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PRECOOLING AGENTS: A BOON TO LOCAL ANESTHETICS

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ABSTRACT

Early childhood experiences with painful injections may lead to anxiety and fear. The fear of pain attributed to anesthetic needle injections is cited as an obstacle in providing appropriate dental care. These reactions need not develop if steps are taken to reduce the pain associated with injections. This review presents recent findings regarding different treatment strategies such as applying pre-cooling agents, topical anesthetics, vibrating applying pressure to the injection site and using a mechanical delivery system. Cryoanesthesia has been reported to be promising to lessen the pain of the injection.

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INTRODUCTION

As a dentist, administering anesthesia to patients, especially children proves to be one of the most difficult parts of a procedure and most commonly fear, anxiety and development of avoidance behavior in children is also due to injection. Researches have shown that most of the pediatric patients postpone their dental visits primarily due to the fear of needles, pain and biting injury from injection (Munshi *et al* 2001, Okawa *et al* 2005). Local anesthesia (LA) are frequently used in dental practice to reduce acute and chronic pain as well as facilitate atraumatic dental treatment, also administered in pediatric dentistry(Malamed SF 2014). Its mechanism is to be deposited as close to the nerve as possible so that optimal diffusion of the drug may occur which provide profound anesthesia and a pain-free dental experience for the kids in treatments like extractions, pulpotomies, root canal treatments/pulpectomies, drainage of abscesses and minor oral surgical procedures.(Ghaderi *et al* 2013, Aminah *et al* 2017). However, the irony of the situation is that local anesthetics which are the most effective drugs for the prevention and management of pain are themselves associated with pain and this pain gets further aggravated due to the fear and anxiety caused by the sight of the needle and has been referred to as needle phobia or blenophobia (Kosaraju 2009). Thus, achieving an appropriate anesthesia is critical in modern dentistry and where the needle phobia has become an obstacle for pediatric patients, administrating various possible pharmacological and non-pharmacological desensitization techniques such as warming, buffering the local anesthesia, pre-cooling the site of injection, vibration or pressure, acupuncture, adjusting the rate of infiltration, hypnosis, applying topical anesthetics, computerized anesthesia delivery system (e.g., WAND), using modern devices like vibra ject, dental vibe, or accupal or jet injectors recently.(Malamed 2014, Aminah *et al* 2017). The most widely advocated technique to minimize the pain of local anesthesia is the use of topical anesthetic agent before injection. Benzocaine due to its prolonged effect and acceptable taste is the most popular topical anesthetic agent used in dentistry. Cryoanesthesia is the application of cold to a localized part of the body in order to block the local nerve conduction of painful impulses. It may be induced either by the use of refrigerant sprays or with the use of ice. The focal application of ice before and sometimes after painful procedures has been practiced for thousands of years and was one of the first source of local anesthesia and analgesia (Lathwal *et al* 2015).

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History

Man has known the use of cold for analgesia for thousands of years. Hippocrates (460-377 BC) left us the first written records of the use of ice for pain relief, describing how snow was brought down from the mountains in ancient Greece and applied to wounds for pain relief. The ancient Egyptians documented the use of low temperature for analgesia. Avicenna of Persia (980-1070 AD) an early physician, described the use of cold for pre-operative analgesia. Jean Larre, Napoleon's Surgeon General, noted in 1812 that half-frozen soldiers in the Moscow battle were able to tolerate limb amputation with little or no pain. In addition, John Hunter noted in 1777 that when roster comb cells were killed by cold, the base of the comb healed without scarring (Andrea 2003). Arnott described the use of severe cold to treat pain in 1848, and by 1851, he was avidly promoted the application of cold to relieve certain types of cancer and nerve pain, using mixtures of ice and salt at –20ºC.He also noted the hemostatic and anesthetic effects of such a mixture. Richardso introduced ether spray in 1866 for topical anesthesia, which was followed by ethyl chloride spray in 1891. Thus "to freeze" became synonymous with "to numb". Trendelenberg in 1917 demonstrated that freezing tissues caused severe nerve damage and loss of function but noted that the nerves regenerated without neuroma formation.

