Effect of Dexamethasone as an Adjuvant to Local Anesthetic in Supraclavicular Brachial Plexus Block

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Abstract

Introduction: Brachial plexus block is the most preferred anesthetic technique for upper limb surgeries. This study was done to study the adjuvant effect of dexamethasone when added with local anesthetics in supraclavicular brachial plexus block.

Objective: The objective of the study was to evaluate dexamethasone as an adjuvant to bupivacaine in patients undergoing upper limb surgeries by supraclavicular brachial plexus block.

Materials and Methods: After Ethics Committee Approval this randomized, double-blinded, control study was conducted in the Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry. A total of 50 patients who met the inclusion criteria were enrolled into the study and were randomized to receive plain bupivacaine and bupivacaine with dexamethasone in supraclavicular brachial plexus block. The onset of analgesia, the onset of motor blockade and hemodynamic parameters oxygen saturation, heart rate, systolic and diastolic blood pressures were recorded during and 1 h after the procedure. The duration of analgesia and motor blockade were also noted in the post-operative period.

Results: There was no statistically significant difference in the onset of sensory and motor blockade between both the groups. The mean duration of sensory blockade in study group was 1075.20 ± 144.831 min and in control group was found to be 288.00 ± 103.923 min and the mean duration of motor blockade in study group was 475.20 ± 114.787 min and in control group was found to be 218.40 ± 64.52 min and was statistically significant ($P \le 0.001$).

Conclusion: We conclude that when dexamethasone used as an adjuvant along with local anesthetic in brachial plexus block, it effectively prolongs the duration of both sensory and motor blockade with no side effects.

Key words: Adjuvant, Brachial plexus, Dexamethasone, Supraclavicular

INTRODUCTION

Brachial plexus block is the most preferred anesthetic technique for upper limb surgeries. It has its own advantages by avoiding untoward effects of general anesthetic drugs and upper airway instrumentation. Various approaches of brachial plexus blocks have been described, but the supraclavicular approach is the easiest and most consistent method for anesthesia and perioperative pain management

in surgery below the shoulder joint.[1] In a supraclavicular approach, the brachial plexus is blocked where it is most compactly arranged at the level of nerve trunks and rapid onset can be achieved, with a high success rate for elbow, forearm, and hand surgery because all the branches of the brachial plexus can be reliably blocked.[2]

Investigators have tried mixing local anesthetic with adjuvant drugs in an attempt to prolong analgesia from nerve blocks. Drugs like morphine, pethidine, clonidine, dexmedetomidine, butorphanol, buprenorphine are commonly used as adjuvant along with local anesthetic. Adjuvants including epinephrine, clonidine,[3,4] opioids,[5,6] ketamine,[7,8] and midazolam[9] have met with limited success.

Recent pre-clinical and clinical studies show that the glucocorticoid dexamethasone appears to be effective as

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an adjuvant to local anesthetics.[10-13] This study was done to study the adjuvant effect of dexamethasone when added with local anesthetics in Supraclavicular brachial plexus block.

MATERIALS AND METHODS

After obtaining approval from the Institutional Ethics Committee approval, this study was conducted in Department of Anesthesiology at Sri Manakula Vinayagar Medical College and Hospital, Pondicherry between November 2013 and May 2015. The study was designed to be of double blinded randomized control study following good clinical practice guidelines of the WHO. After taking thorough history and pre-operative assessment, 50 patients who were satisfying the inclusion criteria were enrolled into the study. The inclusion criteria were defined as patients aged between 18 and 60 years of American Society of Anesthesiologists I to II physical status, who were planned to undergo below shoulder upper limb surgeries (both elective and emergency) under brachial plexus block. Patients who refused to give consent, pregnant women, history of local anesthetics allergy, peptic ulcer disease, diabetes mellitus, peripheral neuropathy and patients with contraindications for brachial plexus block like bleeding disorder, patients on anticoagulants, severe respiratory disease, neurological deficit involving brachial plexus local infection at the injection site were excluded from the study.

