Pomeranian J Life Sci 2025;71(1):31-39 doi: 10.21164/pomjlifesci.1045

Ropivacaine – its pharmacology, properties, and clinical use within orofacial tissues with a particular focus on dental practice

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ABSTRACT

Ropivacaine is a long-acting local anaesthetic from the aminoamide drug class. Synthesized in 1957, it was brought into clinical practice at the end of the 20th century. The drug is used in medicine, especially in the field of general surgery and obstetrics. Unlike structurally akin bupivacaine, which is also sold in cartridges for carpule-type syringes popular in dental practice, no dental formulations of ropivacaine are available to this day. The paper presents the characteristics of ropivacaine and its properties. Particular emphasis is placed on the possible use of ropivacaine within orofacial tissues. Data from trials in dental settings conducted in the past 2 decades were discussed, with implications important for dentists. The drug may be a suitable option for time-consuming oral procedures, particularly when prolonged postoperative analgesia is desirable.

Ropivacaine, with its efficacy, lower propensity for motor block, and reduced potential for central nervous system (CNS) toxicity and cardiotoxicity compared to other long-acting drugs from the class, is an important alternative in regional anaesthesia and the management of postoperative pain and, as such, should not be overlooked in dental practice.

Keywords: ropivacaine; local anaesthetics; local anaesthesia; postoperative pain management; dentistry.

INTRODUCTION

Ropivacaine hydrochloride appeared in medical practice at the end of the 20th century. Synthesized in 1957, it was first brought into clinical application in 1996 in the United Kingdom and British Commonwealth (Naropin, AstraZeneca) and was soon approved in other countries in the years that followed. In Poland, for example, the drug was registered in 2001 [1, 2, 3].

Ropivacaine is an aminoamide-type local anaesthetic and a xylidine derivative. Structurally, the drug is related to mepivacaine and bupivacaine. These 3 agents share a common structure, with the main difference being the substituent bonded to the piperidine nitrogen: for ropivacaine, it is a propyl group; for bupivacaine, a butyl group; and for mepivacaine, a methyl group [4, 5].

The chemical structures of ropivacaine and other xylidine local anaesthetics used in dentistry are shown in Figure 1.

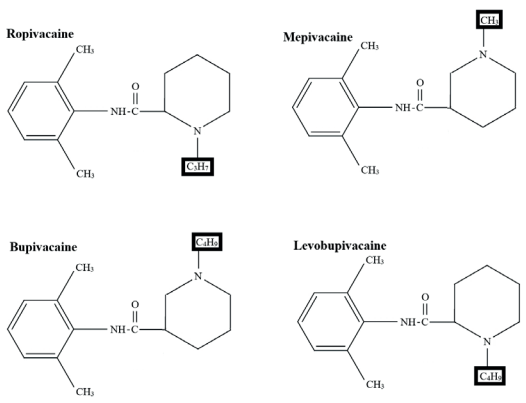

FIGURE 1. Chemical structure of ropivacaine and other xylidine derivatives – mepivacaine, bupivacaine

Ropivacaine is prepared solely as an S-isomer, while mepivacaine is a racemic mixture [6]. Formulations of bupivacaine, in turn, are sold as racemic mixtures, and recently, the hydrochloride of the pure S-enantiomer of the drug (levobupivacaine) has become available [4]. Like other local anaesthetics, ropivacaine blocks impulse conduction in sensory nerve fibres by reversibly inhibiting sodium ion influx [7]. This action is enhanced by dose-dependent inhibition of potassium channels [1, 8].

Like bupivacaine, ropivacaine is characterised by a relatively long duration of anaesthetic effect after administration, while its common feature with mepivacaine is its weak vasodilatory effect, allowing for the use of plain (i.e., without a vasoconstrictor) solutions in clinical practice [5, 9]. Regarding the latency period after ropivacaine administration, information from trials is not unequivocal and varies depending on the solution concentration and the type of block employed. However, it generally appears that the time required for the development of the anaesthetic effect is shorter than that of bupivacaine [2].

