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Original Article

Anaesthesia Section

Effects of Low Dose Dexamethasone as an Adjuvant to Levobupivacaine in Ultrasound-guided Interscalene Brachial Plexus Block: A Randomised Clinical Trial

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ABSTRACT

Introduction: Ultrasound-guided Interscalene Brachial (USG-ISB) plexus block is known to provide effective analgesia for upper limbs surgery. Low-dose dexamethasone as additive with levobupivacaine in USG-ISB plexus block is known to provide effective analgesia for upper limbs surgery.

Aim: To evaluate whether dexamethasone, use as an additive with levobupivacaine during an USG-ISB plexus block for upper limb surgery, has sufficient analgesic effect.

Materials and Methods: The randomised clinical trial was conducted at GGS Medical College and Hospital, Faridkot, Punjab, India, from March 2018 to August 2019. Sixty patients, who were scheduled to have upper limb surgery using USG-ISB with 0.5% levobupivacaine were randomly assigned to one of two groups. Group A (n=30) received one mL of normal saline, while group B (n=30) received 4 mg of dexamethasone. A four-point Verbal Numerical Rating Scale (VNRS) for pain was used to evaluate postoperative analgesia. The duration of analgesia, time to onset and duration of sensory and motor blockade, and pain ratings were measured. Unpaired student's t-test, Chi-square and Fisher's-exact tests were used to analyse the data.

Results: The mean duration of analgesia was significantly longer for group B than for group A (854.67±10.08 min vs 743.00±23.22 min; p-value <0.001). The onset of sensory and motor blocks in group B began to develop earlier (8.42±0.35 min, and 9.72±0.55 min) than those in group A (10.10±0.80 min, and 11.02±0.84 min; p-value <0.001). The duration of the sensory and motor block in group B was longer (653±16.17 min and 582.83±14.18 min) than that in group A (595±17.29 min and 487.33±21.04 min; p-value <0.001).

Conclusion: Perineural dexamethasone with levobupivacaine provides greater postoperative analgesia, also, speed up the onset of sensory and motor effects, and prolongs the duration of interscalene brachial plexus block.

Keywords: Analgesia, Perineural, Surgery

INTRODUCTION

The advent of outpatient surgery in the current clinical setting has given regional anaesthesia for upper limb surgery a lot of attention. Excellent anaesthesia and analgesia, including better postoperative analgesia and haemodynamic stability, are provided by Interscalene Brachial (ISB) [1].

To extend the time that peripheral nerve blocks last, local anaesthetics have been tried in combination with various adjuvants. A more recent local anaesthetic, levobupivacaine, is the S-enantiomer of bupivacaine and has lower cardiac and neural toxicity [2,3]. Many additives, including epinephrine, clonidine, opioids, ketamine, and midazolam, have been researched to lengthen the duration of peripheral nerve blocks, but they may also have unfavourable side-effects [4-6].

It has been demonstrated that dexamethasone works wonders at extending the time that peripheral nerve blocks last. When combined with local anaesthetic, dexamethasone prolongs the effects of peripheral nerve blocks [7]. Dexamethasone works by reducing inflammation, delaying C-fiber impulses, and halting the discharge of ectopic nerves. These effects have a fantastic safety profile, with no complications reported [8-10].

Only a few studies have been conducted on the analgesic effectiveness of low-dose dexamethasone with levobupivacaine in brachial plexus blocks, and the results have been inconsistent [11,12]. Therefore, the present study was carried out to assess the role of additive effects of perineural dexamethasone with levobupivacaine in prolonging the duration of postoperative analgesia, comparing postoperative pain scores, and evaluating block characteristics. The duration of analgesia was the primary outcome. Time to onset and duration of sensory and motor blockade, and pain ratings, were secondary outcomes of the present study.

MATERIALS AND METHODS

The randomised clinical trial was conducted on 60 patients at Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India, from March 2018 to August 2019. The Institutional Ethical Committee had approved the study (no.ECR/836/Inst/PB/2016) and the study is also registered at the Clinical Trial Registry, India (CTRI/2018/07/014795). Written informed consent was obtained from all participants and the entire research protocol was thoroughly explained to them.

Inclusion criteria: Patients aged 25-55 years, of either gender, with an American Society of Anaesthesiologists (ASA) physical status I-II, who were scheduled for upper limbs surgery, above the elbow.

Exclusion criteria: Patients with known hypersensitivity to the study drugs, and contraindication to ISB were excluded from the study.

Sample size calculation: A power analysis was performed to calculate the sample size based on duration of analgesia (primary outcome), where 10 pilot cases were conducted. It was found that a 40% difference in duration of analgesia, can be considered a clinically relevant. With a power of 80%, alpha error of 0.05, and beta error of 0.2%, the minimum sample size was determined to be 30 per group.

Study Procedure

A thorough preanaesthetic evaluation was done and patients were explained about the block procedure, complications, and Verbal

Numerical Rating Scale (VNRS). On the night before the procedure, patient received oral ranitidine 150 mg and alprazolam 0.25 mg.

