

INTERSCALENE BRACHIAL PLEXUS BLOCK: COMPARISON OF EFFICACY OF VARYING DOSES OF DEXAMETHASONE COMBINED WITH LEVOBUPIVACAINE: A DOUBLE-BLIND RANDOMISED TRAIL.Srinivasa Rao Nallam¹**HOW TO CITE THIS ARTICLE:**

Srinivasa Rao Nallam. "Interscalene Brachial Plexus Block: Comparison of Efficacy of Varying Doses of Dexamethasone Combined with Levobupivacaine: A Double-blind Randomised Trail". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 25, June 23; Page: 6900-6908, DOI: 10.14260/jemds/2014/2836

ABSTRACT: INTRODUCTION: To compare the effects of adding two different doses of dexamethasone on the duration and quality of interscalene block in patients undergoing shoulder surgery. **METHODOLOGY:** A total of 90 patients (age 18-65 years) undergoing shoulder surgery under interscalene block were assigned randomly to one of three groups: Control Group-C received injection levobupivacaine (0.5%), 35ml plus 2 ml normal saline Group-L received injection levobupivacaine (0.5%) 35 ml plus dexamethasone 4 mg plus 1 ml normal saline and; Group H received injection levobupivacaine (0.5%) 35 ml plus dexamethasone 8 mg. Assessment of motor and sensory blockade, pulse, systolic blood pressure, respiration and side effects were noted every 5 minutes for first 30 minute and every 10 minute till the end of surgery. Postoperative analgesia was assessed using the numeric rating scores [NRS]. **RESULTS:** The duration of analgesia was significantly prolonged in both Group L (19.2 ± 2.6 h) and Group H (21.3 ± 1.7 h) compared with Group C (11.6 ± 1.1 h) ($p < 0.05$). Similarly, the duration of motor block was longer in both Group L (26.6 ± 2.8 h), and Group H (28.4 ± 2.2 h) compared to Group C (18.6 ± 3.1 h) ($p < 0.05$). Postoperative analgesic consumption for the first 48 hours was significantly lower in Group L (6.5 [4-8] tabs) and in Group H (5.5 [4-7] tabs) vs. 9.5 [8-12] tabs in Group C ($p < 0.01$). **CONCLUSION:** The addition of dexamethasone to levobupivacaine significantly prolonged the duration of the motor block and improved the quality of analgesia following interscalene block. There was no difference in the duration of analgesia and motor block between low-dose and high-dose dexamethasone.

KEYWORDS: Postoperative Pain, Interscalene -block, Levobupivacaine, Dexamethasone.

INTRODUCTION: Pain after orthopedic surgery can be intense.^[1] In particular, managing pain after shoulder procedures poses a challenge to both anesthesiologists and orthopedic surgeons. In an effort to improve analgesia and facilitate mobilization, regional anesthesia in the form of an interscalene approach to the brachial plexus is often used. The use of an interscalene block as the primary anesthetic increases the proportion of patients suitable for post-anesthesia care unit (PACU) bypass and decreases immediate postoperative pain.^[2]

Investigators have tried mixing local anesthetics with adjuvant drugs in an attempt to prolong analgesia from nerve blocks. Adjuvants including epinephrine, clonidine,^[3,4] opioids,^[5,6] ketamine^[7,8] and midazolam^[9] have met with limited success. However, the glucocorticoid dexamethasone appears to be effective in a small number of preclinical^[10,11] and clinical^[12] studies. Steroids induce a degree of vasoconstriction, so one theory is that the drug acts by reducing local anesthetic absorption. A more attractive theory holds that dexamethasone increases the activity of inhibitory

ORIGINAL ARTICLE

potassium channels on nociceptive C-fibers (via glucocorticoid receptors) thus decreasing their activity.

The present work is a prospective, randomized study examining the analgesic properties of low and high doses of dexamethasone.

MATERIALS AND METHODS: The hospital ethical committee approved the prospective, randomized study and a written informed consent from all the patients was obtained. Ninety adult patients (18-65 Years) of either sex, weight range (40- 90 kg), American Society of Anesthesiologists (ASA) grade I, II, scheduled for shoulder surgeries[open reduction and internal fixation for fracture proximal humerus (NEERS type 2 and type 3), modified putti plat technique for recurrent shoulder dislocations.] were randomly allocated into three groups.