After explaining the procedure properly in their native language, a written informed consent was taken from all the participants of the study. The study subjects were randomized by using block randomization using sealed concealed envelopes into two groups namely Group D and Group S each consisting of 25 patients. In the pre-operative room, intravenous access was secured with 18-G cannula on the contralateral hand and baseline parameters such as heart rate, mean arterial pressure, oxygen saturation was observed and recorded.

The brachial plexus block was carried out after thorough explanation of the procedure and emphasizing the need for patient cooperation. In the operation theater, monitors were connected (pulse oximetry, electrocardiography and noninvasive arterial blood pressure monitoring). Oxygen was administered via a Hudson mask at a rate of 5 L/min. Supraclavicular brachial plexus block was performed under aseptic precautions with the patient in supine position, and head turned slightly to the opposite side. A small pillow was placed in between the shoulders. The arm to be anaesthetized is adducted and the hand extended along the side towards the ipsilateral knee as far as possible. We used a nerve stimulator with a 22-G, 5 cm insulated needle

for precise localization of the brachial plexus. A skin wheal with local anesthetic was raised in the 1.5-2 cm posterior to the midpoint of the clavicle. The subclavian artery is usually palpable at this site. The nerve stimulator frequency was set at 1 Hz, and the intensity of the stimulating current was initially set to deliver 2 mA. The insulated needle was inserted through the skin wheal in a posterior, caudal and medial direction until a distal motor response is elicited. The position of the needle was considered acceptable when an output current ≤0.4 mA still elicited a distal motor response. At this point, the local anesthetic mixture was injected in increments after negative aspiration for blood and air. The local anesthetic mixture for patients belonging to respective groups as follows.

Group D (study group): Patients in this group received 0.25% bupivacaine (38 ml) plus dexamethasone 8 mg (2 ml) making a total volume of 40 ml (care was taken not to exceed the maximum drug dosage).

Group S (control group): Patients in this group received 0.25% bupivacaine (38 ml) plus 0.9% normal saline (2 ml) making a total volume of 40 ml.

The site of injection was sealed with a tincture benzoin. During the conduct of block and thereafter, the patient was observed vigilantly for any complications and toxicity of the drugs injected. After injection of the local anesthetic, the following parameters were studied:

1. The onset of sensory block, i.e., the time from injection to onset of analgesia in each of the major peripheral nerve distribution (ulnar, radial, medial and musculocutaneous) was assessed by pinprick using the blunt end of a 27-G needle at 0, 2, 5, 10, 15, 20 and 30 min. Sensory block was graded according to the following scale: 0 = no block (normal sensation), 1 = partial block (decreased sensation), and 2 = complete block (no sensation)

2. Onset of motor block, i.e. the time from injection to the inability of the patient to move his/her fingers or raise hand. Motor block was measured at 0, 10, 20, 30 and 40 min by assessing the following motor functions: Flexion at the elbow (musculocutaneous nerve), extension of the elbow and the wrist (radial nerve), opposition of the thumb and index finger (median nerve), and opposition of the thumb and small finger (ulnar nerve). Motor block was graded according to the following scale: 0 = no block (full muscle activity), 1 = partial block (decreased muscle activity), and 2 = complete block (no muscle activity)

3. A duration of analgesia was assessed during the procedure. Anesthesia was considered satisfactory if the patient did not complain of any pain or discomfort and if no sedation was necessary. Post-operative

follow-up was carried out in the recovery and post-operative ward. The duration of analgesia was noted according to 0-10 visual analogue score (VAS) for pain at every 1 h until first 10 h and thereafter 2nd hourly until 24 h. When the patients began to experience pain (VAS = 4), it was considered that analgesic action of the drugs was terminated, and rescue analgesic (injection diclofenac 1-1.5 mg/kg IM) was given

4. Duration of motor block, postoperatively was assessed every hourly by asking the patients to move their fingers and to see whether the elbow flexion could be done against gravity or not. This time was recorded and taken as cessation of motor block effect

5. Possible complications of brachial plexus block such as pneumothorax, hematoma, signs and symptoms for local anesthetic toxicity was looked for and noted, if any.

The above assessments were carried out by the principal investigator who was blinded to the drugs administered in the plexus block. In the circumstance of inadequate or patchy action of the block, the block was supplemented with general anesthesia. If in case surgery is unduly prolonged and the effect of the block wore off, general anesthesia was given.

