian children have dental phobia,¹⁰ while in Saudi Arabia, this proportion is as high as 34%.¹¹ Effective pain management can create a comfortable experiences for patients in operation processes and reduce their dental anxiety.

At present, LA is used as the main method to eliminate pain in maxillofacial surgery. LA refers to a kind of anesthesia that injects drugs to specific sites, which retains patient's pain and retain their consciousness. The advantage of this procedure is to avoid systemic medication for patients and they also do not need to wait a long time for recovering from anesthesia. Local anesthetics have ability to reduce the permeability of sodium channels in peripheral nerves and bind themselves with Ca^{2+} , which block the transmission of nerve impulses to the brain and make patients painless.^{12,13}

Anesthetics and injection methods, as the most important factors in LA, play a decisive role in the success of anesthesia. On the one hand, clinicians have been trying to optimize the existing anesthetics and develop new ones. Since cocaine was first used in dental LA in 1884, the development of local anesthetics has never stopped.¹⁴ In recent years, opioids have gradually been used in oral and maxillofacial surgery. These drugs has a strong analgesic effect on the operation, moreover they also make patients feel painless for a long time after operation, which reduce the intake of additional painkillers.^{15,16} However, it must be pointed out that all kinds of local anesthetics have their own limitations, including the short anesthesia duration, low anesthetic efficacy and side effects. Procaine, for example, has potential to cause severe allergic reactions

and is rarely used to local anesthesia in maxillofacial surgery. Furthermore, when operators use opioids as anesthetics, patients are prone to nausea vomiting and myelosuppression.¹⁷ Therefore, clinicians should fully consider the actual situation and select the most appropriate anesthetics for every patients.

On the other hand, conventional injection methods in oral and maxillofacial surgery include block anesthesia, infiltration anesthesia, topical anesthesia and freezing anesthesia. Some new technologies, such as computer-assisted intraosseous anesthesia (CAIO) and oral dissolving film (ODF), are gradually applied in clinical practice, and have also been proved to be very efficient.^{18,19} How to make patients get complete anesthesia in maxillofacial operation has been a tricky problem for a long time.²⁰ For example, inferior alveolar nerve block (IANB) is commonly used in the extraction of mandibular posterior teeth, but it has been reported that the failure rate of this injection method was as high as 20–47%.^{21,22} In order to improve the success rate of IANB, scholars have developed new anesthetics,^{23,24} changed patient's position,²¹ and adjusted drug dosage.²⁵ Every single injection method have its own limitations which may cause the failure of LA, but when combined with other ways, the successful anesthesia rate can has effectively increases.

In this review article, we retrospect the latest research on LA in maxillofacial surgery over the past decades and hope to provide guidance for dentists on how to perform LA in clinical practice. We promise that the gathering data do not know the patients before being used for the review articles.

Types of local anesthetics in oral and maxillofacial surgery

The majority of local anesthetics in oral and maxillofacial surgery can be divided into esters and amides. However, esters have been gradually abandoned in dental treatment due to their allergenicity. The basic principle for the development of local anesthetics is that drugs should be non-toxic and effective.^{26–29} Before LA, clinicians must fully understand the anesthetic efficacy, onset time, pharmacokinetics and toxicology of drugs, so as to effectively anesthetize patients and avoid causing additional injury.³⁰ Amides are another kind of local anesthetics in dental treatment, including lidocaine, articaine, procaine, mepivacaine and bupivacaine. Generally local anesthetics in dental treatment are remaining compounds with high fat solubility, so they are often formulated as hydrochloride to increase their water solubility.³¹ Few scholars explored the possibility of using opioids as local anesthetics in maxillofacial surgery, because long-term use of this drug predisposes patients to addiction. However, in recent years, some low-addictive opioids have been shown to have unexpected anesthetic effects in dental treatment.^{32,33} Among kinds of local anesthetics, lidocaine is often used as the gold standard to evaluate other anesthesia drugs in terms of safety and effectiveness.³⁴

Lidocaine

Lidocaine is widely accepted as a drug of first choice for patients with acute myocardial infarction and various rapid ventricular arrhythmias, due to the fact that low doses of lidocaine can promote K^+ outflow from cardiomyocytes and reduce myocardial autorhythmicity. Once injected into body, 90% of lidocaine is metabolized by the liver and 10% is excreted in the original form. The metabolites of lidocaine in the liver still have local anesthetic properties, but their toxicity is enhanced, which means that lidocaine is more toxic than other local anesthetics. The dissociation constant (pKa) of lidocaine is 7.85 and it can be decomposed into numerous re-charged local anesthetic molecules which act on myelin sheath to produce nerve block.^{12,35}