All patients received interscalene brachial plexus block using levobupivacaine 0.5%. A total volume of 35 mL of local anesthetic was selected to provide the highest rate of success of interscalene block administered using the nerve stimulation technique. Patients were randomized using a randomization table for two treatment groups and one control group. Patients were assigned randomly to one of three groups:

Group C: received 35 ml of 0.5% levobupivacaine plus 2ml of normal saline was added, with no addition of dexamethasone; Group L, received 35 ml of 0.5% levobupivacaine plus dexamethasone 4 mg(1 ml) plus 1ml of normal saline and; Group H, received 35 ml of 0.5% levobupivacaine plus dexamethasone 8 mg (2 ml).

The block was performed by an anesthesiologist who was blinded to the preparation and randomization process. After establishing intravenous access, standard ASA monitors were applied, and supplemental oxygen was provided at 2 L/min via nasal cannula. Moderate levels of sedation were provided by intravenous administration of midazolam 1 mg plus fentanyl 30 micrograms before the block. A nerve stimulation technique with a Stimuplex needle and a stimulator were used. After proper location of the nerve the study solution was injected in incremental 5 mL boluses with intermittent aspiration.

Postoperative pain was treated with oral administration of acetaminophen 325 mg as necessary in all patients. Patients were advised to take one or two tablets if the pain intensity exceeded 3 (0, no pain; and 10, worst pain imaginable) on the Numerical Rating Score (NRS). If the pain persisted, patients were advised to take ibuprofen 400 mg. They were asked to indicate the time after discharge when the oral analgesic was taken initially due to pain.

Duration of analgesia was reported as the time in hours from the time of completion of surgery to where the patients felt pain from the incision for the first time at intensity of more than 3 on numerical rating scale [NRS]. Total analgesic use also was recorded as the number of acetaminophen tablets and the amount of ibuprofen consumed by the patient within the first 72 h. Duration of the motor block was calculated from the time of completion of the nerve block to the time when the patient was able to abduct the arm at least 2 inches away from the body.

RESULTS: The average age of the patients was 46.8 ± 4.1 years. All patients except for one in the control group were sedated preoperatively with intravenous midazolam 2 mg. Fentanyl was administered to a higher number of patients in Group L than in Group H and Group C ($p < 0.05$). The mean length of stay in the post-anesthetic care unit was similar in all groups.(Table 1)

ORIGINAL ARTICLE

	Group C (N=28)	Group L (N=28)	Group H(N=30)
Dexamethasone	None	4mg	8mg
Gender (M/F)	22/6	19/9	21/9
ASA Grade (I/II)	20/8	17/11	20/10
Body mass Index (kg/m ²)	28.2+/- 5.1	28.4+/- 4.6	28.7+/- 5
Base Line H.R (bpm)	81.2+/- 13.9	81.3+/- 12.3	81.2+/- 12.6
Base Line M.A.P (mm of Hg)	91.5+/- 8.6	91.9+/- 7.4	91.2+/- 8.2
Base Line Spo2 (%)	96.8+/- 1.2	97.0+/- 1.1	97.2+/- 1.4
Duration of Surgery (mins)	112+/- 37	103+/-38	109+/- 31
PACU Length of Stay (mins)	66+/- 20	64+/- 28	64+/- 18

TABLE 1: DEMOGRAPHIC DATA AND DEXAMETHASONE DOSES

The numerical data are presented as mean \pm SD. There was no statistical significance in these variables (PACU) Post-anesthetic care unit.

The majority of the patients (97.7%) did not receive any supplemental analgesics and were discharged with no pain. The duration of surgery was also similar among the groups. The duration of analgesia was significantly longer in Group L and Group H patients (19.2 ± 2.6 and 21.3 ± 1.7 h) than in Group C patients (11.6 ± 1.1 h, $p < 0.05$).

However, there was no difference in the duration of analgesia between Group L and Group H. Time-to-event analysis of the pain showed that both doses of dexamethasone prolonged the duration of analgesia when compared to levobupivacaine alone (Fig.1). Similarly, both dexamethasone groups had longer durations of motor block [26.2 ± 2.8 h (Group L) and 28.4 ± 2.2 h (Group H)] than Group C (18.6 ± 3.1 h, $p < 0.05$). Once again, there was no difference in the duration of motor block between Group L and Group H. (Table.2)