RESULTS AND OBSERVATIONS

Sample Size Determination

The sample size was determined considering mean difference of 1.75 min as proposed in the previous study done by Talukdar *et al*.,[14] with a confidence interval of 95% and 80% power of the study, the sample size of 23 in each group was considered adequate. Considering non-response, we concluded to a sample size of 25 in each group (total *n* = 50).

The data were analyzed using statistical software using Epi info 3.5.3 and SPSS version 20. Results are represented as mean ± standard deviation. Student's unpaired "*t*" test was used to compare the age, weight, baseline parameters, perioperative parameters and for onset and duration of sensory and motor blockade. Fisher's exact test was used for sex distribution. Chi-square test was used for site of surgery. Mann–Whitney *U*-test was used for assessing VAS score parameters. A *P* = 0.05 or less was considered for statistical significance. The results and observations are summarized as Tables 1-6 and Figures 1-12. Side effects like pneumothorax, hematoma, signs and symptoms for local anesthetic toxicity, nausea, bradycardia, and hypotension were not significant in between the study groups.

The Figure 5 shows the perioperative heart rate changes in both the groups. The Figure 6 the perioperative systolic blood pressure changes in both the groups. The Figure 7 the perioperative diastolic blood pressure changes in both

Table 1: Demographic and clinical characteristics of study participants

Patient characteristics	Group D	Group S	*P* value
Age	36.88±11.501	37.32±11.814	0.894 (NS) - Student's unpaired *t*-test
Sex			
Male	22	19	0.463 (NS) - Fisher's exact test
Female	3	6	
Weight	59.60±4.472	60.04±4.208	0.722 (NS) - Student's unpaired *t*-test
ASA status			
I	19	19	1.000 (NS) - Chi-square test
II	6	6	

NS: Not significant, ASA: American Society of Anesthesiologists

Table 2: Site of surgery distribution

Site of surgery	Study groups		Total
	Group D	Group S	
Arm	4	2	6
Elbow	5	6	11
Forearm	11	12	23
Hand	2	0	2
Wrist	3	5	8
Total	25	25	50

Chi-square test, Degree of freedom=3, *P*=0.849 (not significant)

Table 3: Onset of sensory block

Parameters	Groups	*N*	Mean	SD	*P* value
Onset of sensory (min)	Group D	25	28.00	4.082	0.451 (NS)
	Group S	25	28.80	3.317	

Student's unpaired *t*-test; NS: Not significant, SD: Standard deviation

Table 4: Onset of motor block

Parameters	Groups	*N*	Mean	SD	*P* value
Onset of motor (mins)	Group D	25	38.80	3.317	1.000 (NS)
	Group S	25	38.69	3.317	

Student's unpaired *t*-test; NS: Not significant, SD: Standard deviation

Table 5: Duration of sensory block

Parameters	Groups	*N*	Mean	SD	*P* value
Duration of sensory (min)	Group D	25	1075.20	144.831	<0.001*
	Group S	25	288.00	103.923	

Student's unpaired *t*-test; *Significant

Table 6: Duration of motor block

Parameters	Groups	*N*	Mean	SD	*P* value
Duration of motor (mins)	Group D	25	475.20	114.787	<0.001*
	Group S	25	218.40	64.529	