Lidocaine has ability to dilate blood vessels and most of the drugs are absorbed by the body in a short time. This process not only shortens the duration of anesthesia, but also greatly increases the risk of poisoning.^{36–38} Therefore, when lidocaine is used as local anesthetics, adrenaline is often added into the solution to achieve the purpose of constricting blood vessels and delaying drug absorption.³⁹ Interestingly, in addition to adding adrenaline, Brkovic et al. have demonstrated that an IANB injection of lidocaine with clonidine can effectively prolong the duration of anesthesia in the extraction of impacted mandibular third molars, similar to the effect of an IANB injection of lidocaine with adrenaline.⁴⁰

Lidocaine is the gold standard to evaluate the safety and effectiveness of other LA agents and commonly used in IANB. Nevertheless, in the previous studies, the success rates of lidocaine-IANB with adrenaline varied in different regions.^{41,42} Shabazfar and his colleagues have believed that although IANB has a good anesthetic effect on the teeth, it only exists in cases of effective anesthesia.^{43,44} Some other scholars pointed out that using an IANB injection of lidocaine only effectively anesthetizes the pulp of mandibular anterior teeth, but has limited anesthetic effect on the posterior teeth.⁴⁵ The most likely reasons for this phenomenon are anatomical variations of the mandibular foramen and insufficient diffusion capacity of lidocaine in soft tissues.^{41,42} It may explain why some patients still feel uncomfortable when the mandibular posterior teeth are divided into pieces after IANB.

Since block anesthesia cannot guarantee success in every operation, scholars are trying different injection methods of lidocaine for LA. In Jamil's study, when patients received an infiltration injection of lidocaine, the average duration of lower lip numbness was 2.3 h,⁴⁶ while the same data from Kammer's study was 3.8 h.⁴⁴ It suggested that the infiltration injection of lidocaine may be an alternative way to anesthetize the mandible. Nevertheless, Robertson et al. pointed out that only 45–67% of patients were successfully anesthetized by buccal infiltration (BI) technique when using lidocaine as local anesthetics.⁴⁷ The possible reason for this may be the lack of tissue permeability for lidocaine to fully penetrate the thickened bone plate on the buccal side of mandible.

Lidocaine can be injected into body through the way of periodontal intraligamentary injection (PDL). This method is capable of providing efficient anesthesia for a single

tooth, avoiding the anesthesia of soft tissues, such as lip and tongue, and reducing the postoperative discomfort of patients.⁴⁸ It is worth mentioning that PDL can easily cause periodontal wound and root resorption, because the needle is directly inserted into periodontal tissues.⁴⁹ Apart from direct injection, scientists have made different types of lidocaine, such as gels and sustained-release tablets, in order to simplify procedures or improve efficiency.^{50,51} For example, in the previous study, 100 mg lidocaine sustained-release tablets were proved to have therapeutic potential for dental LA.¹⁷ Furthermore, Kim et al. created a new type of materials (ODF) containing lidocaine and used it in LA for dental treatment.⁵² They found that this new material is able to release 91.7% of lidocaine within the first minute and 96.3% within the first 5 min. And according to cellular uptake study, Kim also found nearly 47% of lidocaine was absorbed by oral cells without any toxicity. It means that ODF containing lidocaine has therapeutic potential to replace conventional anesthesia methods, but more research on this material is further needed.

Articaine

In 1969, Muscchaneashou used a new type of powerful LA agents, namely articaine.¹⁴ The molecular structure of articaine contains a thiophene ring which results in a stronger lipid-solubility for articaine, compared to the benzene ring in lidocaine.^{53,54} What's more, articaine is able to form additional hydrogen bonds after being injected into oral mucosa, which is another key factor to improving the lipid-solubility of articaine.⁵⁵ The greater lipid-solubility means the stronger diffusion capability of articaine in hard and soft tissues, and nerve endings in target organs can be rapidly anesthetized due to strong lipid-solubility of articaine.^{26,53,56} Interestingly, articaine is also considered to have ability to fold their molecules in tissues and promote themselves to penetrate in nerve sheath.³⁸ The protein binding rate of articaine is also the highest among amide local anesthetics (94%), which means articaine has a longer duration of LA in vivo.^{57,58}