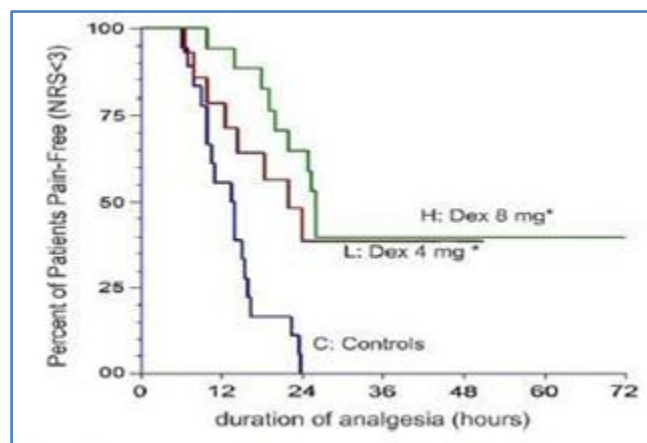


Figure 1

Fig.1: Logrank test (Kaplan–Meier) analysis for the treatment groups from the time of interscalene block to the time at which the patient reported a pain level [3]. Data points were censored if the patient never had this level of pain within the 72 h follow-up period. Asterisk denotes a statistically significant difference from Group C ($p < 0.05$).

ORIGINAL ARTICLE

Postoperative analgesic consumption (the number of acetaminophen tablets) was compiled for the first and second postoperative days. Analgesic consumption for the first postoperative 48 h was significantly lower in Group L (6.5, range [4–8] tabs) and in Group H (5.5, range [4–7] tabs) than in Group C (9.5, range [8–12] tabs) ($p < 0.01$). Although there was a trend for lower analgesic consumption in Group H when compared to Group L, this difference did not reach statistical significance. Analgesic consumption on the third postoperative day was similar in all three groups (Table 2).

	Group C (N=28)	Group L (N=28)	Group H (N=30)
Duration of analgesia (Hrs)	11+/- 3	19+/- 6	21+/- 7
Duration of Motor block (Hrs)	18+/- 11	27+/- 18	28+/- 14
Number of Tablets Consumed in the first post-operative 48hrs (median range)	9.5(8- 12) tabs	6.5 (4- 8) tabs	5.5 (4 - 7) tabs
Number of A tablets Consumed on POD3 (median range)	4.5 (3 - 5) tabs	3.5 (3 - 5) tabs	4 (3 - 5) tabs

TABLE 2: DURATION AND QUALITY OF POST OPERATIVE ANALGESIA

Duration of analgesia is the time reported in hours from discharge to the time that patient first experienced incisional pain of 3 or greater. Data for analgesic consumption are presented as the median [range], and were analyzed using nonparametric analysis of variance (MANOVA). Other continuous data are presented as the mean \pm SD.

L Low-dose dexamethasone 4mg was added to the local anesthetic; H high-dose dexamethasone 8 mg was added to the local anesthetic; POD3 third postoperative day; A tablet acetaminophen 325 mg.

* Signify statistical significance with a p value\0.05 when compared to the control group
 _ Statistical significance when comparing Group H to Group L.

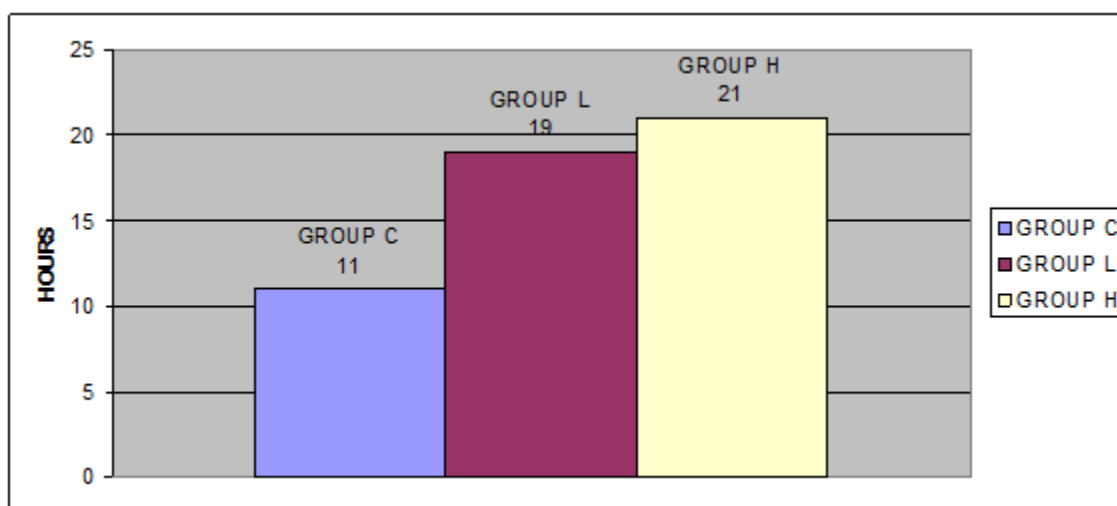


Table 3: Duration of analgesia (Hours)

ORIGINAL ARTICLE

The difference of duration of analgesia between control group and study group was statistically significant but not between group L and group H.