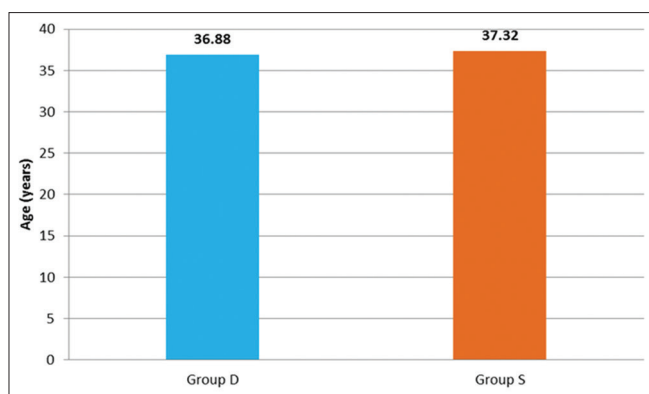Student's unpaired *t*-test; *Significant
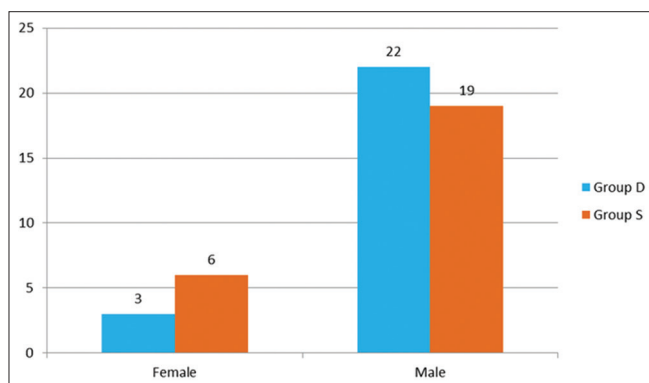
Figure 1: Age-wise distribution of study participants

Figure 2: Sex-wise distribution of study participants

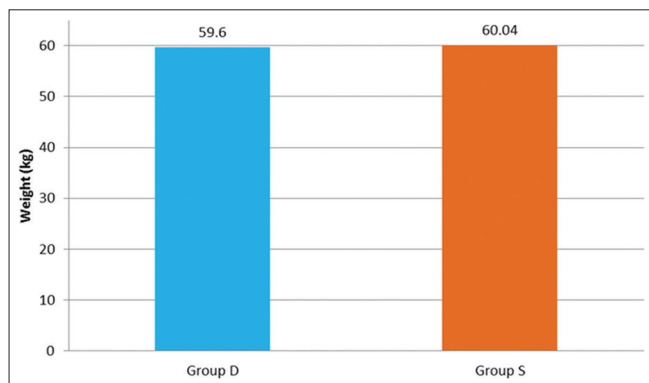Figure 3: Mean weight of the study participants in both groups
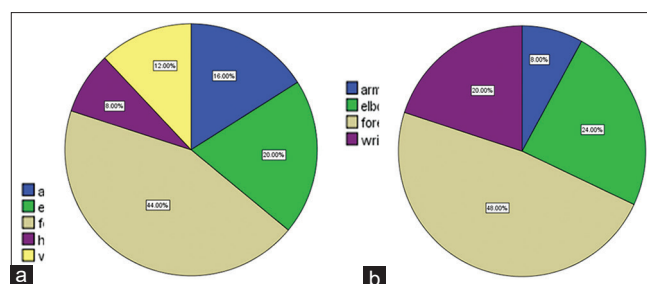

Figure 4: (a) Site of surgery in Group D, (b) site of surgery in Group S
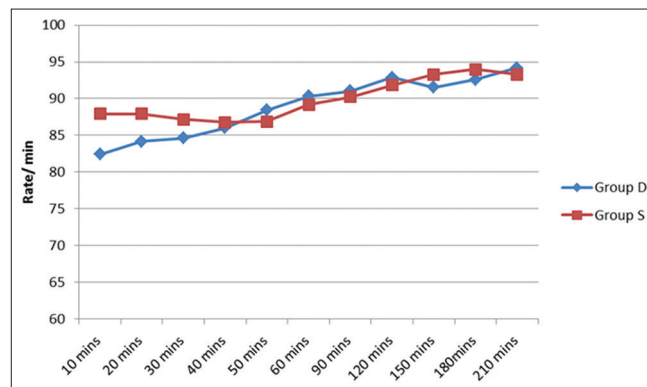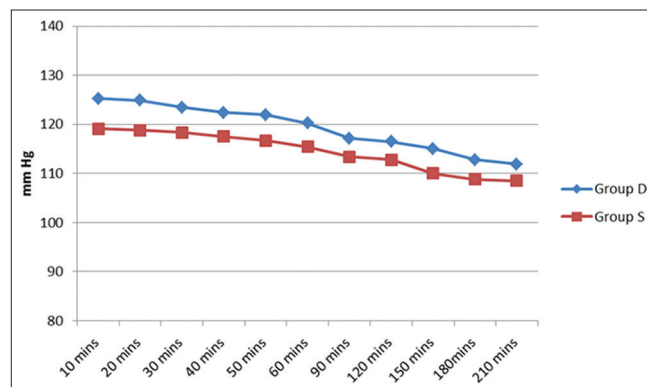

Figure 5: Perioperative heart rate

Figure 6: Perioperative systolic blood pressure

the groups. The Figure 8 shows the perioperative SpO_2 changes in both the groups. The mean duration of sensory blockade in group D was 1075.20 ± 144.831 mins and in group S was found to be 288.00 ± 103.923 mins and was statistically significant (*P* value = <0.001) (Figure 11).

