

Can repeated scorpion bite lead to development of resistance to the effect of local anesthetics? Maybe it does!*

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ABSTRACT

An 80 years old, bronchial asthmatic, male was posted for left cataract extraction with intra ocular lens implantation. He was administered peribulbar block/left facial nerve block. There was no sensory or motor block. Thereafter peribulbar block was repeated. Only partial akinesia was achieved, so under intermittent intra venous sedation, the surgery continued for 40 minutes. In the post-operative period, no signs of any residual/delayed block were noted. On specific enquiry, patient gave history of scorpion bite thrice, at the age of 27 years on his right foot, about 8 - 9 years back and again about 6 - 7 months back on his right hand. On 4th post-operative day after obtaining informed consent, local infiltration of the skin on the ventral aspect of the forearm, using, 6 mL, 2% lignocaine with adrenaline, was carried out. Confirming the suspicion, there was no sensory block after the injection, confirmed by pin prick method. Peribulbar block produces adequate intra-operative analgesia for cataract extraction. The cause of the failures may be due to technical inability to achieve block. However failure that occurs despite of technically correct injection of the correct drug can be mystifying. As the scorpion venom is known to affect the pumping mechanism of

sodium channels in the nerve fibres, which are involved in the mechanism of action of local anaesthetic drugs, it may be responsible for the development of "resistance" to the action of local anaesthetic agents.

Keywords: Resistance to Local Anaesthetics; Multiple Scorpion Bites; Peribulbar Block; Ophthalmic Surgery

1. INTRODUCTION

The ophthalmic surgical procedures are routinely performed under optimum analgesia and operative conditions, using either peribulbar or retro bulbar block with or without facial nerve block. Resistance or "failure to achieve" adequate block by local anaesthetic agents is an uncommon but a known phenomenon [1]. There are reports of "not able to achieve" the optimum sensory/motor effect when given either via neuraxial, peripheral nerve blocks or as local infiltration, where because of lack of any plausible explanation, the absence to achieve the block, had to be attributed to the so called "failure" of local anesthetics [1,2]. Even genetic factors like being a redhead, *i.e.* carrying a variants of the melanocortin-1 receptor (*MC1R*) gene, can lead to resistance to not only local anaesthetics (*i.e.* novocaine, lidocaine) but may make them resistant to effects of inhalational anaesthetic agents like desflurane [3-5].

Envenomation by scorpion is not uncommon occurrence in subtropical countries like India. In fact there are some "endemic" rural areas of very high prevalence of the scorpions, especially in the agrarian societies. We have been encountering unusual phenomena like "failure of action of local anaesthetics" administered via various

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routes like sub-arachnoid block in the patients giving history of scorpion bite, especially when exposure has been more than once, which we have recently reported [6]. We are presenting another one of such cases.

2. CASE REPORT

An 80 years old asthmatic male, belonging to American Society of Anesthesiologists (ASA), grade II, with bilateral mature senile cataract, was posted for left extra capsular cataract extraction with posterior chamber intra ocular lens. On general physical examination, he was found to be cachexic, weighing 45 kilos, edentulous having normal vital parameters and his airway assessment was Mallampati grade II. All the laboratory investigations, including chest X-ray, ECG and 2 Dimensional echo-cardiography were within normal limits.

Inside the operating room intravenous infusion of 5% dextrose in normal saline was started, as he had been kept fasting for more than 6 hours, with a 20 G indwelling intravenous cannula. Standard monitoring including ECG, Oxygen saturation (SpO₂) and noninvasive blood pressure (NIBP) was started.

Left Peribulbar block and left facial nerve block (O'Brien's Technique) was administered with 5 ml of 2% lignocaine with adrenaline using 26G 1.5 inch needle. There was no sensory or motor block or akinesia. Peribulbar block was repeated again with the 3 ml of the same drug mixture, this time at the inferior orbital margin. All the blocks were administered by a qualified and very senior ophthalmologist. Only partial akinesia was achieved this time. Wide fluctuations in pulse were noticed during the conjunctival flap fashioning. Patient became much restless, so injection midazolam 1 mg was administered intravenously for sedation.

At the time of corneo-scleral incision, the patient again became restless, so oxygen was administered with mask and inj. Butorphanol 1 mg was administered intravenously as analgesic-sedative. Anterior capsulotomy and nucleus delivery was done with great difficulty. Further sedation with injection propofol 40 mg as a bolus was administered. Intra ocular lens implantation was done under this sedation, patient kept on squeezing the eyeball, leading to rupture of the posterior capsule and vitreous prolapse occurred suddenly after placement of IOL. So the incremental doses of 10 mg propofol up to total of 30 mg was administered for the vitrectomy. While taking corneo-scleral sutures, it was observed again that, the ocular anesthesia was not sufficient, as the patient was found to be moving with each needle prick in spite of sedation.

At the conclusion of surgery, patient was conscious, oriented and able to sit up on command. When asked specifically, he mentioned that he did not have any per-

sistent/residual block. At this point, after very specific inquiry into past history, patient gave history of scorpion bite thrice, first time approximately at the age of 27 years on his right foot, second time about 8 - 9 years back and again about 6 - 7 months back on his right hand.

Patient was followed up in the post-operative period for next 48 hours, which was uneventful.

On 4th post-operative day after explaining about his possible special condition (Resistance to local anesthetic agents) and obtaining informed consent, patient was administered local infiltration of the skin on the ventral aspect of left arm using 2% xylocaine with adrenaline (total volume 6 ml). Confirming our suspicion, the infiltration did not produce any perceptible sensory loss, when checked by pin-prick method. On further enquiry, patient denied any of the immediate family members, who had undergone surgical procedures, in past exhibiting such "resistance" to action of the local anaesthetic agents. The patient was observed in the recovery room for next 2 hours and then sent back to the ward.