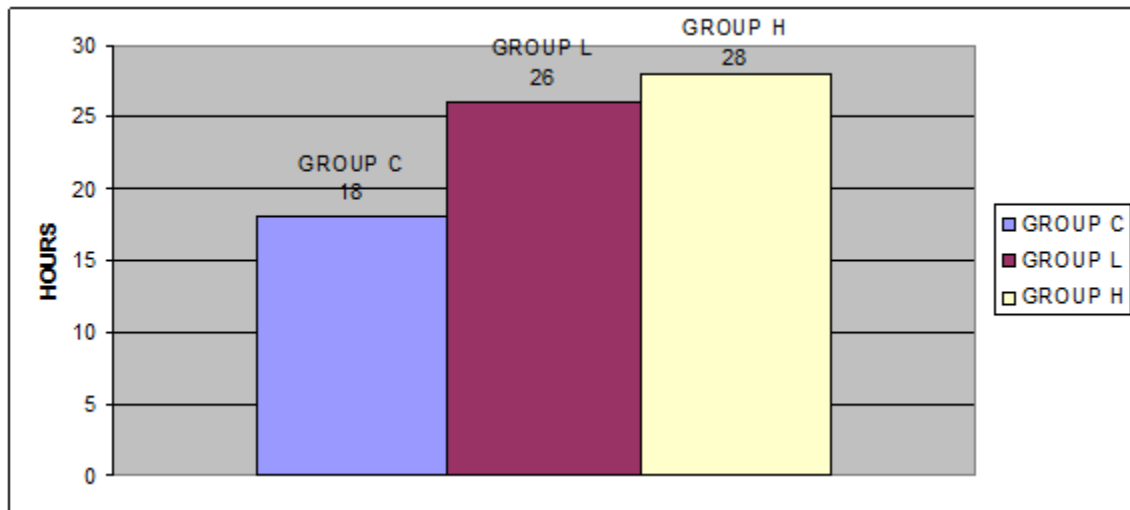


Table 4: Duration of motor block (Hours)

DISCUSSION: Steroids were added to local anesthetic agents in order to prolong the duration of anesthesia and improve the quality of pain relief. This combination was used for both neuraxial route and peripheral nerve blocks.^[13,14,15] We demonstrated that the addition of dexamethasone to levobupivacaine prolongs the duration of the motor block and improves the quality of interscalene block. Our findings also indicated that both 4 and 8 mg doses of dexamethasone were equally effective in prolonging the duration of analgesia and improving the quality of pain relief when mixed with levobupivacaine. Interestingly, the duration of the motor block was also increased when dexamethasone was added to the local anesthetic mixture.

Our finding that dexamethasone can be used to increase the duration of regional analgesia from a peripheral nerve block correlates well with other recently published investigations.^[16] A single dose of dexamethasone added to levobupivacaine has been used successfully to produce a preemptive analgesia following podiatric surgery.^[17] These patients received local infiltration of the local anesthetic in addition to mid-metatarsal nerve blocks. An independent group of investigators observed similar effects when a longer-acting glucocorticoid was added to plain levobupivacaine. These patients experienced prolonged sensory anesthesia (24 h) following a single bolus axillary approach brachial plexus block.^[18]

In a preliminary work by Iyers et al. on 13 patients, adding 4 mg of dexamethasone to 0.5% ropivacaine (similar to Group L in this study) increased the duration of sensory block from 12.7 to 22.2 h after interscalene nerve block. These authors report a similar effect upon adding dexamethasone 4 mg to both levobupivacaine and ropivacaine after femoral blocks.