Ropivacaine exhibits some chondrotoxic properties, less pronounced than those of bupivacaine but more distinct compared to mepivacaine [10, 11]. Additionally, it inhibits platelet aggregation [12]. Ropivacaine has also been observed to exert anti-inflammatory activity, with inhibition of both leukocyte rolling and adhesion appearing to be the underlying mechanism [13]. Unlike other drugs commonly used in local anaesthesia, the cationic form of ropivacaine lacks antimicrobial and antiviral properties [10, 14, 15].

After administration, ropivacaine undergoes significant hepatic metabolism into 4 inactive products, with only an estimated 1% of the administered dose excreted unchanged in the

urine [16]. The drug is primarily used in medicine, particularly in general surgery and obstetrics [1, 12, 17].

Unlike bupivacaine, which is also available in cartridges for carpule-type syringes commonly used in dental practice (e.g., Marcaine 0.5% bupivacaine with epinephrine 1 : 200,000, Septodont), no dental formulations of ropivacaine are available to this day [2, 5, 18, 19]. Currently, the only ropivacaine formulation available in Poland is sold in 10 mL ampoules (Ropimol, Molteni), which, although usable in dentistry, is far less convenient [20]. However, despite the lack of dental-specific formulations, the last 2 decades have seen trials and attempts to use ropivacaine in this field. This paper focuses on trials and reports concerning the use of ropivacaine within orofacial tissues, with a particular emphasis on dental practice.

ROPIVACAINE – INSIGHT IN ITS PROPERTIES

Ropivacaine formulations contain only the S-enantiomer, which has been proven to be less toxic than its chiral counterpart [21]. The concentration of ropivacaine solutions used in medicine ranges between 0.2–1% [5, 22]. The optimal concentration of ropivacaine in dentistry is not well-established, but researchers tend to choose concentrations between 0.5–1%, as more diluted solutions have been observed to be less effective [2, 6]. In conducted trials, 0.5% and 0.75% concentrations were found to have a rapid onset and produce good surgical conditions lasting more than 3 h [2]. Lower concentrations of ropivacaine (0.25% and 0.375%) have a selective analgesic effect, as they clinically block thin Aδ and C nerve fibres more readily than large Aβ fibres. Although at lower concentrations the drug may be suitable for providing postoperative analgesia, higher concentrations (0.5% and 0.75%) are required for effective surgical anaesthesia [23].

The vasoactive properties of the drug are another feature dependent on its concentration. Generally, most local anaesthetic drugs used in dentistry exhibit inherent vasodilator activity [24]. This effect is intrinsically linked to their mechanism of action and results from blocking small sympathetic vascular nerve fibres [5]. The only local anaesthetics with pronounced vasoconstrictive properties are cocaine and centbucridine [25]. Among aminoamide anaesthetics, mepivacaine – a drug structurally similar to ropivacaine – exhibits the least vasodilatory effect [7]. Mepivacaine induces vascular contraction mediated by calcium ion influx through voltage-opened calcium channels (VOCCs) and calcium release from the endoplasmic reticulum. Therefore, the vasodilatory effect of the drug, caused by blocking small sympathetic vascular nerve fibres, is counteracted by slight vasoconstriction resulting from an intracellular calcium increase in endothelial cells at the site of administration [26].

Ropivacaine is the only local anaesthetic that exhibits a biphasic vascular effect [27]. At lower concentrations (0.063–0.5%), the drug affects calcium ion currents in smooth muscle cells of the vascular endothelium, leading to vasoconstriction, which is even more pronounced than that of mepivacaine. However, at its highest concentration (1%), vasodilation becomes the predominant effect [28, 29]. The vasoconstrictive mechanism is responsible for the skin blanching observed after subcutaneous infiltration with lower concentrations of ropivacaine [30]. Interestingly, the addition of epinephrine does not seem to improve the quality or duration of the anaesthetic effect, making the use of a vasoconstrictor unnecessary for ropivacaine in dentistry when administered in concentrations below 1% [2, 31]. On the other hand, some trials have employed 0.5% and 0.75% ropivacaine solutions with epinephrine in inferior alveolar nerve blocks (IANBs) and in maxillary and palatal infiltrations, reporting desirable effects [6, 23, 32, 33].

