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Review Article

Anaesthesia Section

Mannitol an Adjuvant in Local Anaesthetic Solution: Recent Concept & Changing Trends (Review)

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ABSTRACT

Various adjuncts have been utilized with lignocaine to decrement tourniquet pain and prolong postoperative analgesia and its efficacy during dental extraction and various other restorative procedures in dentistry. An obligatory part of the dental process is to sanction a patient to feel comfortable and pain-free during operational and remedial dental procedures. The most popular local anaesthetic injection for lower teeth is the inferior alveolar nerve (IAN) block. Instead of this the percentage of ineffectiveness is higher is inferior alveolar nerve block as compared to other local anaesthetic nerve block. The goal of cumulating different drugs is to engender the best therapeutic effects with the fewest or no unpropitious effects. There are fewer researches and evidence present which recommend and promote the application and effectiveness of mannitol other than in the administration in decreasing raised intracranial pressure. It is paramount to know how the drug interacts with each other to minimize the unexpected or perilous effects.

Keywords: Anaesthetic, Diuretic, Efficacy mannitol, Osmotherapy

INTRODUCTION

Mannitol (A carbohydrate derivative) first introduced by Wise and Chater in 1962 [1] and is probably the most widely used agent as osmotic diuretics due to its availability and efficiency and remains mostly in extra. Mannitol is a naturally befalling sugar alcohol employed clinically principally for its osmotic diuretic properties. Mannitol does not penetrate cells, and it simply denotes of clearance from the plasma is by glomerular filtration. Mannitol is a scavenger of oxygen-free radicals, which may limit cellular swelling and decrease renal tubular interference. Mannitol does not enter cells, and its only denotes of clearance from the plasma is by glomerular filtration.

Mannitol has become the mainstay of ICP management protocols. An osmotic diuretic, mannitol draws dihydrogen monoxide from the brain and other tissues into the intravascular compartment. Mannitol may adscititiously lower ICP by decrementing blood viscosity and expanding plasma volume that increase CBF (cerebral blood flow). When autoregulation is intact, this prompts vasoconstriction to renovate CBF towards mundane.

Mannitol is widely utilized in the management of raised intracranial pressure (ICP), for renal bulwark in cardiac, vascular, and renal transplantation surgery, and in the management of rhabdomyolysis. It has withal antecedently been utilized for bowel preparation before colorectal surgery [2].

DIURETICS

Mannitol is remarkably efficient in decreasing ICP (intra cranial pressure). Mannitol is commonly used in neuro-anaesthesia as a hypertonic infusion to reduce intracranial pressure and volume. It achieves the present by its osmotic action producing brain shrinkage and by producing vasoconstriction subsequent to a decline in viscosity. The outcomes start within 10 min and rise at about 60 min provided the ultimate importance of promoting the CBF to preclude cerebral ischemia, and given the least side effects of mannitol assuming in order that any unconscious head injured patient should be given the mannitol approximately 1.5gm/kg as shortly as is possible. Despite, whichever is said to be mannitol, given rapidly, may produce profound hypotension (not hypertension) and should be administered over 20 min. The additional important side effect of rapid administration of mannitol is transient hyperkalemia.

Marsh et al., [3] stated that mannitol begins to exert an effect within 10 to 15 min and is effective for about 2 h. There is little difference in the effect of this dose range on intracranial pressure, but the larger dose may last longer.

LOCAL ANAESTHESIA [NEW CONCEPT]

Drug interaction results immediately upon the effect of one's drug and is changed by the concurrent administration of another and more possible cause for failure of local anaesthesia in dental and oral surgical procedure is that the perineurial barrier around the nerve may not sanction consummate diffusion of anaesthetic solution into the nerve trunk.

