



Vasoconstrictor for Local Anesthetics

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Dental local anesthetics contain vasoconstrictors, such as adrenaline and felypressin, to enhance the anesthetic effects and reduce bleeding in the surgical field.

Adrenaline has been used for long periods of time as an additive to local anesthetics. With a typical dose range of 10 - 12.5 μg /mL, adrenaline is believed to prolong duration by its vasoconstrictive properties that prevent systemic reabsorption of local anesthetics. Several reports have warned against the use of dental local anesthetics containing adrenaline in patients with cardiovascular diseases [1, 2]

On other hand, felypressin, a non-catecholamine vasopressor that is chemically related to vasopressin, has been used as a safe vasoconstrictor in patients with compromised cardiovascular status in Japan and European Union nations [3]. However, there have been reports that, in a dog study, clinical doses of felypressin caused decreases in coronary blood flow [4]. But, in felypressin contained propitocaine, felypressin have maintained oxygen supply in myocardial tissues by maintained myocardial blood flow [5].

An α -2 adrenoceptor agonist, clonidine, combined with a local anesthetic, has been found to extend the duration of the peripheral nerve block. The action of clonidine was suggested to be due to local vasoconstriction [6]. But, clonidine is not particularly specific for α -2 adrenoceptors and acts via α -1 adrenoceptors at comparatively high concentrations. Thus, it is unclear whether it acts via α -2 adrenoceptors. And despite substantial study, it is not clear which doses of clonidine are optimal for prolongation of analgesia after peripheral nerve blocks. The use of perineural clonidine is not currently recommended for clinical use [7].

On the other hand, another α -2 adrenoceptor agonist, dexmedetomidine, acts more specifically against α -2 adrenoceptors and has more than 7-8 times the affinity for α -2 adrenoceptors of clonidine. Dexmedetomidine, which produce sympatholytic, sedative, analgesic, antihypertensive and bradycardiac effects when combined with a local anesthetic agent, have been found to extend the duration of local anesthesia effect by causing local vasoconstriction. Dexmedetomidine is a selective α -2 adrenoceptor agonist. α -2 adrenoceptors are subdivided into four subtypes: α -2A, α -2B, α -2C and α -2D. The α -2A, α -2B and α -2C adrenoceptors have been well identified pharmacologically and have been shown to cause vasoconstriction [8-10]. The other possible mechanism for enhancement and prolongation of local anesthetic action by dexmedetomidine is its direct effect on peripheral nerve activity. A direct action of dexmedetomidine has been reported on exposure of isolated sciatic nerve fibers to dexmedetomidine [11]. However, direct effect of dexmedetomidine on peripheral nerve activity was not observed *in-vivo* [12]. It is reported that dexmedetomidine administered alone for epidural anesthesia, at the concentration that was shown in this study to effectively enhance local anesthetic action, produced no local anesthesia effects [12]. A possible explanation for this discrepancy is that epidural anesthesia involves injection of the local anesthetic solution into the epidural space, which includes loose connective tissue. The pterygomandibular space, which is the region where the drug is injected for Inferior Alveolar Nerve Block, also includes loose connective tissue, making it similar to the epidural space. In conduction anesthesia involving penetration of a nerve fiber in connective tissue and jawbone, dexmedetomidine enhances the local anesthetic action of lidocaine by vasoconstriction via α -2A, α -2B and α -2C adrenoceptors around the site of injection. Based on the mechanism that the local anesthesia reinforcement action of dexmedetomidine depends on local vasoconstriction, using a sedated tail-



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flick and epidural animal model, we previously reported that prolongation of the local anesthetic effect by dexmedetomidine was concentration-dependent [12,13].

We studied dexmedetomidine for local anesthetic, now. Use of a new drug, dexmedetomidine, that can replace adrenaline and felypressin for the safe enhancement of local anesthesia effect in patients with cardiovascular diseases, may be recommended.

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