The maximum adult dose of ropivacaine is 675 mg, while in children, it is 3 mg/kg body weight. However, even at higher doses, neurotoxic effects were often absent [5, 34]. A closer examination of ropivacaine's properties inevitably leads to comparisons with its structurally related long-acting counterpart, bupivacaine, which is already used in dentistry and oral surgery [5, 35, 36]. The physicochemical properties of ropivacaine compared to bupivacaine are summarized in Table 1.

The dissociation constant (pKa) is one of the most important properties of local anaesthetics. Local anaesthetics used in dentistry are salts of a weak organic base and a strong acid (usually hydrochloride). In solution, an ionised (cationic) and an un-ionised (basic) form of the drug exist in dynamic equilibrium. For an anaesthetic to exert its effect, it must cross the lipid cell membrane and block the voltage-gated sodium channel from the inside – only the lipophilic, un-ionised form can achieve this. The pKa is the pH at which the concentrations of the 2 forms are equal [7]. The lower the pKa, the higher the concentration of the basic form under physiological conditions, resulting in a shorter onset time for the anaesthetic effect [24].

The pKa value for ropivacaine is identical to that of bupivacaine, both being 8.1 – the highest among amino-amide local anaesthetics used in clinical practice [5]. This means that at the physiological pH of healthy tissues (approx. 7.4), only 15% of the drug is in the un-ionised form, capable of crossing the neuronal cell membrane [36]. However, despite having the same pKa value, ropivacaine has a faster onset than bupivacaine due to its weaker binding to extraneural and submucosal tissues, resulting from lower lipophilicity [2, 35]. Lower lipid solubility leads to a higher free concentration of ropivacaine, allowing more molecules to bind to and penetrate the nerve sheath, facilitating more rapid diffusion to the site of action [2, 37].

Furthermore, due to its lower lipophilicity, ropivacaine is less likely to penetrate large myelinated motor fibres, resulting in a relatively reduced motor blockade. The motor block induced by ropivacaine is slower in onset, less intense, and shorter in duration compared to an equivalent dose of bupivacaine [35]. Motor nerve block is a more significant concern in epidural or spinal anaesthesia. In dental procedures, motor fibres are generally not affected unless the drug is inadvertently deposited near the facial nerve, such as when the parotid gland is entered during an inferior alveolar block [36]. The sensory block provided by ropivacaine is comparable to that of an equivalent dose of bupivacaine in both extradural and peripheral nerve blocks [35]. Reduced lipophilicity is also associated with a lower potential for cardiotoxicity and central nervous system (CNS) toxicity [12].

TABLE 1. Comparison of the physicochemical characteristics of ropivacaine and bupivacaine

Feature	Ropivacaine	Bupivacaine	Practical impact
MW	274	288	the MW of both agents is relatively high, resulting in the slow diffusion of their molecules through membranes
pKa	8.1	8.1	a longer latency period is usually observed compared to agents with a lower pKa value; however, the pKa value is not the only factor influencing the length of the latency period (see remarks in the rows "Partition coefficient" and "pH of the formulations")
Plasma protein binding	94%	95%	only an unbound drug can cross the membranes, and since sodium channels are composed of protein subunits, high protein binding values indicate a long duration of action and relatively low bioavailability for both agents
Partition coefficient (N-heptane/ buffer)	2.9	10	ropivacaine is less lipophilic than bupivacaine, resulting in lower toxicity and potency, but also lower efficacy after topical administration; the lower lipophilicity of ropivacaine shortens the latency period compared to bupivacaine, as less of the drug binds to extra-neural tissues
Toxic plasma concentration	>4 μg/mL	>1.5 μg/mL	ropivacaine is less toxic than bupivacaine
pH of the formulations	about 5.5	about 4.0	the less acidic character of ropivacaine formulations contributes to less pronounced pain and discomfort during administration; additionally the higher pH value results in a higher concentration of the un-ionised form of the drug, leading to a faster onset of action