The precise mechanism by which dexamethasone prolongs the duration sensory block is not completely understood. Although the mechanism of action for dexamethasone was not examined by this study, direct antinociceptive effects have been described following the local administration of steroids. Johansson et al.^[19] demonstrated that locally administered steroids inhibit the signal

ORIGINAL ARTICLE

transmission of nociceptive C-fibers and by modifying the membrane lipid phase equilibrium. Interestingly, myelinated nerve fibers were spared from these changes. The biologic half-life of dexamethasone is between 36 to 54 h, and its effects are most apparent in the first 48 h.^[20] Our results showed that dexamethasone prolonged the duration of analgesia for approximately 24 h. Opioid sparing effect of dexamethasone were apparent only on the first and the second postoperative days.

Dexamethasone alone lacks any analgesic property in thermal injury and secondary hyperalgesia.^[21] Inclusion of dexamethasone in bupivacaine microspheres injected in animal experiments results in prolonged duration of analgesia. In a study done by Kohane et al.^[22] Coencapsulation of tetrodotoxin (TTX) in controlled-release devices containing bupivacaine and dexamethasone resulted in exceedingly prolonged nerve blocks. Kopacz et al. found similar clinical effects following the addition of dexamethasone in bupivacaine microcapsules used for intercostal blocks in healthy volunteers. These investigators found an increase of at least 96 h in the duration of intercostal block.^[23]

The safety of the perineural administration of dexamethasone may raise some concerns, especially when it contains benzyl alcohol. It is important to note that a small fraction of this additive is given and that it is diluted in a volume of 40 mL, so the chance of causing nerve damage under this circumstance is low.^[24] In an animal study, dexamethasone reduced blood flow to the normal nerves for 4 h after topical application.^[25]

However, the reduction is generally below the threshold for developing ischemic changes in peripheral nerve fibers. Rare reports of nerve injury associated with dexamethasone injection are generally due to direct needle trauma.^[26] Intrafascicular injection of dexamethasone produces minimal injury, while methyl prednisolone has shown to cause intermediate damage.^[27]

Intrafascicular steroid injections produced a harmful effect on nerve fibers; however, there were no reports of long-term local effects on peripheral nerves. We continue to follow our patients through periodic phone calls, and have established a self-reporting mechanism that allows the patients to report any untoward reaction that can remotely mimic late-onset neuropathy for a period of 1 year.

We understand that the terms of the sensory and motor blockade used in this study may not correlate well with other investigations in which these variables were examined by a health professional. The source of information for our results was the survey questionnaires collected from the patients. Assessment of pain can potentially be affected by the time and pattern of sleep, unless the severity of the pain arouses the patient from sleep.

Although these patients were educated preoperatively by an anesthesiologist and a study nurse, and coached through the postoperative period over the phone by the study nurse, almost all of the sensory block assessments were subjective. This issue will remain a significant limitation for any human study in the outpatient setting, due to the operational logistics of outpatient surgery centers. It is therefore acceptable to use the time to report surgical pain as a surrogate marker for the duration of sensory block.

Our results indicated that the addition of dexamethasone to levobupivacaine prolonged motor weakness following interscalene block. Since the duration of the motor block is a semi-objective measure, it was recorded from the time of block as the reference time point. As for the duration of analgesia (a purely subjective measure), we used the time of discharge as our reference

ORIGINAL ARTICLE

point. As there was no difference in the length of hospital stay among the groups, our results for the duration of analgesia were not affected. Only one patient was dissatisfied from prolonged motor weakness postoperatively.

We should note that the reported motor block considered only abduction of the arm (deltoid muscle) in this study. The majority of the patients were able to use their fingers while arm abduction was still blocked.

We conclude that adding dexamethasone to the levobupivacaine significantly prolonged the duration of analgesia and motor blockade, and reduced opioid consumption for 48 h postoperatively. Although there was no report of adverse events related directly to the dexamethasone–levobupivacaine mixture interscalene block in our case mix during the four-week follow-up period, we are unable to comment on the safety of this therapeutic approach due to the relatively small sizes of our study groups.

Overall, patients were satisfied with the postoperative analgesic control. As a result of this study, we believe that this technique may be a good alternative to the continuous perineural block if technical and logistic issues are of concern. Future studies may need to examine the effectiveness of dexamethasone when it is added to ropivacaine, and to determine whether the duration of sensory blockade is comparable to levobupivacaine with a shorter motor blockade.

