



Effect of Local Anaesthesia in Young Pulpal Cells - A Review

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ABSTRACT

Pulp cells are essential for tooth development, dentin repair and regeneration. In addition these cells have been identified as an important stem cell source. Local anaesthetics are widely used in dental clinics, as well as the other clinical disciplines. Local anaesthetics work by binding to voltage-gated Na⁺ channels in nerves, therefore block sodium transportation and nerve conduction. The commonly used local anaesthetics contain a vasoconstrictor to prolong the anesthetic effect. Vasoconstrictors interfere with pulpal blood flow by reducing diameter of the blood vessels. Lignocaine, Articaine, bupivacaine, mepivacaine and prilocaine are the commonly available local anaesthetics. It has been suggested to interfere with human permanent tooth development and induce tooth agenesis through unknown mechanisms. Literature survey shows novel evidence that local anaesthetics could affect tooth cell growth that potentially can have impacts on tooth development. It is important to understand the effects of LA on the young pulpal cells as it affects the vitality of the tooth. Local anaesthetics reduce SP levels in the pulp, thereby reducing the pulpal blood flow leading to pulpal degeneration. LA administered to young children when the third-molar tooth bud is immature may stop third-molar development. Bafilomycin A1 is an autophagy inhibitor, which can be used if needed. The aim of the review is to understand the effect of local anaesthesia in young pulpal cells.

Keywords: Local anaesthetics, pulpal cells, autophagy, tooth development.

INTRODUCTION

Local anaesthesia is the loss of sensation in an area of the body caused by an inhibition of the peripheral nerve conduction or a depression of excitation in nerve endings¹. Local anaesthetic solutions have been used for dental procedures to eliminate pain associated with invasive procedures^{2,3}. Local anaesthetics work by binding to voltage-gated Na⁺ channels in nerves, therefore block sodium transportation and nerve conduction^{2,4}. The commonly used local anaesthetics contain a vasoconstrictor to prolong the anesthetic effect⁵. Vasoconstrictors interfere with pulpal blood flow by reducing diameter of the blood vessels^{6,7}. Lignocaine, Articaine, bupivacaine, mepivacaine and prilocaine are the commonly available local anaesthetics⁸. Dental Practitioners have the responsibility to alleviate pain. Fear of pain prevents many patients from obtaining dental care, so to eliminate pain and the fear of the patient local anaesthetics are provided.

Local anaesthetics used in dentistry are weak bases, and so are combined with an acid to form a salt (hydrochloride salt) to render them water-soluble, which creates a stable injectable anesthetic solution. The addition of hydrochloric acid creates undesirable qualities such as stinging and burning upon injection, relatively slow onset of action, and unreliable or no anesthesia when injected into infected tissues⁹. Local anaesthetics are generally much less effective when administered to patients with inflamed tissue¹⁰. A recent clinical epidemiological study showed that local anesthesia can potentially interfere

with human permanent tooth development and induces tooth agenesis through unknown mechanisms¹².

Local anaesthesia mainly causes autophagy and cell death in the pulp cells. Autophagy is a catabolic process involving the degradation of unnecessary or aberrant cellular components through hydrolysis of lysosomes. It therefore controls the turnover of organelles and proteins within cells, and of cells within organisms. During this process, targeted cytoplasmic constituents are isolated within autophagosomes, which then fuse with lysosomes to form autolysosomes where the cellular material is degraded or recycled¹³. It was previously observed that anesthesia drugs could induce vacuolation¹⁴. Molecular studies have led to the channel's pore neuronal depolarization consisting of four transmembrane domains, much like staves forming a barrel. Local anaesthetics bind to sites located on all four of these domains and thereby block sodium in flow^{10,15}.

Nerve fibres in the pulp

The large mass of pulp is present within the pulp chamber of the tooth. The shape of each pulp chamber chamber has coronal pulp and radicular pulp¹¹. The dental pulp is densely innervated with sensory fibers containing immunomodulatory neuropeptides such as Substance P (SP) and Calcitonin gene related peptide (CGRP). There are unmyelinated and myelinated fibres in the pulp corresponds to the shape of the tooth, and thus is individualized for every tooth; the pulp tissue in the pulp. Unmyelinated C fibers are the most sensitive to local anesthetic blockade, followed by the lightly myelinated neurons (A-delta fibers), with the heavily myelinated



neurons (A-beta fibers) being the least sensitive to these drugs¹⁶. In a normal circumstance, any pain perception is mediated by the C and A-delta fibers, whereas touch and proprioception are mediated by the A-beta fibers¹⁶.

Complications following local anaesthesia

Complications related to local anesthesia can be divided into two categories: preoperative and postoperative complications. Preoperative complications mainly include anxiety, fear of the needle etc., The Postoperative complications include pain, bleeding and hematoma formation, nerve injury, infection, ischaemic necrosis. Local anesthetic overdose results in excitation followed by depression of the central nervous system and to a lesser extent of the cardiovascular system.

Local anaesthetics and pulpal microcirculation

Pulp microcirculation maintains tissue homeostasis by the transportation of oxygen and nutrients and the removal of metabolic waste products¹⁷. The control of pulpal blood flow is regulated by neuropeptides released from pulpal nerve fibers, including SP, which is a potent vasodilator that regulates vascular permeability and modulates pain transmission via binding to its NK1 cell receptor^{18,19}. It has been shown that 4% prilocaine without vasoconstrictor maintains SP basal levels^{20,23}. It has been shown that neuropeptide expression is attenuated by alpha-adrenergic agonists like vasoconstrictors²⁴ because they generate vascular smooth muscle contraction; therefore reducing blood flow²⁵. Lidocaine with epinephrine competes with SP for the NK1 receptor. This could result in a reduced neuropeptide-receptor interaction, and, consequently, SP-dependent pulp defense mechanisms may be affected²⁶. Moreover, control of pulpal blood flow and tissue homeostasis regulated by SP could also be affected^{18,27}. This could have a clinical significance in terms of hemodynamic changes that need to take place when pulp dentin complex is being exposed to dental procedures²⁸. In addition to the role of SP in generating neurogenic inflammation, it has been shown that SP has a mitotic effect on fibroblasts and endothelial and smooth muscle cells²⁹. SP also has an effect in the recruitment of immunocompetent cells, thus playing a role in pulp healing and reparation³⁰. As dental pulp is in the low compliance environment, excessive vasodilation can cause a deleterious effect on the pulp by inducing pulpal inflammation via vessel damage³¹. As a result of all this, Local anaesthetics may lead to autophagy of the pulp. Bafilomycin A1 is an autophagy inhibitor. Bafilomycin A1 prevents maturation of autophagic vacuoles between autophagosomes and lysosomes by inhibiting fusion process by inhibiting vacuolar H⁺ ATPase. Treatment with 100 nM bafilomycin A1 for one hour blocks the fusion of autophagosomes with lysosomes in the rat hepatoma H-4-II-E cell line, based on data from electron microscopy.³²

CONCLUSION

In conclusion, it is evident that previous studies showed that Local anesthetics, especially with vasoconstrictors reduce SP levels in the pulp, thereby reducing the pulpal blood flow leading to autophagy or ischaemic necrosis. Local anaesthetics should be used only at needed times. Not all procedures in dentistry require local anaesthetics. Long term exposure of local anaesthetics can affect the development of permanent tooth in primary dentition. Bafilomycin A1 is an autophagy inhibitor, which can be used if needed.

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