MW – molecular weight; pKa – dissociation constant

Another important property to compare is protein binding. Local anaesthetics bind to plasma proteins, primarily albumin and α1-acid glycoprotein [24]. The plasma protein binding of ropivacaine is slightly lower than that of bupivacaine (94% vs. 95%) [35, 38]. Since only the unbound fraction of the drug is free to cross membranes, and given that sodium channels are protein-based structures, the high degree of protein binding contributes to the prolonged anaesthetic effect [24, 38]. The toxic plasma concentration threshold is significantly higher for ropivacaine than for bupivacaine (>4 μg/mL vs. >1.5 μg/mL, respectively), indicating a more favourable safety profile for ropivacaine [24].

Lastly, a key difference between these 2 structurally related xylidine derivatives is the pH value of their available formulations. The higher pH of ropivacaine (typically around 5.5) compared to bupivacaine (4.0) results in a higher concentration of the basic form, which more readily crosses the neuronal membrane. Additionally, this contributes to reduced discomfort during administration, as even slightly acidic solutions can cause an unpleasant, sometimes burning sensation – an issue well known in dental practice [5, 33, 39, 40]. A simple method to improve patient comfort and accelerate the onset of anaesthesia is warming the solution to body temperature before administration. However, alkalinisation (buffering) of ropivacaine with sodium bicarbonate, a technique commonly used with other aminoamide anaesthetics, is not recommended, as ropivacaine precipitates more rapidly than other local anaesthetics under such conditions [41].

THE USE OF ROPIVACAINE IN OROFACIAL TISSUES – THE OUTCOMES FROM TRIALS IMPORTANT FOR DENTISTRY AND ORAL SURGERY

The clinical applications and outcomes relevant to dentistry and oral surgery, as evaluated in trials conducted over the last 2 decades, are summarised in Table 2.

The main indications for the use of long-acting local anaesthetics in dentistry include extensive dental procedures requiring pulpal anaesthesia for more than 90 min and postoperative pain management [42]. The usefulness of ropivacaine in dentistry has been assessed in IANB, infiltrative and intraligamentary blocks, and topical anaesthesia. Beyond postoperative pain management, the long anaesthetic and analgesic effects of ropivacaine have also been examined in trigeminal neuralgia (TN).

Inferior alveolar nerve block is the most common conduction anaesthesia technique employed by dental practitioners [7]. The anatomical structure of the mandibular bone, specifically the thick cortical bone on the buccal side of the alveolar ridge in the lower posterior teeth region, necessitates the use of this block for intraoperative pain control, especially in procedures involving mandibular premolars and molars in adults [43]. The anatomy of the mandible in children differs, as the cortical bone is thinner, yet infiltrative blocks for lower molars may not be sufficient for intraoperative pain control, making IANB necessary [34].

Initial trials aimed at determining the appropriate concentration of ropivacaine for IANB found that 0.5% and 0.75% solutions were the most effective [44, 45]. Both concentrations provided effective IANB with a reasonable onset time and prolonged anaesthesia in pulp, bone, and soft tissues [46]. Importantly, 0.5% ropivacaine was effective in achieving pulpal anaesthesia in lower molars with symptomatic irreversible pulpitis, a common challenge in daily dental practice [47]. The administered volumes ranged 1–3.5 mL, most commonly using 1.8 mL, equivalent to a standard dental cartridge [27, 37, 48, 49, 50]. A shorter onset time was observed with higher concentrations and larger volumes, likely due to the drug's low lipophilicity, which increases the availability of ropivacaine molecules to penetrate the nerve sheath more efficiently [45, 48]. The duration of anaesthesia was also concentration-dependent, with 0.75% ropivacaine typically lasting over 6 h [44].