On 6th post-operative day after satisfactory recovery from the surgical procedure, he was discharged from the hospital.

3. DISCUSSION

Peribulbar block is a very effective method, having success rate of about 95% with only 5% - 10% patients requiring supplementation [7,8]. The causes of failures may be due to technical difficulty and inability to inject the correct drug in appropriate dosage in correct place, which is obvious at that moment and is understandable. The explanation for peribulbar (or any other) blocks' failure which occurs despite using apparent technically correct method of injection of the correct drug can be mystifying. True local anesthetic resistance is difficult to diagnose and may be greeted with skepticism [9]. However, since local anesthetics work via the sodium channel, it is theoretically possible that mutations in this channel might lead to differing responses to these medications [10].

An extensive literature search has revealed isolated case reports of local anaesthetic resistance, mainly in dental practices where repeated procedures are more likely to happen [11]. There is one reported pilot study conducted in a Pain Centre in Florida evaluating the prevalence of apparent local anaesthetic resistance to mepivacaine, lignocaine and bupivacaine. Of the 1198 patients interviewed, 250 were tested. 90 (7.5% of the total patients) were found to be hypoesthetic only to mepivacaine, and an additional 43 (3.8%) only to lignocaine. The rest were hypoesthetic to all or bupivacaine [11].

One of the postulated mechanisms for local anaesthetic resistance is receptor mutation associated with

sodium channel abnormalities. An atypical receptor site might result from genetic variation in the amino acid sequence within the sodium channel. Specifically; the sodium channel has been found to consist of alpha (α), beta-1 (β_1) and beta-2 (β_2) subunits [9]. The alpha subunit involves four homologous domains (I-IV) and each of these domains is made up of six trans membrane segments (S1-S6). Local anaesthetic action is believed to be due to an interaction with the sixth segment of domain four of the alpha subunit (IV-S6), involving sites of phenylalanine and tyrosine amino acid residues [12]. Therefore, it is possible that genetic variation that alters the site of action as stated above can be the cause of resistance to local anaesthetics [13].

In our country, scorpion bites are a relatively a common phenomenon. We do not give much importance to the past history of the scorpion bite as a relevant and significant factor, when patient comes for unrelated medical/surgical condition. Scorpion's venom contains numerous toxins, biogenic amines, enzymes, salts, unidentified substances and water. Based upon the composition, the toxins are divided into two main groups namely Buthidae and the Chactoids. For clinicians, Buthidae is of more significance, as these toxins are known to affect sodium ion channels, potassium ion channels and calcium ion channels with regards to electrolyte balance. Disturbance of electrolyte balance can affect the following: Sodium and calcium permeability affects the heart, sodium and potassium affect the nerve transmission and cell membrane integrity, sodium affects the homeostasis by kidney, calcium affects the muscles and is an important secondary messenger [14].

The neuromuscular intoxication by scorpion venom may be due to its ability to act on exposed fibres or on muscles directly or through motor nerves [15]. Since an intact nerve trunk appears to be impermeable to the venom, the venom makes contact with the nerve tissue at the exposed presynaptic terminals at the neuromuscular junction. The resulting muscular twitchings and fibrillations may be due to a stimulation of the release of the transmitter substance [16,17]. It appears that scorpion neurotoxins (which are low molecular weight, thermostable, basic proteins), possess the general ability to depolarize excitable membranes. This is due to an increase in the sodium permeability of the resting membrane and reduction of the rate and amount of sodium inactivation [18]. It is suggested that scorpion venom may modify the sodium pumping mechanism within fibres as well as affecting the passive and active sodium permeability systems.

We are situated in a very predominantly endemic area of scorpion existence and have actually been experiencing similar apparent "resistance" in quite a few patients (with history of single or multiple scorpion bites), where

the local anaesthetics had been administered via different routes like sub-arachnoid [6], supraclavicular brachial block and as happened in this case, peribulbar block. The complete failure of local infiltration, highlights the possibility of development of "resistance" to local anaesthetics and appears to be the most likely and plausible explanation of "failure of peribulbar block". For the sake of argument, one may put forward, a hypothesis that, the patient might have been inherently resistant to the local anaesthetics as such, because there is no past history of the use of local anaesthetics before the occurrence of scorpion bite. This may be a remote possibility, but one has to accept the irrefutable fact that, this man had been bitten by scorpion not once, twice but three times, and last one only about six months back. It is our hypothesis that, it is the antigenic nature of scorpion venom that makes it more significant as it may evoke a very potent antigen-antibody response. This might have led to the development of antibodies against the scorpion venom, which may be circulating even at the time of administration of local anaesthetics and may have produced competitive antagonism with them at the "receptor site" *i.e.* that particular component of sodium channels {sixth segment of domain four of the alpha subunit (IV-S6)}, where the local anaesthetics are supposed to act [12]. As a result there may be "development of resistance leading to failure of action of local anaesthetics". We at present are still experimenting to verify our antigen-antibody hypothesis, but by the process of exclusion, we believe that we have found a correlation between these two occurrences.

4. CONCLUSION

After coming across many such cases, we are putting forward the hypothesis, that "single or multiple scorpion bites" may cause development of resistance to the effect of local anesthetic drugs used to achieve blocks by various routes.

5. AUTHOR CONTRIBUTIONS

All the authors participated in the interview, examination and care of this patient. All authors have read and approved the final manuscript.

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