Effect of previous scorpion bite(s) on the action of intrathecal bupivacaine: A case control study

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ABSTRACT

Background: During the routine practice in the institution, it was observed that there were persistent incidents of inadequate/failed spinal anaesthesia in patients with a history of single or multiple scorpion bite/s. To test any possible correlation between scorpion bite and the altered response to spinal anaesthesia, a case control study was conducted involving patients with a history of scorpion bite/s and without such a history. **Methods:** Randomly selected 70 (n=70) patients of either sex and age range of 18-80 years, were divided into two equal groups, giving past history of one or multiple scorpion bites and giving no such a history. The anaesthetic management was identical inclusive of subarachnoid block with 3.5 ml. 0.5% bupivacaine heavy. The onsets of sensory, motor and peaks of sensory and motor blocks were observed with the pin-prick method and Bromage scale. After waiting for 20 min, if the block was inadequate, then balanced general anaesthesia was administered. The analysis of the data and application of various statistical tests was carried out using Chi-square test, percentages, independent sample t-test and paired t-test. **Results:** Demographically both groups were comparable. In scorpion bite group, the time of onsets of both sensory and motor blocks and time for the peak of sensory and motor blocks were significantly prolonged, 4 patients had failed/inadequate sensory block and 5 patients had failed/inadequate motor block while all the patients in non-bite group had adequate intra-operative block. **Conclusion:** We conclude that there appears to be a direct correlation between the histories of old, single or multiple scorpion bites and development of resistance to effect of local anaesthetics administered intra-thecally.

Key words: Failure of local anaesthetics, randomized case control study, route of administration, history of scorpion bite, subarachnoid block

INTRODUCTION

Spinal block is a common anaesthetic technique implemented in a wide variety of surgical procedures.[1] Nevertheless, failure of spinal block may occur even in expert hands.[2,3] Causes of failure of spinal block may be technical difficulty, poor positioning of patient, incorrect needle insertion, abnormalities of spine (kyphosis, scoliosis, ligament calcification, disc-fusion), obesity, pseudo successful lumbar puncture, solution injection errors, wrong dose selection misplaced injection, inadequate intra-thecal spread, ineffective drug action, chemical incompatibility caused by adjuvant and local anaesthetic 'resistance'.[4]

The resistance to local anaesthetic injected in the Subarachnoid space is difficult to diagnose.[5] Considering the mechanism of action of local anaesthetics via the sodium channels, possible mutations of this channel may alter the response to local anaesthetics.[6] Inadequacy or failure of effect of local anaesthetics like 0.5% bupivacaine administered by neuraxial routes in patients with a history of single or multiple scorpion bites has recently been reported.[7]

The aim of the present study was to compare the efficacy of spinal block produced by bupivacaine in patients with a history of one or more scorpion bites and in patients with no such history.

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METHODS

After excluding the ethical aspects, 70 patients (n=70) of either sex, in the age range of 18 and 80 years and American Society of Anesthesiologists (ASA) physical status I to III were included in the study. All were registered and admitted patients for planned surgery under proposed spinal anaesthesia. Informed and written consent was obtained for the surgery and anaesthesia and for inclusion in the study.

The study period was between January 2012 and June 2012. Patients with of one or more scorpion bites undergoing spinal anaesthesia comprised the case group (Group S). These patients were compared to an equal number of controls; that is patients undergoing surgery under spinal anaesthesia but with no history of scorpion bite (Group C). The details of the scorpion bite(s) was noted in Group S.

All patients were pre-operatively assessed and were scheduled to undergo various types of elective surgeries under spinal anaesthesia (hernioplasty, hysterectomy, hydrocoele repair, Freyer's prostatectomy, Proximal Femoral nailing, tibia-fibula nailing etc.). In the operating room, A 20 Gz. Intravenous cannula was inserted in a peripheral vein and an infusion of Lactated Ringer was started. The standard monitoring (Electrocardiography, heart rate, non-invasive blood pressure and pulse oximeter) was implemented.

Spinal needle (27 gauze Quincke) was placed with the patient in the sitting position in the L3-L4 or L4-L5 intervertebral space and 3.5 ml (17.5 mg) of 0.5% bupivacaine heavy was injected over 10-15 s and barbotage was not carried out. The anaesthesiologist's experience varied between 6 months to 20 years Subsequently patients were placed in the supine position and the following parameters were recorded: T0-time of the spinal injection, T1-onset of the sensory block, T2-onset of motor block, T3-peak of sensory block and T4-peak of motor block.