Unlike lidocaine, articaine is not only metabolized in the liver but also in the blood.⁵⁹ With the existence of carboxylic ester groups in molecular structure, articaine can be decomposed in the liver, but only 10–15% of drugs go through this process.⁶⁰ In blood, the remaining 85–90% of articaine is inactivated to articainic acid which is nontoxic and inactive as anesthetics, with the formation of extra ester bonds in chemical structure of articaine.^{53,59}

Because of its strong tissue permeability, articaine is commonly used in infiltration injection to anesthetize jaw bone, especially in the area of maxillary posterior teeth.^{61,62} Some scholars even believe that articaine has excellent permeability in maxilla and 70.4% of patients in their studies who receive an BI of articaine have a sensation of anesthesia in palatal soft tissues, while the same data is only 29.6% in mepivacaine groups.⁶³ At present, the controversy of using articaine in infiltration injection to mandible has caught the attention of scientists. Kanaa and Robertson et al. have considered that the BI of articaine on mandibular molars showed obvious advantages in anesthetic effect and speed.^{47,61} Betaineh even thought that

articaine has potential to completely anesthetize mandibular molars through BI, instead of IANB.⁶² Maruthingal et al. have proved that 87.5% of patients obtained perfect anesthetic effect after receiving a BI injection of articaine to mandible and have a mean time of onset 6.92 min.¹⁴ However, some scholars have hold the opposite view.⁶⁴ For instance, in Nydegger's study, articaine was not able to effectively anesthetize the mandibular canines and second molars.³⁸ The reason may be that buccal bone plate thickens and the mandibular canal deviates to the lingual side in these areas. Furthermore, he also pointed out that only 55% of the patients who received BI of articaine obtained a painless treatment process which illustrate this anesthesia method is not enough for clinical promotion. Haas and his colleagues have even believed that articaine is not suitable to be used as LA agent with BI in mandible.⁶⁵ Several factors, such as the thickness of buccal bone cortex, position of mental foramen and direction of mandibular canal, affect the success rate of BI of articaine.⁶⁶ However, there is a view which is generally accepted that it is after IANB, the additional BI of articaine is able to prolong the anesthetic duration.⁶⁷

Although the molecular structure of articaine indicates that it has strong diffusion capability in tissues, Prof. Bonar did not recommend using articaine in IANB,⁶⁸ due to their consideration of the high risk of nerve damage. In recent years, CAIO has been introduced into maxillofacial surgery for LA. In 2015, Sixou found that with the help of CAIO technique, both permanent teeth (97.2%) and primary teeth (94.1%) could get extremely high rate of successful anesthesia when used articaine with 1:400,000 adrenaline as anesthetics.⁶⁹ However, the clinical popularization of this technique still needs to solve many problems, such as high economic cost and pain management during injection.

Prilocaine

Prilocaine is another type of amide local anesthetics. There are many similarities between prilocaine and articaine in clinical characteristics and chemical structures, but it should be pointed out that prilocaine has a benzene ring rather than a thiophene ring like articaine.⁵⁶ Prilocaine is the weakest vasodilator among amide local anesthetics, so it can be used in patients who have contraindications to adrenaline.⁷⁰ Burton et al. found that the patients injected with prilocaine were more comfortable than those with lidocaine, which indicated that the toxicity of prilocaine was lower than that of lidocaine.⁷¹ As shown in the previous studies, the onset time of prilocaine was faster than that of lidocaine.⁵⁶ On one hand, the weak vasodilator effect of prilocaine makes more local anesthetics stay in specific areas and promote their rapid arrival to target organs.^{36,72} On the other hand, the pKa (7.7) of prilocaine is slightly smaller than that of lidocaine (pKa = 7.85), indicating that prilocaine can produce more uncharged base molecules in the body to body accelerate the anesthesia processes,⁷² which is consistent with the viewpoint in pharmacology (the lower the pKa of a drug, the faster it works in vivo).^{56,73}

Prilocaine is metabolized not only in the liver, but also in the kidneys and lungs, while lidocaine is only metabolized

in the liver, which gives prilocaine a faster metabolism.^{36,56,72} Specifically, the metabolic process of prilocaine can be divided into two stages. The first stage occurs in the kidney and lung tissues, and the metabolites are decomposed in the liver within the following stage.^{74,75} This multi-level procedure makes the drugs metabolized faster and easier and less likely to cause poisoning to patients.⁷⁶