All local anaesthetics are nerve membrane layer stabilizing drugs; they reversibly minimize the rate of depolarization and repolarization of excitable nerve membranes (as nociceptors). Although many different drugs, also produce membrane stabilizing characteristics, not each and every drug are used as local anaesthetics (propranolol, for example). Local anaesthetic drugs act principally by hindering sodium influx through sodium-specific ion channels in the neuronal cell membrane, in particular the so-called voltage-gated sodium channels. When the influx of sodium is hindered, an action potential cannot rise and wave conduction is inhibited. The receptor site is believed to be found at the cytoplasmic (inner) portion of the sodium channel. Local anaesthetic drugs adhere more readily to sodium channels in an activated state; hence incipience of neuronal blockade is faster in neurons that are rapidly firing. This is mentioned to as essential dependent blockade. Sodium is diluted in this retained water in the renal tubules, leading to the limited reabsorption of this ion. As a consequence of this osmotic outcome in the renal tubular fluid, there is an osmotic diuretic result with urinary excretion of water, sodium, chloride, and bicarbonate ions. Antonijevic et al., observed that a 0.5 M solution of mannitol was most effective in opening the perineurial membrane to allow for enhanced penetrability for macromolecules and/or ions.

The inferior alveolar nerve (IAN) block is the most frequently used injection technique for achieving local anaesthesia for mandibular restorative and surgical procedures. However, the IAN block does not always result in successful pulpal anaesthesia [1-6]. Failure rates (never achieving 2 consecutive 80 readings with the electric

pulp tester) of 10 to 39% have been reported [1]. A possible reason for failure is the perineurial barrier around the nerve may not allow complete diffusion of the anaesthetic solution into the nerve trunk.

DISCUSSION

The composition is a mixture of a local anaesthetic agent and a sugar alcohol (Mannitol). The sugar alcohol opens the protective covering of sensory nerves, allowing the anaesthetic agent to enter the innermost parts of the nerves it is meant to numb or anaesthetized.

When local anaesthetic efficacy is compared, it is consequential that a reproducible outcome measure be obtained. Operative dental procedures will engender uncontrolled stimuli, so a reliable alternative is required. The utilization of electrical stimulation is considered a safe and precise method of evaluating pulpal anaesthesia in vital asymptomatic teeth [4-6]. The absence of perception to the maximum output of the pulp tester (80 reading) has been widely utilized as a criterion for pulpal anaesthesia [7-10].

Tofolli G R et al., investigated articaine in IANB using an electric pulp stimulator to measure pulpal anesthesia onset and duration periods [11] However, inclusding Tofolli G R et al., and few more authors [11] compared articaine solutions containing epinephrine (1:100,000 and 1:200,000), but not with lidocaine solution containing epinephrine (1:100,00) and concluded a mean interval of approx 245 minutes.

Local anesthesia is not always effective in dentistry. It would be expected that a higher degree of success is achieved with infiltration anesthesia because it is an easier technique to perform, and it should not be affected by collateral nerve supply. Nevertheless, infiltration injection is not always 100% successful. Success is reported to range from 50 to 100% in maxillary teeth [12,13,14].

When only the anterior maxillary teeth are considered for the anesthetic, success has been reported to range from 68 to 100% for the lateral incisor, with local anesthetic volumes ranging from 0.5 to 1.8 mL [15-19].

Rood and Sowray [20] also described a series of cases where 5% lidocaine provided adequate pain control when 2% lidocaine was inadequate. Lastly, Sandy and Rood [21] discussed the use of 5% lidocaine in children. They showed a 5% lidocaine solution was helpful in achieving anesthesia when 2% lidocaine was inadequate.

Wolf et al., [22] demonstrated that lidocaine in combination with 0.5M mannitol (defined as the total of all the times of pulpal anesthesia [80 readings] significantly improved the success of the IAN block. The proposed mechanism was that mannitol opens the perineurial membrane to allow for enhanced penetrability for lipophilic compounds (such as lidocaine), and it may also directly affect nerve conduction.