DISCUSSION

The word "pain" derived from the Latin word "*Poena*" which means penalty or punishment. International society for the study of pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Inadequate pain relief in the perioperative period increases the patient morbidity and often associated with poor surgical outcomes.

Regional anesthesia is a boon in the present era of patient care because of its simplicity of the technique, preservation of consciousness, avoidance of airway instrumentation and rapid recovery with adequate post-operative analgesia (Miller's, 1994). The techniques of peripheral neural blockade were developed early in the history of anesthesia. The American surgeons Halsted and Hall[15] described the injection of cocaine into peripheral sites, including the ulnar, musculocutaneous, supratrochlear, and infraorbital nerves, for minor surgical procedures in the 1880s. Regional
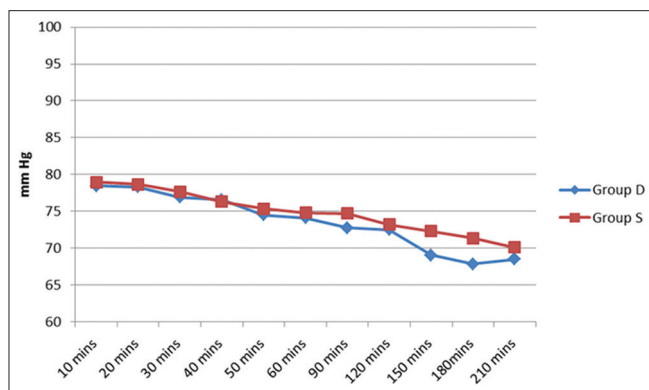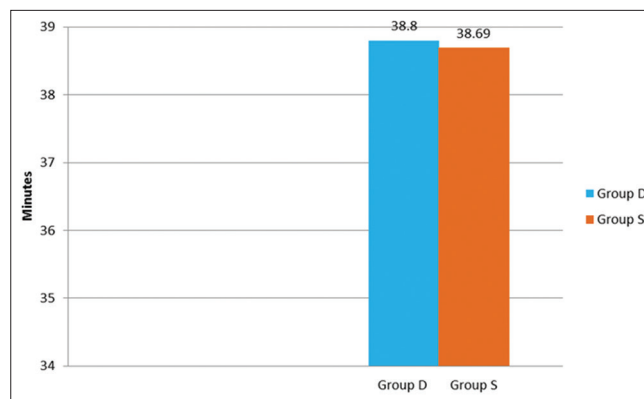
Figure 7: Perioperative diastolic blood pressure

Figure 8: Perioperative SpO$_2$

Figure 9: Mean onset of sensory block in both groups

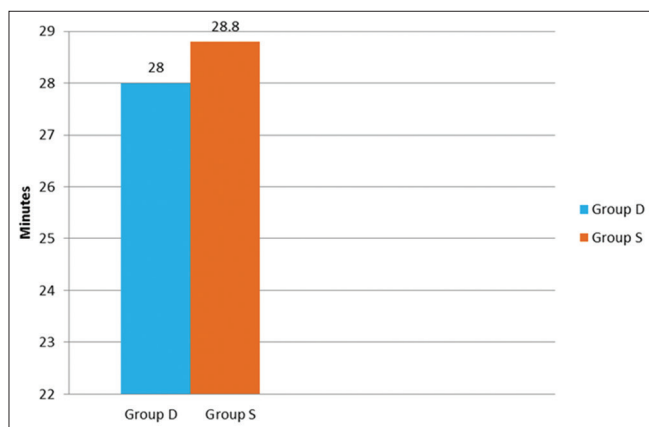**Figure 10: Mean onset of motor block in both groups**