Prilocaine is considered to be as effective as lidocaine and articaine in oral and maxillofacial surgery.^{56,65,77} With its good safety, it is a good choice for children, the elderly and patients with adrenaline contraindications.^{72,73,78} In a previous study of pulp anesthesia for the mandibular first molars, the success rates of 4% lidocaine and 4% prilocaine were very close, 33% and 32% respectively.³⁸ Similarly, Gazal et al. have proved that there was no significant difference in the onset time and depth of anesthesia between 4% articaine and 3% prilocaine.⁷⁰ When used in IANB, the anesthetic ability of 4% prilocaine with 1:200,000 adrenaline and 2% lidocaine with 1:100,000 adrenaline are very similar.⁷⁶ As for other injection methods, Haas also believed that there was no significant difference in the success rate of anesthesia between 4% prilocaine and 4% articaine in BI of the maxillary second molars and canines.^{79,80}

Although the anesthetic efficacy of prilocaine is similar to that of lidocaine and articaine, Brown and Ward et al. have proved that prilocaine had a short anesthetic duration of anesthesia and belonged to short acting LA agent,⁸¹ due to the fact that they thought prilocaine was rarely used with adrenaline, which shortened the duration of drug efficacy. Some scholars have hold a view that patients should receive an injection of prilocaine with felypressin to prolong the duration of anesthesia. Nonetheless, this drug combination has some negative effects on the cardiovascular system and clinicians should conduct comprehensive assessments if necessary.⁸² In addition, there is a potential risk of developing methemoglobin in patients with the injection of prilocaine.^{83,84}

Mepivacaine

Mepivacaine has been used in oral and maxillofacial surgery for nearly 50 years, and its safety and effectiveness have been fully recognized.⁵⁷ The pKa of mepivacaine is also lower than that of lidocaine, which gives drugs the characteristics of quick action and long-term effect.⁸⁵ Like prilocaine, mepivacaine, which has a good application in children's dental treatment, has weak vasorelaxation and can promote long-time pulp anesthesia.⁸⁶ That is to say, mepivacaine and prilocaine are the only two LA agents which can be injected without adrenaline in maxillofacial surgery.^{87,88} In a previous animal study, mepivacaine may cause bradycardia in animals, but there was no evidence that the same phenomenon may occur in humans.⁸⁹ Mepivacaine was almost completely metabolized in the liver, and 1–6% of drugs were excreted into urine as the original form. Thanks to its excellent pharmacological properties, mepivacaine has been considered as the preferred LA drug for people who have cardiovascular diseases.^{90,91}

Azed compared the permeability of articaine and mepivacaine in the jaw bones.⁶³ He found that about 70.4% of patients in articaine group did not need supplementary

palatal anesthesia after BI in the maxilla, while in mepivacaine group, the percentage was 29.6%. It indicated that the permeability of mepivacaine was not as great as that of articaine in the maxilla, which is in accordance with the standpoint of Gazal et al.^{53,92,93} Gazal has also proved that when used in infiltration anesthesia, mepivacaine has a longer average time of onset (4.22 min) than that of articaine (2.98 min).⁵³ Similar to prilocaine, mepivacaine is always used without adrenaline so that some scholars consider mepivacaine as a kind of short-acting LA agents, but this viewpoint is still controversial in academic circles.^{94,95}

The clinical advantage of mepivacaine is its anesthetic effect on inflamed pulp. According to the literature, the anesthesia success rate of inflamed pulp is much lower than that of normal pulp,^{96–98} and the appearance of mepivacaine seems to provide a new strategy to solve it. In the study of Rodríguez-Wong et al., they found teeth with irreversible pulpitis which received an IANB injection of the mepivacaine alone has a higher success rate of anesthesia (67.9%) than receiving other LA agents injection.⁹⁸ Visconti and his colleagues have also believed that mepivacaine has high anesthetic effect on inflamed pulp tissues and makes more adults with pulpitis feel comfortable in the process of pulpotomy.⁸⁵ However, it should be pointed out that mepivacaine can increase the risk of buccal bite when it is used in medium length operation.⁸⁶