Michael Whitcomb et al., [23] concluded in a study that buffering a 2% lidocaine with 1:100,000 epinephrine with sodium bicarbonate, didn't statistically decrease the pain of injection, provide faster onset, or increase the profoundity of anesthesia when compared with unbuffered 2% lidocaine with 1:100000 epinephrine for an IAN block. The improved efficacy of local anesthetic solution with 0.5 mol/L. Mannitol is due to increased permeability of perineurium brought about by mannitol. Thus there is better distribution of local anesthetic macromolecules resulting in increase in its efficacy and reduction in pain response on endodontic access and initial instrumentation. As there is a possibility of failure of local anesthetic in IAN block, there is a need to increase the efficacy of IAN block [24]. Since mannitol opens the perineurial membrane to allow for enhanced penetrability for macromolecules (and/or ions) [25] and may effect nerve conduction, [26] it may also increase the success of an IAN block when administered concurrently with a local anesthetic solution. Researchers found that the new composition of mannitol in local anaesthetic agent could increase the efficacy of local anaesthetic agent and completely numb the anesthetized region in about 90 percent of cases, as opposed to about 50 percent of cases using only the local anaesthesia in the standard dosage.

Timothy Kreimer et al., [26] does a study on 2 prospective, randomized, single-blind studies was to determine the anaesthetic efficacy of lidocaine with epinephrine compared with a combination lidocaine with epinephrine plus 0.5 mol/L mannitol in Patients with Symptomatic Irreversible Pulpitis and concluded with a conflict of previous research that for mandibular posterior teeth in patients with symptomatic irreversible pulpitis, the addition of 0.5 mol/L mannitol to 1.9 mL of lidocaine (76.4 mg) with epinephrine resulted in a statistically higher success rate. However, the combination lidocaine/mannitol formulation would not result in predictable pulpal anaesthesia.

CEREBRAL EFFECTS

Mannitol does not overpass the blood brain barrier, therefore, an elevated plasma osmolality due to an infusion of hypertonic mannitol is efficient in eliminating fluid from the brain. This is called 'mannitol osmotherapy'.

Mannitol admixtures are beneficial to acutely decrease elevated intracranial pressure due to an intracranial outer space residing lesion. A standard application would be in a patient with intracerebral hematoma due to intense traumatic head injury. The outcome is rapid in onset (min) although just temporary (as the mannitol is excreted) however, its use acquires time for critical definitive therapy.

SOME MORE EFFECTS OF MANNITOL

Due to hypertonicity osmotic effect of mannitol are Intracellular dehydration, Expansion of ECF volume (except brain ECF) Haemodilution and Diuresis due osmotic effects and ECF expansion. While non-osmotic effects of mannitol are decreased blood viscosity (with enhanced tissue blood movement) with Possible Cytoprotective consequence (due to free radical scavenging) and cardiovascular consequences are subsequent to expanded intravascular volume (e.g., increased cardiac output, hypertension, heart failure, pulmonary oedema).

Jeffrey J Fletcher et al., [27] stated that Mannitol has been shown to damage endothelial cells and activate coagulation pathways leading to intravascular thrombosis. Dehydration and hemagglutination have also been associated with mannitol use, although the risk of clinically evident venous thromboembolism (VTE) disease is not well-defined. In conclusion, despite a significant change in the pattern of osmotic therapy used at our institution, the proportion of patients with VTE remained unchanged. They found no evidence that mannitol use was associated with VTE compared to hypertonic saline alone.

Use of hypertonic mannitol as an osmotic agent was reported with success by Barry et al.,[28] in cases with functional renal failure and oliguria and has since then had been an accepted part of therapy. Mannitol was also found a very effective agent for reducing cerebro-spinal fluid pressure. Wise and Charter [29] demonstrated, in anaesthetized dogs after ligation of renal arteries, that the cerebrospinal fluid hypotensive effect of mannitol was independent of its diuretic effect without secondary rebound overshoot of pressure.

MANNITOL IN CATARACT SURGERY

Osmotic agents like urea, mannitol, and glycerol have been effectively used earlier to lower both the cerebro-spinal pressure and intra-ocular pressure. Mannitol is a hexahydroxy alcohol related to mannose. It occurs as a white, crystalline powder and is soluble in water and stable at room temperature.