Unfortunately it is teasable that to eliminate pain we must create a painful stimulus at any moment. Cryo-anaesthesia is the application of cold to a localized part of the body in order to block the local nerve conduction of painful impulses. It can be induced either by the use of refrigerant sprays or with the use of ice(Priyatham and Nuvvula 2016). Most useful factor of cryoanesthesia is that it acts on all the cells of the part and not just on the nerve cells as other topical anesthetics and analgesics do, that is why it produces an immediate anesthesia. The anesthesia produced by cryoanesthesia is of very short duration (2 to 5 second) but is sufficient enough to reduce the discomfort caused by the insertion of a needle. It is believed that topical cold application stimulate myelinated A delta fibers, activating inhibitory pain pathways, which in return increases the pain threshold. It let down the nerve conduction, causing temporary vasoconstriction. Gate control theory of pain is the base of analgesic effect of vibration and it was prescribed to minimize concurrent pain. The use of a refrigerant such as ice and a refrigerant spray to reduce the pain experienced during administration of a maxillary palatal injection has been described in technique articles in the dental literature. The authors of one article described a technique in which a cotton pellet was saturated with a dichlorodifluoromethane refrigerant spray and then was placed in contact with the palatal tissue for five seconds before the injection was administered (Duncan *et al.,* 1992).

Table 1. Various studies with their results (Priyatham and Nuvvula 2016)

S. No	Author year	Intervention	Results
.1	Lathwal et al., 2015	Children age 5-8 years. One minute ice cone vs 5 seconds refrigerant spray vs benzocaine for IANB and Greater palatine block.	Ice cone showed higher efficacy as compared to benzocaine and refrigerant.
2.	Ghaderi et al., 2013	Children age 8-10 years buccal infiltration (Benzocaine) on one side (control) for 1 min and topical anaesthetic agent plus one minute of ice pack on the other side	Significantly reduced pain was perceived by pediatric patients.
3	Aminabadi et al., 2009	Children aged 5-6 years of age. Benzocaine for 1 min followed by a 2-min application of ice before injection of local anaesthetics.	Minimize the discomfort and reduce anxiety associated with the injection procedure

First, Harbert presented the idea of precooling technique for palatal injection technique. He observed that prior palatal cooling is efficient for relieved pain perception and claimed that cooling reaches the nerves through the tissue and blood supplies (Davoudi *et al.,* 2016). Further, there have been numerous studies in medicine where pre-cooling has been used to relieve pain from a local anesthetic injection, and prevent edema. Ghaderi *et al.* (2013) found in their study that cooling the injection site before infiltration of local anesthetics for 1 min, significantly reduces the pain perceived by pediatric patients (Aminah *et al.,* 2017). Reviews on intraoral precooling agents in pediatric dentistry are lacking so this review was undertaken with the aim to provide an insight about these agents and their application in various intraoral operative procedures with a special focus on applications in pediatric dentistry and their specific clinical recommendations. One of the most common problem encountered by pediatric dentists is dental anxiety and fear of needle. Many methods have been suggested to lower the discomfort of local anesthesia injection for dental procedures among which desensitizing the injection site is a recommended strategy. Conventional pain control techniques, but it deals with one aspect of pain control, which is pharmacological/sensory and the psychologic component is often left unresolved. This is especially true of the pediatric population where the fear of needle is a major deterrent to quality dental care.

The authors of another article described the use of ice frozen on a stick that was applied to the palatal tissue in conjunction with the injection. There also is anecdotal evidence that dental providers have used off-label products such as 1,1,1,2 tetrafluoroethane (Endo-Ice, Hygenic, Akron, Ohio) for this purpose; however, to our knowledge, no researchers have investigated the effectiveness of a refrigerant in reducing injection pain for dental procedures (Abbot and Fowler-Kerry 1995). The refrigerant 1,1,1,3,3-pentafluoropropane/ 1,1,1,2-tetrafluoroethane (Pain Ease, Gebauer, Cleveland) received U.S. Food and Drug Administration approval in March 2004, and it is safe for use on "skin, intact mucous membranes (oral cavity, nasal passages and lips) and minor open wounds.(Kosaraju and Vandewalle, 2009)

Anesthetic agents

Oraqix: Oraqix which is a topical anesthetic agent which consists of Lidocaine 2.5% & Prilocaine gel 2.5%. It is a needle-free sub gingival anesthetic used to provide localized anesthesia in periodontal pockets during scaling and/or root-planning procedures. According to research, Oraqix is oil at room temperature, which helps it to be applied easily into periodontal pockets requiring root planning and scaling. Once applied, it solidifies at body temperature into an elastic gel, enabling it to remain in place while the anesthetics take effect. It is applied on to the minimal margin around the

selected tooth using a blunt-tipped applicator. (Singh *et al* 2017). The Periodontal procedure can be started in thirty seconds after the application, and the anesthetic effect remains for approximately 20 minutes. Oraqix has minimal risk for allergic reaction. Adverse reactions are similar as of injectable amides.