Bupivacaine

Bupivacaine is a type of aniline anesthetics and is considered as the most successful long-term LA drugs.⁹⁹ At present, bupivacaine is commonly used in some minor operations in general surgery and less used in maxillofacial surgery. The reason is that small operations in dental clinics usually last within 30 min, while bupivacaine has a longer anesthesia time than the operation time, which may bring discomfort to patients with the numbness of soft tissues.⁹⁹ On the contrary, in transurethral resection of the prostate, the average anesthesia time of bupivacaine for surface anesthesia (141 min) is consistent with the operation time.¹⁰⁰

In special cases, bupivacaine can show its unique advantages in oral and maxillofacial surgery. For example, compared to lidocaine, bupivacaine plays a greater role on tetrodotoxin (TTX) resistance channels which are extremely important for the local anesthesia of inflamed dental pulp.¹⁰¹ When used in IANB, several studies have explored the successful anesthesia rate of bupivacaine.^{102–104} It has been shown that lidocaine has a better anesthetic effect than bupivacaine in the anesthesia of the mandibular second molar.¹⁰⁴ However, more scholars have demonstrated that the anesthetic efficacy of lidocaine and bupivacaine was almost the same in the IANB injection.^{102,103,105} With the long-term anesthetic effect, bupivacaine can even make patients have a sense of anesthesia 8 h after operation.^{106–108}

Bupivacaine is often made into ointment for topical anesthesia. Nevertheless, the poor adhesiveness of ointment shortens the residence time on mucosa and it is easy to cause incomplete LA.¹⁰⁹ Fortunately, Satya Bhushan

et al. created a new gel material containing bupivacaine or lidocaine and they also explored the possibility of them being used in topical anesthesia in maxillofacial surgery.⁹⁹ The study found that gel containing lidocaine reached its anesthesia effect peak in 8–11 min, while the number for bupivacaine-gel was 15–18 min. Furthermore, the anesthesia duration of bupivacaine-gel was 25–30 min, compared to lidocaine-gel was 15–18 min. It could be seen that bupivacaine had ability to provide twice as long anesthesia time as lidocaine in topical anesthesia, which is enough for clinicians to do the extraction of a single tooth. Additionally, Satya Bhushan also pointed out that this new type of bupivacaine-gel could only be used for the extraction of grade II or III mobile teeth, otherwise, patients may feel severe pain during teeth extraction. Scholars attributed this phenomenon to the poor permeability of bupivacaine. When used in topical anesthesia, bupivacaine can not completely penetrate the jaw bones and reach to apical regions, which makes the pulp anesthesia incomplete.

Khorshidi used 0.5% bupivacaine solution to rinse alveolar fossae after the extraction of mandibular third molars and they were surprised to find that there was no obvious pain within 24 h after surgery.¹¹⁰ This anesthesia way is convenient and simple, and provides a prospective strategy for the clinical application of bupivacaine.

Others

Opioid drugs which belong to potent analgesics are alkaloids extracted from plants and can interact with central specific receptors to relieve the pain of patients.³³ Although opioids, like morphine, codeine and fentanyl, have analgesic effects on inflammatory tissues, there are few studies on the application of these drugs in maxillofacial surgery.^{111,112} After injecting morphine into the periodontal ligament of patients with periodontitis, Hargreaves found it can effectively relieve pain.¹¹³ The success rate of LA for the extraction of pulpitis teeth has always been problematic to clinicians. For this kind of teeth, conventional local anesthetics can not obtain satisfactory anesthetic effect. Uhle et al. injected fentanyl into the periodontal ligament and made patients with pulpitis obtained painless treatment processes.¹¹⁴ In the study of Elsharrow et al., only a small dose of fentanyl can produce obvious anesthetic effects on teeth with pulpitis, which is much stronger than that of mepivacaine.³² The reason for this phenomenon could be the acidic environment of inflamed pulp tissues promote the ionization of opioids and maintain a high concentration effective drugs in local area. As a result, opioids may have great potential in LA, clinicians should pay close attention to the addiction of opioids and control the dosage of this type of drugs.