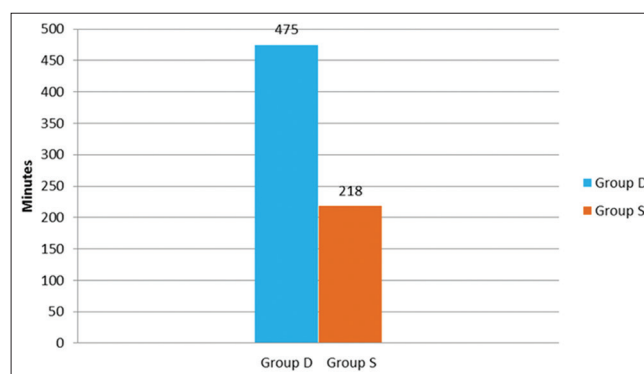**Figure 11: Comparison of mean duration of sensory block**

Figure 12: Comparison of mean motor block

anesthesia of the upper extremity requires knowledge of brachial plexus anatomy from its origin, where the nerves emerge from the intervertebral foramina to its termination in the peripheral nerves. Kulenkampff introduced the supraclavicular brachial plexus block[16] a few months after Hirschel described the axillary approach. Kulenkampff injected his own plexus with 10 mL of procaine at complete anesthesia of the arm.

The supraclavicular brachial plexus block provides a satisfactory anesthesia and analgesia for the upper extremity

surgery and also provides anesthesia of the entire upper extremity in the most consistent manner of any brachial plexus techniques. Currently, local anesthetics can provide analgesia for limited period of time when used as a single injection. When plain Bupivacaine used as a sole anesthetic in brachial plexus block, it produces a block with the relative duration of action with bupivacaine is 2-4 h[17] and also it has its own unfavorable properties like cardiac toxicity and slower onset of action.

Different drugs have been used as adjuvant to achieve quick, dense and prolong block.[18] Adjuvant improves analgesia,

reduces systemic side effects and reduce total dose of local anesthetic required. Drugs like morphine, pethidine, clonidine, butorphanol, midazolam are commonly used along with local anesthetics for this purpose. Clonidine has been used as an adjuvant to local anesthetics since the 1980s in various regional techniques to extend the duration of block because of the side effects like heavy sedation, respiratory depression and psychomimetic effects seen with morphine, pethidine, butorphenol.

There has always been a search for adjuvants to the regional nerve block with drugs that prolong the duration of analgesia but with lesser adverse effects. The search for the ideal additive led us to try the novel glucocorticoids-dexamethasone as an adjuvant to local anesthetics in brachial plexus block in this study because respiratory depression is not a major problem with its use. Steroids have nerve block prolonging effects. They block the nociceptive impulse transmission along the myelinated C fibres.[19,20] Steroids are very potent anti-inflammatory and immunosuppressive agents. Perineural injection of steroids is reported to influence post-operative analgesia.

We assessed sensory blockade using pin prick method using the blunt end of a 27-G needle at 0, 2, 5, 10, 15, 20 and 30 min. In our study, the mean time taken for onset of sensory blockade in dexamethasone group was 28.00 ± 4.082 min and in the saline group was 28.80 ± 3.317 min; we did not find any statistically significant difference between both the groups in terms of time taken for onset of sensory blockade ($P = 0.451$).

We assessed the motor blockade at 0, 10, 20, 30 and 40 min by assessing the motor functions of each nerve individually. The mean time taken for onset of the motor blockade in dexamethasone group was 38.80 ± 3.317 min and in the saline group was 38.80 ± 3.317 min; we did not find any statistically significant difference between both the groups in terms of time taken for onset of motor blockade ($P = 1.000$).

With our observations, we found out that addition of dexamethasone did not have any impact on the time taken for onset of sensory and motor blockade.