EMLA

EMLA which can be described as Eutectic Mixture of Local Anesthetics. It is oil in water emulsion i.e. 5% cream of 25mg/g lidocaine, 25mg/g prilocaine in a ratio of 1:1 by weight. It is supplied in 5 or 30 g tube or as EMLA anesthetic patch or disc in a laminated foil bound with adhesive tape. It is applied orally for 2.5 to 5 minutes to achieve beneficial psychological or pharmacological effects prior to needle penetration. EMLA is effective as a Pediatric local anesthesia and for minor soft tissue surgical procedures. It is contraindicated in patients with congenita or idiopathic methemoglobinemia or patient with known sensitivity to amide type local anesthetic, where it may cause allergic dermatitis, transient skin blanching and erythma. (Singh *et al.,* 2017)

Recent Advances

Injection and vibing technique

Vibratory stimulation is one of the several non-pharmacological techniques used to reduce pain. Previously, vibration was applied using a hand-held massager/a vibrating cotton swab. As the vibration of the hand-held massager cannot be monitored throughout, there may be variations in frequency and pressure applied from subject to subject over time (Shilpapriya, 2015). The vibration technique was first prescribed to minimize concurrent pain. The gate control theory of pain, which was explained previously, is the base of the analgesic effect of vibration. Vibration and touch receptors stimulate inhibitory interneurons in the spinal cord and results in elimination of pain transmit information by A-δ and C fibers.

Different brands and devices are available, in which the vibrating stimuli are produced such as VibraJect, DentalVibe, and Accupal. Released data about these devices are not vast enough. However, based on available executed studies, controversial effects of these systems are published. About VibraJect, two studies suggested using the device in contrast to another study. The same controversy can be found about DentalVibe.

VibraJect

It is a small battery-operated attachment that snaps on to the standard dental syringe. It delivers a high-frequency vibration to the needle that is strong enough for the patient to feel. Nanitsos *et al*. and Blair, (2010) have recommended the use of VibraJect for painless injection. It enables less painful palatal injection because it delivers small amounts of anesthetic solution over a period.

Dental Vibe

Another system that uses vibration diversion based on the pain gate theory is recently introduced Dental Vibe (BING Innovations LLC, Crystal Lake, IL, USA). It is a cordless, rechargeable, hand-held device that delivers soothing, pulsed, percussive micro-oscillations to the site where an injection is being administered and gently stimulates sensory nerves. Its U-shaped vibrating tip attached to a microprocessor - controlled Vibra-Pulse motor gently stimulates the sensory receptors at the injection site, effectively closing the neural pain gate, blocking the painful sensation of injections. It also lights the injection area and has an attachment to retract the lip or cheek (Saxena *et al.,* 2013). It sends intermittent micro-sonic oscillations to the brain's neurological pain sensors, closing the pain gate, blocking the pain of injections and is also more useful for pediatric patients and those who have a phobia of intraoral injection or pain as there is an audible distraction (70-75db) provided. Additionally, the comfort tip provides gentle massaging of the injection site, through Vibra-Pulse Technology and prevents a swelling of the bolus of the anesthetic solution as it is injected. This causes dissipation of the solution faster, and causes a profound anesthetic effect and further on application of increased pressure the device shuts down automatically (Shilpapriya, 2015).

Accupal

The Accupal (Hot Springs, AR, USA) is a cordless device that uses both vibration and pressure to precondition the oral mucosa. Accupal provides pressure and vibrates the injection site 360° proximal to the needle penetration, which shuts the "pain gate," according to the manufacturer. After placing the device at the injection site and applying moderate pressure, the unit light up the area and begins to vibrate. The needle is placed through a hole in the head of the disposable tip, which is attached to the motor. It uses one AAA standard battery (Saxena *et al.,* 2013).

Computer-aided delivery systems

The main factors for pain-induced is the volume and rate of drug infiltration. That is why computer-controlled local anesthetic delivery (CCLAD) systems were designed for the better manipulation and delivery of local anesthesia. Maximum researches support the efficacy of using these delivery systems in reducing the pain of local anesthesia injection. It is essential to deliver local anesthetic solution at a constant rate and slower speed to avoid causing discomfort to the patient. While Conventional syringes do not allow precise control of flow rate, and injections into dense tissues like palate needs adequate pressure which is difficult with conventional syringes and using all the calculations a research in 1997 delivered a system using computer technology to control the rate and flow of anesthetic solutions evolved, and are called as computer controlled local anesthetic delivery systems. The very first computer controlled local anesthetic delivery systems is the Wand, followed by Wand Plus and CompuDent. The Wand has 3 components: Base unit, Foot pedal and Disposable Hand piece assembly. Base unit consists of a microprocessor and connects to the foot pedal and Hand piece assembly that accepts the LA cartridge. LA solution from the cartridge passes through the microbore tubing in the Hand piece assembly and attached needle into the target tissue. The Light weight hand piece is held in a pen-like grasp that provides the user with greater tactile sensation and control compared to the traditional syringe. The available flow rates of LA delivery are controlled by a computer and thus remain consistent from one injection to the next and are delivered with a foot-activated