Tramadol hydrochloride, which belongs to a kind of non-opioid agents, is similar to morphine and codeine in structure, and is also commonly used to relieve pain in patients. Interestingly, tramadol hydrochloride can also be used as LA agent in oral and maxillofacial surgery.¹¹⁵ 5% tramadol hydrochloride with adrenaline had ability to provided safe and effective LA during and after the maxillofacial operation.^{16,116} In 2013, Alsandook et al. respectively used lidocaine and tramadol hydrochloride in IANB, and found that

the anesthetic efficacy of these two drugs were close.¹¹⁷ Jaber et al. firstly found muopioid receptor existed in dental pulp tissue in 2003, which laid a theoretical foundation for tramadol hydrochloride to be used as LA agent in dentistry.¹¹⁸ However, there was evidence that the onset time of tramadol hydrochloride is significantly slower than that of lidocaine and Dalkilic, inferred that compared to the Na⁺ channels of the slow conducting fibers, tramadol had a greater influence on that of the fast conducting fibers.^{119–121}

Several main factors affecting the outcome of anesthesia

Besides the selection of LA agents, there are still many subjective and objective factors that may affect the success rate of anesthesia. For example, bone structures, experience of the operators and pulp status, all have a profound impact on the results of LA.^{41,42} The experience of clinicians can be gradually improved as time goes on, so the success rate of experienced doctors in LA operation is usually higher than that of young doctors. Some patients with dental anxiety may be afraid of needles and this also affects the outcome of LA. However, these factors can be improved by training doctors and enlightening patients. Clinicians need to focus on the following three objective factors that affect the success rate of LA: the selection of infection methods, pulp status and bone structures.

The selection of injection methods

The conventional injection methods of LA in maxillofacial surgery include block anesthesia, infiltration anesthesia, topical anesthesia and freezing anesthesia. At present, block anesthesia is mainly used in mandibular local anesthesia, while infiltration anesthesia is often used for maxilla.⁶¹ However, the success rates of single injection methods are often unable to achieve the desired goals. Actually, the failure rate of IANB is 20–47%.^{21,22}

In recent decades, clinicians have been exploring the possibility of combining two or more injection methods. Rogers et al. pointed out that the anesthetic effect of an BI injection of 4% articaine as supplementary anesthesia after IANB is much better than a single IANB injection, especially in the continuity of anesthesia.¹²² Meanwhile, patients in another study got a successful anesthesia rate of 84% after receiving a supplementary BI injection when previous IANB failed.¹²³

What's more, whether choosing block anesthesia or infiltration anesthesia, it can't avoid inserting needles into soft tissues and sometimes it even brings extra pain to patients. Some clinicians used 5% lidocaine as surface anesthetic onto the operation area to eliminate the following injection pain.⁹⁹ However, whether topical anesthesia can completely eliminate injection pain, the outcome of worldwide research was very different, because of the different size of needles and qualifications of doctors.¹²⁴ Therefore, some scholars have just believed that 5% lidocaine could only reduce the pain of needle insertion, but the pain of drug injection still existed unless

there was a long waiting time.¹²⁵ Even several scientists believe that topical anesthesia has little effect on relieving pain during injection process.¹²⁶ However, the authors support the view that topical anesthesia can enhance the success rate of anesthesia. It is worth mentioning that freezing anesthesia seems to improve the anesthetic efficacy of topical anesthetics.¹²⁷ Lathwal et al. think it can stimulate myelinated fiber A and slow down the transmission of nerves that sense pain.^{128,129}

The emergence of some new types of LA techniques has not only replaced the conventional ones, but also greatly improved the success rate of anesthesia. In children's dental treatment, using CAIO technique for anesthesia in children can increase the success rate of anesthesia to 91.2–97.2%.¹⁸ When doctors injected articaine with 1:400,000 adrenaline through this technique, there was a high success rate of anesthesia in permanent teeth (97.2%) and deciduous teeth (94.1%).⁶⁹ Anyway, CAIO still has potential to make patients feel pain with the intraosseous injection. Recently, Wang and his colleagues reported a new kind of bone putty containing lidocaine. When this biomaterial is placed in the oral, the anesthetic effect patients obtained is 10 times higher than that of the injection of lidocaine, and at the same time, it could also fill the alveolar fossae.¹³⁰

Pulp status of teeth

The abnormal pulp condition usually causes difficulties to LA in dental treatment. Any singular changes in dental pulps make these closed tissues more sensitive to pain.¹³¹ Especially when the dental pulp is inflamed, the resting membrane potential of nerve changes and the excitability threshold of teeth also decreases.^{75,132} In addition, pulpitis is often accompanied with acidosis, and as mentioned above, acidic environment is not conducive to the decomposed of amides.