TABLE 2. Possible clinical applications of ropivacaine with important results for dental practice

Clinical application	Results from trials	Can ropivacaine be used in this application?	Outcomes important for dental practice
IANB	0.5% and 0.75% ropivacaine, administered in volumes of 1–3.5 mL, provides effective intraoperative pain control in procedures within the fields of oral surgery and conservative dentistry	yes	0.5% and 0.75% ropivacaine (the latter concentration may be a better choice for more painful procedures) can be used in oral surgery and dentistry, particularly when longer-than-usual anaesthesia is required and the use of a vasoconstrictor should be avoided; this type of block is not recommended for children younger than 12 years or patients with mental disabilities due to the higher risk of self-inflicted injuries to anaesthetised soft tissues
Infiltrative anaesthesia	ropivacaine in a 0.5% concentration, when administered in volumes of at least 1.8 mL, provides effective pulpal and soft tissue anaesthesia, ensuring satisfactory intraoperative pain control; a 0.75% concentration is effective when administered in volumes of at least 1 mL, although better effects were observed when the volume was equal to or exceeded 1.8 mL; a 1% concentration also proved effective	yes	the choice of volume is important and should be greater than 1 mL; the duration and intensity of the anaesthetic effect appear to increase with the concentration used; the onset of action is faster than that of bupivacaine, while the effect obtained is long-lasting
Intraligamentary anaesthesia	0.75% and 1% ropivacaine provided insufficient and short-duration anaesthesia of the pulp and adjacent soft tissues	no	the use of ropivacaine in periodontal ligament anaesthesia is not recommended
Topical anaesthesia	cotton swabs soaked with a 1% solution, as well as 1% and 2% liposomal ropivacaine gel, provided sufficient anaesthesia in the oral mucosa but were not effective in the region of the hard palate	yes (but further research is needed)	direct topical application of swabs soaked with 1% ropivacaine solution can be used as a symptomatic measure for painful conditions of the oral mucosa; caution should be exercised regarding potential systemic absorption of the drug through lesions; experimental liposomal ropivacaine gels (1% and 2% concentrations) have been proven effective in the oral vestibule but not in the palatal mucosa
Postprocedural pain management in oral surgery	0.5%, 0.75%, and 1% ropivacaine, when used as additional blocks or as the sole means of anaesthesia, can be beneficial for postoperative pain control, although the results remain inconclusive	yes (but further research is needed)	IANB and infiltration with 0.5% and 0.75% ropivacaine have been proven effective for post-procedural pain management in oral surgery performed under general anaesthesia; post-procedural pain control was also achieved when 0.5% and 0.75% ropivacaine was used as an anaesthetic in IANB; however, regarding ropivacaine used in infiltration anaesthesia, the results from trials remain inconclusive; topical application of 1% ropivacaine (using a swab soaked in the drug solution) has been proven effective in post-procedural pain management in ENT surgery, encouraging similar trials in oral surgery, particularly after tooth extraction
Nerve blockade in TN	ropivacaine at concentrations of 0.25–0.75% has been used in peripheral blocks in trigger zones	yes	(note that patients with TN should be referred to a neurology specialist); solutions used for peripheral blocks in trigger zones by infiltration and topical administration (intranasal application for sphenopalatine ganglion block) were effective in TN pain management; however, better results were achieved when peripheral blocks with ropivacaine were combined with low doses of oral anticonvulsants such as gabapentin or carbamazepine

ENT – ear, nose, throat; IANB – inferior alveolar nerve block; TN – trigeminal neuralgia

Both concentrations effectively facilitated painless completion of various oral surgery procedures, including extractions and implant placement [27, 42, 51, 52, 53]. However, in a study by Bhargava et al., 0.5% ropivacaine induced soft tissue numbness but did not provide sufficient intraoperative pain control for surgical extraction of impacted lower wisdom teeth, leading the authors to recommend the use of 0.75%, which proved effective [54]. Conversely, Goyal et al. found 0.5% ropivacaine successful for IANB in the same indication [50]. Based on research findings, 0.5% and 0.75% plain ropivacaine solutions administered in IANB appear to be valuable options for intraoperative pain control in various dental and oral surgery procedures, particularly when prolonged anaesthesia is needed and vasoconstrictors are contraindicated. However, the prolonged soft tissue anaesthesia achieved excludes the use of IANB with ropivacaine in children under 12 years of age and patients with mental disabilities, as these groups have a higher risk of self-inflicted oral injuries due to prolonged numbness [34].