REFERENCES:

1. Rawal N, Hylander J, Nydahl PA, Olofsson I, Gupta A. Survey of postoperative analgesia following ambulatory surgery. *Acta Anaesthesiol Scand* 1997; 41: 1017–22
2. Hadzic A, Williams BA, Karaca PE, et al. For outpatient rotator cuff surgery, nerve block anesthesia provides superior same-day recovery over general anesthesia. *Anesthesiology* 2005; 102: 1001–7
3. Andan T, Elif AA, Ayse K, Gulnaz 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, 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, Buyukgoz F, Baris S, Guldogus F, Tur A. Addition of fentanyl to bupivacaine prolongs anesthesia and analgesia in axillary brachial plexus block. *RegAnesth Pain Med* 2001; 26: 434–8
6. Fanelli G, Casati A, Magistris L, et al. Fentanyl does not improve the nerve block characteristics of axillary brachial plexus anesthesia performed with ropivacaine. *ActaAnaesthesiolScand* 2001; 45: 590–4
7. Clerc S, Vuillermier H, Frascarolo P, Spahn DR, Gardaz J. 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

ORIGINAL ARTICLE

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. *AnesthAnalg* 2006; 102: 263–7
13. Shrestha BR, Maharjan SK, Tabedar S. Supraclavicular brachial plexus block with and without dexamethasone—a comparative study. *Kathmandu Univ Med J.* 2003; 1:158 60.
14. Banaszkiwicz PA, Kader D, Wardlaw D. The role of caudal epidural injections in the management of low back pain. *Bull HospJt Dis.* 2003; 61: 127–31.
15. Bansal S, Turtle MJ. Inadvertent subdural spread complicating cervical epidural steroid injection with local anaesthetic agent. *Anaesth Intensive Care.* 2003; 31:570–2.
16. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. *AnesthAnalg.* 2006; 102: 263–7.
17. Salerno A, Hermann R. Efficacy and safety of steroid use for postoperative pain relief update and review of the medical literature. *J Bone Joint Surg Am.* 2006; 88: 1361–72.
18. Stan T, Goodman EJ, Bravo-Fernandez C, Holbrook CR. Adding methylprednisolone to local anesthetic increases the duration of axillary block. *Reg Anesth Pain Med.* 2004; 29:380–1.
19. Johansson A, Hao J, Sjolund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. *Acta Anaesthesiol Scand.* 1990; 34: 335–8.
20. Copur MS, Ledakis P, Norvell M. Prevention of delayed emesis caused by chemotherapy. *N Engl J Med.* 2000; 343: 888–9.
21. Werner MU, Lassen B, Kehlet H. Analgesic effects of dexamethasone in burn injury. *Reg Anesth Pain Med.* 2002; 27: 254– 60.
22. Kohane DS, Smith SE, Louis DN, Colombo G, Ghoroghchian P, Hunfeld NGM, Berde CB, Langer RS. Prolonged duration local anesthesia from tetrodotoxin-enhanced local anesthetic microspheres. *Pain.* 2003; 104: 415–21.
23. Kopacz DJ, Lacouture PG, Wu D, Nandy P, Swanton R, Landau C. The dose response and effects of dexamethasone on bupivacaine microcapsules for intercostals blockade (T9 to T11) in healthy volunteers. *Anesth Analg.* 2003; 96: 576–82.
24. Goodman E, Stan T. Potentially concerning reason why adding methylprednisolone to local anesthetic may increase the duration of axillary block. *Reg Anesth Pain Med.* 2005; 30:114–5.
25. Shishido H, Kikuchi S, Heckman H, Myers RR. Dexamethasone decreases blood flow in normal nerves and dorsal root ganglia. *Spine.* 2002; 27:581–6.
26. Stahl S, Kaufman T. Ulnar nerve injury at the elbow after steroid injection for medial epicondylitis. *J Hand Surg.* 1997; 22: 69–70.
27. Mackinnon SE, Hudson AR, Gentili F, Kline DG, Hunter D. Peripheral nerve injection injury with steroid agents. *Plast Reconstr Surg.* 1982; 69: 482–90.

ORIGINAL ARTICLE

AUTHORS:

1. Srinivasa Rao Nallam

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesiology, Malemaruvathur Adhiparasakthi Institute of Medical Sciences, Malemaruvathur, Tamilnadu, India.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Srinivasa Rao Nallam,
Flat No. 105, Sai Krishna Appartments,
Besides Balireddy Hospital,
Co-operative Colony, Kadapa-516002,
Andhra Pradesh
Email: drvaasu@gmail.com

Date of Submission: 31/05/2014.
Date of Peer Review: 01/06/2014.
Date of Acceptance: 13/06/2014.
Date of Publishing: 18/06/2014.