control. The greater control over the syringe and the fixed flow rates of the LA drug are responsible for a significantly improved injection experience, as demonstrated in many clinical studies conducted with CCLAD devices in dentistry and medicine. As per our data collected from Internet Fifty blindfolded dentists participated in a controlled clinical study (they received the injection) comparing the standard manual syringe to a CCLAD system (the Wand) for palatal injections. Forty-eight (48%) preferred the CCLAD injections. Overall, pain perception was reduced two- to threefold when compared to the standard manual syringe. (Saxena *et al.,* 2013, Kumar 2015).

The investigators in the study increasingly preferred to perform all injections with the CCLAD technology. Seventeen of the 20 subjects reported a slight or no-pain rating on a visual analogue scale (VAS) for palatal injections administered with CCLAD. They concluded that "the new system provides comfortable anesthesia for patients and can be a good alternative for conventional manual syringe injection. We have three modes of flow rate available: slow, fast and turbo mode. In 2001, the Comfort Control Syringe was marketed as an alternative to the Wand and has two components; base unit and syringe and there is no foot pedal. The most important functions of this unit is injection and aspiration can be controlled directly from the syringe. Five different basic injection rate settings for specific applications, block, infiltration, PDL, IO and Palatal regions. The unit uses two stage delivery rates for every injection. It initially expresses the LA solution at an extremely low rate and after 10 seconds the rate slowly increases to the pre-programmed value for the selected injection technique. Disadvantage is, the syringe is bulky and cumbersome to use when compared to the wand hand piece.Several CCLAD systems are available including the Wand/CompuDent system, QuickSleeper, SleeperOne, Ora Star and Anaeject. Both the Comfort Control Syringe and the Anaeject regulate the speed of injection, starting slowly and accelerating the speed of injection to minimize pain. The Comfort Control Syringe has five preprogrammed speeds for different injection techniques and can be used for all injection techniques. The Anaeject has three pre-programmed speeds. CCLAD allows LAs to be administered comfortably to the patient in virtually all areas of the oral cavity. This is of greatest importance in the palate, where the level of patient discomfort can be quite significant. Computerized delivery of local anesthesia for palatal infiltrations has been found to result in low levels of stress and a low pain reaction, with the stress and pain reaction equivalent to that experienced following buccal infiltrations without computerized delivery (Kumar, 2015).

Jet injectors

Mechanical energy is behind the principal of using Jet injection technology. It creates a pressure sufficient to push a liquid medication through a very small orifice, that it can penetrate into the subcutaneous tissues without a needle. Some of the mentioned examples of Jet Injection are painless injection, less tissue damage, faster injection and faster rate of drug absorption into the tissues. But there are certain drawbacks of this technology which is that it cannot be used for nerve blocks, only infiltration and surface anesthesia are possible. Dabarkis *et al* report 17.6% patients experienced pain during injection of the anesthetic; and 32.3% reported feeling dread or fear from the explosion of the injector as it released the anesthetic.egs, are Injex, Syrijet, Mark II and MED-JET H III (Kumar, 2015). In MED-JET H III the solution is injected through orifice which is 7 times smaller than the smallest available needle in the world. The procedure how jet injectors work is to create and release sufficient energy to push out the anesthetic drug through the soft-tissue without using any needle. They are supposed to induce no or little pain by injecting the drugs without needles by being fast and less irritative. According to the dental researches, they are not as much effective as expected and similar pain was induced during injection in comparison to conventional needle syringes.

Dentipatch [Intraoral Lignocaine Patch]

Amount of lidocaine Dentipatch contains is 10-20 %, which is placed on dried mucosa for 15 minutes. Hersh *et al.* (1996) studied the efficacy of this patch and recommended it for use in achieving topical anesthesia for injections in both maxilla and mandible. It is not recommended in children. Disadvantages include central nervous system and cardiovascular system complications.

Conclusion

Pre-cooling the injection site significantly reduced the pain perception in pediatric patients when compared to topical anesthetic gel application and buffered local anesthesia application. With little difference compared with pre-cooling even vibration stimulus was found to be effective when applied extra-orally while administering local anesthesia. Also various distraction techniques and using euphemistic phrases were found to help in reducing anxiety among pediatric subject population. Pre-cooling of the injection site before infiltration anesthesia is an easy, reliable, and an effective technique with no additional cost and was found to be beneficial to be applied to all pediatric patients which reduces discomfort and facilitates clinical management.

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