Infiltration anaesthesia is commonly used for dental procedures in the upper jaw, where the relatively thin cortical bone facilitates diffusion of the local anaesthetic solution. This technique is effective for all buccal roots of the upper teeth, while palatal roots of molars and premolars require additional palatal infiltration [55]. In the mandibular anterior region of adults, where the cortical bone is thinner, infiltration can be effective, whereas in children, this method suffices for procedures up to the first lower molars [43].

Early trials using ropivacaine for infiltration anaesthesia yielded discouraging results at all tested concentrations (0.2%, 0.5%, and 0.75%), likely due to the small administered volumes (0.5–1.0 mL) [44]. However, subsequent studies using 0.75% ropivacaine reported favourable outcomes. Bansal et al. found that 0.75% ropivacaine (0.5 mL) provided adequate pulpal anaesthesia and numbed adjacent soft tissues, including the palate, eliminating the need for palatal infiltration, which suggests good diffusion properties [56]. Axelsson and Isacsson demonstrated that 1 mL of 0.75% ropivacaine provided sufficient anaesthesia for pulpal and soft tissues in the upper jaw, with an increased duration when the volume was doubled [48].

When 0.5% ropivacaine was administered in volumes between 1.8–2.5 mL, it provided satisfactory pulpal and soft tissue anaesthesia and was successfully used in periodontal surgery [33, 57, 58]. Additionally, 0.75% ropivacaine in volumes between 1.8–3 mL proved effective for various oral surgery procedures [49, 59]. Studies comparing infiltration anaesthesia using 0.5%, 0.75%, and 1.0% ropivacaine suggest that at a fixed volume (2.5 mL), the duration and intensity of anaesthesia increase in a concentration-dependent manner [60]. The use of 1% ropivacaine for long-duration procedures in the maxilla is an attractive option; however, the drug's vasodilatory properties at this concentration need further investigation [2, 60]. A recent meta-analysis concluded that ropivacaine produces a similar anaesthetic effect to other local anaesthetics, with a prolonged duration of action – shorter only than bupivacaine – and a favourable onset time, faster than that of bupivacaine [61].

Ropivacaine was also assessed for intraligamentary anaesthesia, but results were discouraging. When compared to 2% lidocaine with epinephrine 1 : 80,000, plain ropivacaine (0.75% and 1%) was less effective, and, unexpectedly, the pulpal anaesthesia achieved was shorter [62]. Intraligamentary anaesthesia requires adequate vasoconstriction for optimal efficacy, and its effectiveness is more dependent on the vasoconstrictor concentration than the anaesthetic itself [63, 64]. While 0.75% ropivacaine exhibits some vasoconstrictive properties, they are insufficient to ensure success in this type of block [6, 62]. Additionally, the typical small injection volume (0.2 mL per single-rooted tooth) may have contributed to its ineffectiveness, as low volumes were also found ineffective in infiltration anaesthesia [44].

Topical anaesthesia differs from the other types of dental blocks already mentioned. While in the case of IANB, infiltration, and intraligamentary anaesthesia the drug is administered in close proximity to a sensory nerve trunk or its endings, in surface anaesthesia it is applied on the mucosa and reaches free nerve terminals after passing through its layers [65]. The topical use of ropivacaine solution has been assessed in medicine. Among others, it was reported in the field of laryngology, where the anaesthetic properties of 0.75% ropivacaine spray were employed to reduce irritation caused by endotracheal intubation, and in dermatology, where the analgesic action of the drug in lower concentrations (0.2%) allowed for the alleviation of ailments related to aplasia cutis congenita (ACC; the congenital absence of skin in parts of the body, usually the scalp) in hereditary epidermolysis bullosa [66, 67]. Within the oral cavity, ropivacaine has been proven to be an effective tool in combating pain in oral aphthosis. A simple measure proposed by Gasparini et al. was the direct application of a cotton pad soaked with 1% ropivacaine solution on the affected oral mucosa [68].