According to the previous literature, the lowest success rate of anesthesia for pulpitis affected teeth is 37%, which is far lower than that of normal teeth.⁸⁵ Even Simpson et al. thought that using a supplementary BI injection of 4% articaine to anesthetic mandibular molars with pulpitis was almost ineffective when the previous IANB was unsuccessful, and the final anesthesia success rates was only 24%–38%.¹³³ Mepivacaine and bupivacaine are considered as the first choice to anesthetize pulpitis affected teeth.^{85,105} The reason is that the pKa of mepivacaine is low so that it can dissociate relatively more free uncharged base molecules in acidic environment.⁸⁵ As to bupivacaine, it can play a greater role on TTX resistance channels in inflammatory dental pulps.¹⁰¹ However, mepivacaine and bupivacaine do not guarantee good anesthesia for all pulpitis patients. In recent years, the study of opioids in dental treatment seems to offer clinicians new ideas, but it should be used extremely carefully.³²

It is very important to correctly judge the dental pulp status for the selection of appropriate LA agents and injection methods. Wrong judgments are able to lead to a significant reduction in the success rate of anesthesia and bring unnecessary pain to patients.

The structure of soft and hard tissues

The structures of bones determine the success of LA in oral and maxillofacial surgery to a great extent. Mandible foramen is the key position of inferior alveolar nerve (IAN), buccal nerve and lingual nerve (LN) in and out of mandible. In general, the mandible foramen is located posterio-superior to the midline of ramus.¹³⁴ According to the statistical analysis of Thangavelu et al., the mandible foramen were located at an average of 2.75 mm behind the midline of the mandibular ramus and 19 mm away from the coronal notch.¹³⁵ However, clinicians should not only focus on the average position of mandible foramen, and anatomical variations of each patient should be fully considered.

Infiltration anesthesia is often used as the main injection method in maxilla due to the porous structure of maxilla, while it doesn't work in mandible. Although some successful cases of mandibular infiltration anesthesia have reported, the success rate is low or need to combine with other injection methods.^{136,137} Some scholars have thought that only when the thickness of buccal cortical bone plate is less than 3 mm, BI to mandible can be efficient.¹³⁸ It can be inferred that if BI is necessary in the mandible, the surgeons should try to avoid the area of thickened buccal cortical bone plate, such as the mandibular second molars and canines.⁶⁴ What's more, when infiltration anesthesia is performed in the mandible, attention should also be paid to the position of mental foramen. The closer the insertion point is to the mental foramen, the better the anesthesia effect is.³⁵

The communication among mandibular nerve branches also leads to the failure of LA.^{42,139} Desantis and Liebrow reported the possibility of anatomical variation of IAN, including bifid mandibular nerve.¹⁴⁰ Although the incidence of bifid mandibular nerve is only 0.35–1%, it also has a profound impact on the success rate of IANB. In addition, patients with bifid mandibular nerve sometimes also have two mandible foramina and a part of IAN enter into two mandibular foramen at the same time, which makes it difficult for patients to obtain complete anesthesia.^{141–143} In summary, if successful LA wants to be achieved, doctors must have a deep understanding of the anatomical variations of each patient.

Conclusion

Oral and maxillofacial surgery is an important part of dental treatment and effective LA is able to improve the treatment effect and eliminate patients' anxiety. Since cocaine was first used in maxillofacial surgery for local anesthesia in 1884, the development of LA agents has experienced a golden stage. The new anesthetics has replaced the conventional drugs. For example, procaine, which is widely used in the last century, is almost invisible in dental clinical because of its own allergenicity. With the first appearance of lidocaine, amides have gradually become the main stream in dental LA, and then some other amides, such as articaine, mepivacaine and bupivacaine, have been derived. Injection technique of LA has also been optimized with the development of science. For instance, with the

emergence of computer-aided injection system, there seems to be a prospective to improve success anesthesia rate of LA. Though, in less developed areas, the popularization of computer is unrealistic, and the successful LA depends more on the experience of clinicians.

In the rapid development of LA in oral and maxillofacial surgery, we must also be aware that there is still a long way to go to acquire the best LA method. How to further improve the success rate of anesthesia, develop efficient and safe LA agents, and provide a better pain management should become the focus in scientists' study. We believe that in the field of LA in oral and maxillofacial surgery, there are still many scientific research topics worth exploring.

Declaration of competing interest

The authors declare no conflict of interests.

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