To assess sensory block, pinprick was applied to all patients with a blunted 24 g hypodermic needle and the onset of sensory block was defined as the time when the patient could not feel the pain. Motor block was assessed with the Bromage scale (Grade 3: Complete block, unable to move feet or knees, Grade 2: Almost complete, able to move feet only or plantar flexion of the big toe, Grade 1 partial, just able to flex/move knees, Grade 0: None, full flexion of knees, feet, and hip). The onset of motor block was considered as the time when patient could not flex the hip. The time of peak sensory and peak motor levels were considered when the maximum/upper most level of the block was achieved and there was no further progression of either the sensory or motor blockade, above that level.

The Anaesthesiologist who assessed the sensory and motor spinal blocks for all patients was blinded to the group of the patient. The assessment was performed as per established checklists.[8] The block was considered to be adequate when level of sensory/motor block of up to T6-T8 was achieved. If after a 20 min period the block was not adequate, general anaesthesia was administered. At the end of surgery, all patients were transferred to surgical Intensive Care Unit for post-operative monitoring during the first 24 h.

Statistical Analysis of the data and application of various statistical tests were carried out with the help of Statistical Package for Social Services (SPSS version 18). Data were compiled, analysed and presented as frequency, proportions, mean, standard deviation, the significance tests, Chi-square test, percentages, independent sample *t*-test and paired *t*-test. A $P<0.05$ was considered as statistically significant. Continuous covariates (age) were compared using the independent sample *t*-test, with the *P* being reported at the 95% confidence interval. Categorical covariates (sex, ASA grade) were explained using the Chi-square test as comparisons amongst the 2 groups. Covariates (number of bites) were explained using the frequency and percentage. The results were expressed as Mean ± SD and *P*.

RESULTS

Seventy patients of both the sexes, aged between 18 years and 80 years were included in the study. The experience of Anaesthesiologists administering spinal anaesthesia was comparable between the two groups (Group S: 144 months (240-6 months), Group C: 132 months (240-6 months)-values in median, maximum, and minimum).

The groups did not differ in age, age group, and gender or ASA physical status as shown in Table 1. The frequency and the percentage of patients with scorpion bites 1, 2, 3 or 4 are shown in Table 2. About 65.7% of the cases had single scorpion bite.

Group S exhibited longer time for the onset of the sensory and motor block and longer time to reach the peak of both sensory and motor block than the control group as shown in Table 3.

In the Group S, four patients exhibited incomplete sensory block, five patients had incomplete motor block and in two patients both modalities of spinal block failed. All these patients received general anaesthesia.

The time of onset of sensory and motor blocks and time to achieve peak sensory and motor block and the relation to scorpion bites are shown in Table 4.

Table 1: Characteristics of patients in the two groups

Parameters	Group S *N* (%)	Group C *N* (%)	Total	*P* value
Age in years (range)				
Less than 24 years	1 (2.9)	3 (8.6)	4 (5.7)	
25-34 years	3 (8.6)	3 (8.6)	14 (20.0)	
35-44 years	3 (8.6)	11 (31.4)	12 (17.1)	
45-54 years	8 (22.9)	4 (11.4)	4 (5.7)	
55 years and above	20 (57.1)	14 (40.0)	34 (48.6)	
Age in years (mean±SD)	55.06±15.81	48.46±16.43	51.96±16.30	0.112
Gender				
Male	22 (62.9)	17 (48.6)	39 (55.7)	0.229
Female	13 (37.1)	18 (51.4)	31 (44.3)	
ASA grade				
1	6 (17.1)	11 (31.4)	17 (24.3)	0.378
2	22 (62.9)	18 (51.4)	40 (57.1)	
3	7 (20.0)	6 (17.1)	13 (18.6)	

ASA – American society of anaesthesiologists

Table 2: Frequency and percentage of scorpion bites in the Group S

Number of bites	Number of patients	Percentage
1	23	65.7
2	4	11.4
3	3	8.6
4	5	14.3
Total	35	100

DISCUSSION

The study shows that in patients with history of previous scorpion bites, spinal anaesthesia is associated with an inadequate or failed block. In all such patients, spinal anaesthesia administration with bupivacaine was associated with delay in onset and the peak effect of both sensory and motor blockade as compared to the control group of patients with no history of scorpion bite. It was also noted that multiple and most recent scorpion bites (those less than 8 months in the past) were associated with complete failure of the spinal block and necessitated conversion to general anaesthesia. Patients with scorpion bites older than a year showed delayed onset and delayed peak of the sensory block or the motor block or both. On the contrary patients with no scorpion bite history exhibited an adequate spinal block.