Other types of experimental ropivacaine formulations that seem to be the most promising in topical anaesthesia are those employing liposomes. Liposomes are spherical nanovesicles consisting of a phospholipid bilayer, lipophilic on the outside and hydrophilic on the inside. This dual nature of these particles allows for the encapsulation of local anaesthetic solutions, facilitating their diffusion through the mucosal layers and providing sustained release [69].

Applied to the upper buccal fold of the oral vestibule, liposome-encapsulated 1% ropivacaine gel provided satisfactory soft tissue anaesthesia and was effective in pain reduction during needle insertion, performing equally to a eutectic mixture of local anaesthetics (EMLA), prilocaine and lidocaine, and better than unmodified 1% ropivacaine gel [70]. In the same area, 2% liposomal ropivacaine was proven to be equally effective as 20% benzocaine gel, a widely used topical anaesthetic in many countries [71]. However, neither 1% nor 2% liposomal ropivacaine gel was effective enough to reduce pain during needle insertion into the palatal mucosa [72]. This failure is most likely due to the anatomical characteristics of this region. The palatal mucosa is keratinised and tightly bound to the underlying periosteum (the so-called mucoperiosteal complex), and its sensory nerve supply is abundant [7, 73].

In general surgery, ropivacaine is frequently used for postoperative pain management. Its efficacy for postoperative epidural pain relief has been demonstrated in numerous studies. The relatively reduced motor block makes ropivacaine a preferred choice over other long-acting amino-amides like bupivacaine or etidocaine [74]. These findings encouraged further trials in oral surgery.

Within orofacial tissues, ropivacaine has been successfully used for postoperative pain management in maxillofacial surgery performed under general anaesthesia. When 0.5% ropivacaine was administered via IANB, it not only resulted in low postoperative pain scores after sagittal split mandibular osteotomy but also restricted intraoperative bleeding due to its inherent vasoconstrictive properties [75]. Additionally, ropivacaine infiltration proved effective in managing postoperative pain after cleft palate repair in younger patients [76, 77]. In oral surgery procedures performed under general anaesthesia, infiltration with 0.75% ropivacaine for third molar extraction also yielded beneficial outcomes, reducing postprocedural pain on the first day after surgery [78].

The excellent results of topical ropivacaine in postoperative pain control in ear, nose, throat (ENT) surgery, such as the application of a swab soaked with 1% ropivacaine after tonsillectomy, suggest that a similar approach could be beneficial following tooth extractions. Since this technique has already been proven effective with bupivacaine, further research on ropivacaine in this context is warranted [79, 80].

The use of ropivacaine in postoperative pain management is not limited to additional administration during or after the procedure. Due to its long anaesthetic action and analgesic properties, the drug can be employed for both intraoperative and postoperative pain control [81]. Several previously mentioned studies reported such outcomes after IANB with 0.5% and 0.75% ropivacaine [19, 23, 27, 42, 50, 51, 53]. One could argue that the discomfort caused by prolonged lip numbness after IANB with ropivacaine is offset by the reduction in postoperative pain [82].

Interestingly, postoperative pain control with IANB was also achieved when ropivacaine was combined with another local anaesthetic. In a study by Hemmi et al., a 1 : 1 mixture of 2% lidocaine with epinephrine and 0.75% ropivacaine provided effective anaesthesia and was efficient in managing postoperative pain following third molar extraction [83]. In cases of IANB with 1% ropivacaine, postoperative pain control in surgical extractions of impacted mandibular wisdom teeth was found to be superior to intraoperative anaesthesia, supporting the use of 1% ropivacaine as a supplemental nerve block after surgery [18]. Regarding infiltration blocks, the results varied across different concentrations (0.5%, 0.75%, and 1% ropivacaine), with surprisingly better outcomes observed at the lowest concentration [58, 60].