Intravenous administration of mannitol induces diuresis by elevating the osmotic pressure of the glomerular filtrate to such an extent that tubular re-absorption of water and sodium is hindered. Mannitol

also promotes excretion of chlorides. It itself is excreted unchanged in the urine. In the present series, a study is made to evaluate the use of mannitol in cataract surgery. Reduction of intra-ocular pressure prior to cataract surgery is essential to keep vitreous in its "physiological position" after lens extraction and to minimise post-operative complications.

Virno and others [30] studied oral glycerol efficacy in glaucoma cases and, found it most effective in reducing ocular tension in cases of acute angle closure glaucoma. The ease of oral administration, lack of - toxicity, promptness and intensity of action of glycerol made them recommend its use prior to cataract surgery. Jaffe and Light [31] recorded 5.4 mm average fall ocular tension with glycerol as compared to 0.4 mm average fall of ocular tension in control series. Though the hypotensive effect of glycerol was moderate, unpleasant side effects like nausea and vomiting due to the bad taste of glycerol were quite frequent.

MANNITOL IN BOWEL ANALYSIS

The small bowel has always been a challenging area to assess for surgeons and gastroenterologists owing to its long length and complexity of the loops. Yesteryear's barium investigations were most often non-specific with a very low diagnostic yield. Technological advances in multidetector computed tomography (MDCT) have revolutionized imaging field and have added new concepts to solid and hollow viscera imaging.

The success of accurate interpretation of bowel pathologies requires an optimal preparation and acquisition. This requires an oral contrast agent, which should cause uniform intraluminal attenuation, high contrast between luminal content and bowel wall, minimal mucosal absorption leading to maximum distension, absence of artifact formation and no significant adverse effects.

Mannitol as endoluminal contrast increases the diagnostic accuracy of the investigative studies in comparison to water and iodine-based contrast by producing significantly better bowel distension and visibility of mural features with improved image quality without additional adverse effects. K Prakashin et al., [32] stated that Mannitol proved to be better both quantitatively and qualitatively in bringing out small and large bowel distension, delineation of wall, IC valve visualization, and in providing improved overall image quality. It is also a cheap, effective, and well tolerated endoluminal contrast agent with minimal adverse effects and could produce CT enteroclysis equivalent bowel distension.

Jun Yoshikawa et al., [33] does a research to promote the effective use of raw glycerol, 13 yeast strains with the ability to produce mannitol from glycerol were isolated from environmental samples. Of the 13 strains, strain 7-12G was selected as an efficient mannitol producer from 25% (w/v) glycerol and was identified as Candida azyma by morphological, physicochemical, and phylogenetic analyses and found that it candida azyma exhibited the highest production level (31.8 g/l). Culture in jar fomenters was next investigated, and mannitol production reached 50.8 g/l over 7 d, corresponding to 0.30 g/g-glycerol. They have concluded that according to their best of knowledge, this was the highest reported level of mannitol produced by a microbe from glycerol under batch-type culture conditions.

CONCLUSION

We concluded that integrating 0.5 M mannitol to 127.2 mg lidocaine with 50 µg epinephrine was significantly more efficacious in achieving a more preponderant percentage of total pulpal anaesthesia's than a 127.2 mg lidocaine with 50 µg epinephrine formulation without mannitol. Injection pain and post injection pain were not statistically varied between the lidocaine/mannitol formulation and the lidocaine formulation without mannitol. Although its influence is temporary, mannitol has the positive outcome of opening the perineurial membrane. In cases of IAN block failure, it is assumed that the perineurial barrier around the nerve does not permit complete dispersion of the anaesthetic into the nerve trunk.

The summation of mannitol evidently permits heightened permeability, improving the success of an Inferior alveolar nerve block when administered concurrently. Further studies, in punctiliously controlled experimental and randomized clinical tribulations, are required to determine the safety, timing of onset of treatment, the optimum duration of benefit and the particular other injury paradigms that are most liable to benefit from this treatment. Until these definitive tribulations are performed, caution is advised in clinical utilization of these solutions as an adjuvant with lignocaine to increment efficacy of local anaesthetics.

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