An extensive literature search revealed isolated case reports of local anaesthetic resistance.[6,9] Patients with Ehlers Danlos Syndrome, Type III (EDS III), now known as EDS hypermobility type and considered to be identical to Joint Hypermobility Syndrome, are reported to be resistant to the effect of local anaesthetics.[10]

Table 3: The onset of sensory and motor block, time to peak of sensory and motor block

Points in time	Group S	Group C	Total	*T* value (*P*)
Onset of sensory block (min)	2.31±1.68	1.63±0.84	1.97±1.36	4.67 (0.034)
Onset of motor block (min)	2.91±1.80	1.80±0.83	2.36±1.50	10.998 (0.001)
Peak of sensory block (min)	6.45±2.83	3.66±0.94	4.97±2.47	30.48 (0.000)
Peak of motor block (min)	7.83±3.95	4.46±1.40	6.02±3.31	22.36 (0.000)

Values are mean±SD

Table 4: Relation of number of scorpion bites to the time (min) to the onset of sensory and motor block, time to peak of sensory and motor block

Number of bites	Onset of sensory block	Onset of motor block	Peak of sensory block	Peak of motor block
0 (Group C)	1.63±0.84	1.8±0.83	3.66±0.94	4.46±1.4
1 (Group S)	2.48±1.85	3.0±2.02	6.62±3.09	8.2±4.54
2 (Group S)	2.25±2.06	2.5±1.29	5.67±2.08	6.75±1.71
3 (Group S)	2.0±1.0	3.67±2.31	9.5±0.71	9.0±1.24
4 (Group S)	1.8±0.84	2.4±0.55	5.0±1.41	7.0±3.16
F value	1.45	3.19	10.25	5.81
P	0.228	0.019	0.000	0.001

Values are mean±SD

The "resistance" to local anaesthetics may be attributed to mutations in the receptors located in sodium (Na^+) channels.[11] An atypical receptor site might result from genetic variation in the amino acid sequence involving sites of phenylalanine and tyrosine amino acid residues within the sodium channel. Specifically, the sodium channel has been shown to consist of alpha, beta-1 and beta-2 subunits. 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 6th segment of domain four of the alpha subunit (IV-S6).[11] Resistance to local anaesthetics may be related to the alpha subunit of the sodium channel and more specifically to the 6th segment of domain four of this subunit.[12]

Local anaesthetics act by binding with Na^+ channels in the closed, open, and inactivated states. These reach their binding sites via intracellular and extracellular pathways. One of the hypotheses proposed for resistance of local anaesthetics is coupled movement of Na^+ and local anaesthetic in the closed channel. This explains seemingly contradictory data on how the outer pore mutations as well as tetrodotoxin and μ-conotoxin binding, affect the ingress and egress of local anaesthetics.[13]

The voltage-gated sodium channels are involved in the generation and propagation of action potentials and transmitting them in excitable cells.[14-16] These channels are targeted by neurotoxins presenting as a large variety of chemically distinct compounds that bind to several receptor sites on the pore-forming α-subunit.[16-18] Scorpion toxins show a preference for specific sodium channel subtypes of mammals or insects[15,17-20] The antigenic nature of scorpion venom may evoke a very potent antigen-antibody response, especially, if the same individual has been bitten multiple times. Our hypothesis is these antibodies circulating even at the time of administration of local anaesthetics, may have produced competitive antagonism with them at the "receptor site" i.e., that particular component of sodium channels (6th segment of domain four of the alpha subunit (IV-S6)), where the local anaesthetics are supposed to act.[11]

Limitations of the study are that we did not define the primary and secondary outcomes when we designed the study protocol. Another limitation is the wide range of experience of the Anaesthesiologists who performed the spinal anaesthesia, 6 months to 20 years. Furthermore, we did not exclude patients with other comorbidities from the nervous system like diabetic neuropathy.

In India, scorpion bites are a relatively common phenomenon in the countryside. Unfortunately the history of scorpion bite is not taken into consideration when patients are admitted to hospital for unrelated medical or surgical problems. Geographically, the area around the place where our hospital is situated is infested with scorpions. We have come across with 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 such as spinal, epidural, supraclavicular brachial plexus block and peribulbar block.[7,21] The failure of local infiltration with local anaesthetics, highlights the possibility of development of 'resistance' to local anaesthetics in patients with scorpion bite history and is consistent with the failures of spinal block presented in the present study.

CONCLUSION

Patients with a history of scorpion bite exhibited apparent resistance to bupivacaine spinal block. This resistance manifested as inadequate block or block failure requiring conversion to general anaesthesia. More than one scorpion bites and more recent bites are associated with failure of the spinal block rather than inadequate spinal block.

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