Our observations in terms of time taken for onset of the sensory blockade and motor blockade concur with the studies done by Parringtonet,[21] Movafegh *et al.*,[12] and Shaikh *et al.*[22]

We assessed the duration of analgesia among study subjects by using VAS score every hourly in the first 12 h and every 2nd hourly in the next 12 h. The mean duration of analgesia in the study subjects belonging to the dexamethasone group

was 1075.20 ± 144.831 min and the normal saline control group was 288.00 ± 103.923 min. The mean duration of analgesia in dexamethasone group was statistically significant ($P \leq 0.001$). The mean duration of analgesia was 3 times more prolonged in the dexamethasone group compared to the control groups.

In our study, the patients belonging to dexamethasone group had no pain from 1st-10th h, The VAS score remained within a range of 4-6 until 14 h of post-operative period. The VAS score in both the groups were similar in the first 3 h after initiation of block; later the VAS score in the control group started to rise progressively and by the 6th h majority of the patients had inadequate pain relief necessitating rescue analgesia. Our observations show that comparatively dexamethasone group had 3 folds prolonged post-operative analgesia with respect to the control group.

Our findings in terms of duration of analgesia concur with the studies done by Shrestha *et al.*,[23] Cummings *et al.*,[24] Pathak *et al.*,[25] and Choi *et al.*[26]

Dexamethasone used as an adjuvant in brachial plexus blocks clearly prolongs the duration of sensory and motor blockade.

Limitations of our study are we did not use ultrasound-guided block because of unavailability in our institution during the study period. We did not study the impact of dexamethasone on glucose homeostasis on wound healing and we did not follow-up the patients for long periods, i.e., >3 months for chronic neurological effects of dexamethasone.

Recent studies point out that caution must be used while using dexamethasone as an adjuvant in patients with diabetic neuropathy, because of their property to exacerbate neuropathy.[27,28] The outcomes associated with perineural dexamethasone is still unexplored, Christopher *et al.*,[15] from his meta-analysis on multiple studies which used dexamethasone as an adjuvant, did not find any favorable evidence pointing out to dexamethasone-induced neuropathy or neurotoxicity.

From the available data, we can cautiously conclude that perineural adjuvant dexamethasone is not overtly neurotoxic at 8 mg and has the potential for safe use as an adjuvant in regional anesthesia.

Furthermore, more randomized controlled trials would require prohibitively large sample sizes. The dose what we used in our study is a safe dose, which was proved in several clinical trials and no significant side-effects were noted in the study group in our study.

CONCLUSION

We conclude that when dexamethasone used as an adjuvant along with local anesthetic in brachial plexus block, it effectively prolonged the duration of both sensory and motor blockade with no side effects.