The last practical application of ropivacaine in orofacial tissues that has been studied is TN management. The trigeminal nerve is the largest cranial nerve and has 3 branches that provide sensory innervation to the anterior ⅔ of the head and face. Trigeminal neuralgia is characterized by sudden, severe, brief, and stabbing recurrent episodes of facial pain affecting 1 or more branches of the trigeminal nerve. These pain attacks can occur spontaneously or be triggered by non-noxious stimuli. Some patients also experience persistent background pain, which, along with autonomic signs and prolonged disease duration, is associated with poorer treatment outcomes. The management of TN extends beyond routine dental practice and requires multimodal strategies, often involving collaboration with a neurologist. It is now widely accepted that neurovascular compression at the trigeminal root entry zone is an anatomical abnormality strongly correlated with classical TN [84].

One of the strategies for pain management in TN is the use of long-acting local anaesthetics for peripheral nerve blocks in trigger zones. Ropivacaine solutions have been reported to be beneficial even at relatively low concentrations (e.g., 0.25% ropivacaine, 4 mL, administered via infiltration for post-traumatic TN) [85].

An interesting approach for self-administration of ropivacaine in maxillary nerve (V2) neuralgia was proposed by Lima et al. The sphenopalatine ganglion, located in the pterygopalatine fossa, is anatomically accessible via the nasal cavity. This location allows for self-administration of a sphenopalatine ganglion block using nasal swabs soaked in 0.75% ropivacaine [86].

Although ropivacaine alone has demonstrated adequate analgesia for TN, superior results have been obtained when peripheral nerve block therapy was combined with low-dose orally administered antiepileptic drugs such as gabapentin or carbamazepine [87].

CONTRAINDICATIONS, SIDE EFFECTS

Ropivacaine is generally a safe drug, well tolerated regardless of the route of administration [88]. The only absolute contraindication to ropivacaine is known hypersensitivity to ropivacaine or any amide-type local anaesthetic [1]. Due to its high protein binding, extreme caution should be exercised when administering ropivacaine to patients with hypoalbuminaemia. Low albumin concentrations in such cases favour higher plasma concentrations of the drug, which contributes to toxic effects. The recommended approach in this situation is to use lower doses [89].

Local anaesthetic systemic toxicity (LAST) primarily affects the CNS and cardiovascular system. Local anaesthetics can be classified using a cardiovascular collapse (CC) to CNS ratio, which represents the dose required to cause CC compared to the dose required to produce seizures. Ropivacaine has a higher CC to CNS ratio than bupivacaine and levobupivacaine, indicating a greater margin of safety. Compared with other amino-amide local anaesthetics, ropivacaine has a greater arrhythmogenic cardiac effect but affects heart contractility to a lesser extent [90]. However, arrhythmia caused by ropivacaine overdose tends to be milder and easier to manage compared to similar effects observed with bupivacaine overdose [5]. Pregnancy may influence the CNS toxicity potential of ropivacaine, as trials have shown that the cumulative dose

required to induce convulsions was lower in pregnant animals compared to non-pregnant ones [88].

Adverse events with ropivacaine are rare when properly administered [1]. Data from general surgery indicate that the most common side effects, ranked by prevalence, are: hypotension (32%), nausea (17%), vomiting (7%), bradycardia (6%), and headache (7%) [1]. However, reports from trials involving ropivacaine use in orofacial tissues, as summarized in this paper, have not documented similar outcomes [49, 57]. The doses of ropivacaine used in dental procedures, based on research findings, are significantly lower than those routinely employed in general surgery, making adverse reactions less likely in dental practice [33].

SUMMARY

Local anaesthesia forms the backbone of dental practice, and local anaesthetics are the most frequently used drugs by dentists. Ropivacaine is a long-acting amide-type anaesthetic that can be useful in various everyday procedures, particularly in oral surgery, where it may serve as a valuable alternative to bupivacaine due to its significantly greater safety margin [2]. The drug may be suitable for time-consuming oral procedures, especially when prolonged postoperative analgesia is desirable.

Thus, ropivacaine, with its efficacy, lower propensity for motor block, and reduced potential for CNS toxicity and cardiotoxicity compared to other long-acting drugs in the same class, is an important option for regional anaesthesia and postoperative pain management and should not be overlooked in dental practice [6].

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