REFERENCES

1. Tetzlaff JE. Peripheral nerve blocks. In: Edward Morgan Jr G, Mikhail MS, Murray MJ, editors. Clinical Anesthesiology. 3rd ed. New York: McGraw Hill Professional; 2002. p. 289-90.
2. Yentis S, Hirsch N, Ip J, Smith G. Anaesthesia and Intensive Care A-Z: An Encyclopaedia of Principles and Practice. 3rd ed. UK: Butterworth Heinemann; 2004. p. 93.
3. Adnan T, Elif AA, Ayse K, Gülnaz A. Clonidine as an adjuvant for lidocaine in axillary brachial plexus block in patients with chronic renal failure. Acta Anaesthesiol Scand 2005;49:563-8.
4. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S. Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: A randomized, controlled study. Br J Anaesth 2005;94:112-6.
5. Karakaya D, Büyükgöz F, Baris S, Güldogus F, Tür A. Addition of fentanyl to bupivacaine prolongs anesthesia and analgesia in axillary brachial plexus block. Reg Anesth Pain Med 2001;26:434-8.
6. Fanelli G, Casati A, Magistris L, Berti M, Albertin A, Scarioni M, *et al.* Fentanyl does not improve the nerve block characteristics of axillary brachial plexus anaesthesia performed with ropivacaine. Acta Anaesthesiol Scand 2001;45:590-4.
7. Clerc S, Vuilleumier H, Frascarolo P, Spahn DR, Gardaz JP. Is the effect of inguinal field block with 0.5% bupivacaine on postoperative pain after hernia repair enhanced by addition of ketorolac or S(+) ketamine? Clin J Pain 2005;21:101-5.
8. Noyan A. On effects of ketamine to axillary block in hand surgery. J Reconstr Microsurg 2002;18:197.
9. Jarbo K, Batra YK, Panda NB. Brachial plexus block with midazolam and bupivacaine improves analgesia. Can J Anaesth 2005;52:822-6.
10. Colombo G, Padera R, Langer R, Kohane DS. Prolonged duration local anesthesia with lipid-protein-sugar particles containing bupivacaine and dexamethasone. J Biomed Mater Res A 2005;75:458-64.
11. Drager C, Benziger D, Gao F, Berde CB. Prolonged intercostal nerve blockade in sheep using controlled-release of bupivacaine and dexamethasone from polymer microspheres. Anesthesiology 1998;89:969-79.
12. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. Anesth Analg 2006;102:263-7.
13. Vieira PA, Pulai I, Tsao GC, Manikantan P, Keller B, Connelly NR. Dexamethasone with bupivacaine increases duration of analgesia in ultrasound-guided interscalene brachial plexus blockade. Eur J Anaesthesiol 2010;27:285-8.
14. Talukdar M, Begum H, Shoman MM, Khatu UH. Anaesthetic and analgesic effects of adding dexamethasone to bupivacaine in supraclavicular brachial plexus block – A comparative study. J Bangladesh Coll Phys Surg 2013;31:11-7.
15. Noss C, MacKenzie L, Kostash M. Dexamethasone a promising adjuvant in brachial plexus anesthesia? A systematic review. J Anesth Clin Res 2014;5:1-7.
16. Kulenkampff D. Anesthesia of the brachial plexus. Zentralbl Chir 1911;38:1337-40.
17. Bazin JE, Massoni C, Bruelle P, Fenies V, Groslier D, Schoeffler P. The addition of opioids to local anaesthetics in brachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia 1997;52:858-62.
18. De Oliveira GS Jr, Castro Alves LJ, Nader A, Kendall MC, Rahangdale R, McCarthy RJ. Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: A meta-analysis of randomized controlled trials. Pain Res Treat 2014;2014:179029.
19. Benzon HT. Epidural steroids. In: Prithvi Raj P, editor Pain Medicine, A Comprehensive Review. UK: Mosby Publications; 1999. p. 259-63.
20. Evers A, Maze M. Anesthetic Pharmacology: Physiologic Principles and Clinical Practice. New York: Churchill Livingstone; 2004. p. 814-29.
21. Parrington SJ, O'Donnell D, Chan VW, Brown-Shreves D, Subramanyam R, Qu M, *et al.* Dexamethasone added to mepivacaine prolongs the duration of analgesia after supraclavicular brachial plexus blockade. Reg Anesth Pain Med 2010;35:422-6.
22. Shaikh MR, Majumdar S, Das A, Saha TK, Bandyopadhyay SN, Mukherjee D, *et al.* Role of dexamethasone in supraclavicular brachial plexus block. IOSR J Dent Med Sci 2013;12:1-7.
23. Shrestha BR, Maharjan SK, Tabedar S. Supraclavicular brachial plexus block with and without dexamethasone - A comparative study. Kathmandu Univ Med J (KUMJ) 2003;1:158-60.
24. Cummings KC 3rd, Napierkowski DE, Parra-Sanchez I, Kurz A, Dalton JE, Brems JJ, *et al.* Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine. Br J Anaesth 2011;107:446-53.
25. Pathak RG, Anand PS, Rajendra NK. Supraclavicular brachial plexus block with and without dexamethasone – A comparative study. Int J Sci Res Publ 2012;12:1-7.
26. Choi S, Rodseth R, McCartney CJ. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: A systematic review and meta-analysis of randomized trials. Br J Anaesth 2014;112:1-13.
27. Ibinson JW, Mangione MP, Williams BA. Local anesthetics in diabetic rats (and patients): Shifting from a known slippery slope toward a potentially better multimodal perineural paradigm? Reg Anaesth Pain Med 2012;37:574-6.
28. Echevarria M, Hachero A, Martinez A, Ramallo E, García-Bernal D, Ramos M, *et al.* Spinal anaesthesia with 0.5% isobaric bupivacaine in patients with diabetes mellitus: The influence of CSF composition on sensory and motor block. Eur J Anaesthesiol 2008;25:1014-9.