Using a computer-generated programmer, 60 patients were randomly divided into two groups- Group A, (n=30) and Group B, (n=30). Sixty sealed envelopes were prepared to ensure concealment of randomisation. The study drug was prepared by the anaesthesiologist, who was not involved in the study. The anaesthesiologist, who conducted and evaluated the ISB was blinded to the study drug. Every 5 minutes up to 30 minutes, and then every 30 minutes throughout the study, the following vitals were measured: Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), peripheral Oxygen Saturation (SpO_2), and a 3-lead Electrocardiogram (ECG).

Patients were positioned in a supine position with their heads turned to the non operating side. After draping the area and ensuring complete asepsis, 2% lidocaine was applied locally to the skin. A high-frequency (5-10 MHz) ultrasound probe (Esaote Europe BV) was placed over patient's neck, positioned transversely over the sternocleidomastoid at the level of the cricoid cartilage. After locating the jugular vein and carotid artery, the probe was moved posteriorly until the brachial plexus nerve roots were visible. At this level, transverse view was obtained in the interscalene groove to see the brachial plexus nerves, which was hypoechoic and clearly shaped like an oval or round between the anterior and middle scalene muscles. The block was performed using an in-plane technique with 50 mm 22 G insulated short-beveled stimulation needle (Stimuplex A, B. Braun Melsugen AG, Germany).

Once the needle tip reached the brachial plexus cluster on the ultrasound image, drug was deposited as per group allocation in the study.

- **Group A:** Patients received 24 mL of 0.5% levobupivacaine mixed with 1 mL of normal saline.
- **Group B:** Patients received 24 mL of 0.5% levobupivacaine mixed with 4 mg of dexamethasone (1 mL).

Following that, patients were assessed every minute until the successful onset of the sensory and motor block. Pin-prick testing was used to assess sensory block in the distribution of five nerves using a three-point scale: (0=normal sensation, 1=loss of pinprick sensation (analgesia), 2=loss of touch sensation (anaesthesia). The same nerves were assessed for motor block, which was graded on a 3-point scale: (0-No block, 1-Decreased motor strength, 2-Complete motor blockade). Time to achieve adequate sensory and motor block were noted. The duration of analgesia was the primary outcome, whereas time to onset and duration of sensory and motor blockade, and pain ratings, were secondary outcomes of the present study.

Block Parameters

1. **Onset of nerve blockade**

- For sensory: The time from the end of the injection for the ISB to reduction in sensibility equal to scale-2.
- For the motor: The interval between end of the brachial plexus block injection to reduction in muscle power to scale-2.

2. **Block duration**

- For sensory block, the patient was instructed to document the return of normal sensations which is equal to scale 0.
- For the motor: The patient was instructed to move their shoulder.

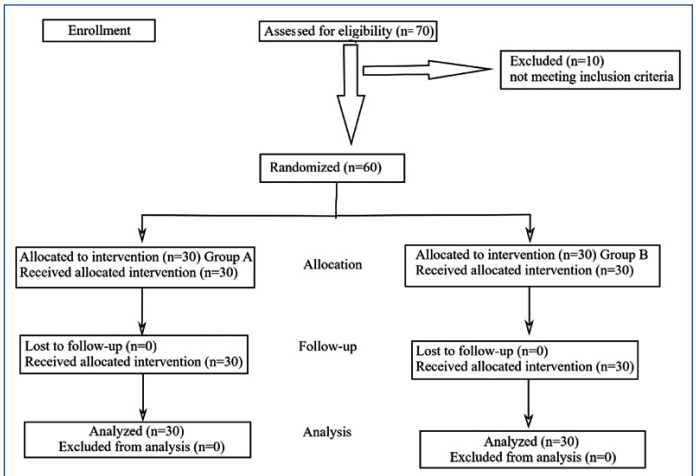
3. **Verbal Numeric Rating Scale (VNRS):** Upon entry into the postanaesthesia care unit, patients were given a four-point VNRS to rate their level of pain on the movement of the operated arm (0=no pain, 1-3=mild pain, 4-7=moderate pain, and 7-10= severe pain).
4. **Duration of analgesia:** From the time of onset of sensory block, to when the patient started to experience considerable pain of VNRS >3, and rescue analgesic injection diclofenac 75 mg was administered intravenously. The total number of rescue injections administered during the initial 24 hours following surgery, was noted. Postoperative follow-up was done hourly for the first six hours, then three hourly for the next 24 hours. Haemodynamic parameter, as well as, any complications was also recorded.

STATISTICAL ANALYSIS

After completion of study, data were compiled and analysed using Statistical Package of Social Sciences (version 21.0, SPSS Inc., USA). While categorical variables were presented as percent, continuous variables were presented as mean and Standard Deviation (SD). Unpaired student's t-test was used to analyse continuous variables, and Chi-square and Fisher's-Exact tests were used to analyse categorical variables. Statistical significance was set at p-value <0.05. Microsoft word and excel were used to create tables and graphs.

RESULTS

A total 70 patients were approached to participate in the present study. Ten patients did not meet the inclusion criteria. A total of 60 patients were recruited, and randomly assigned to their treatment group. The block was effective in all patients. Finally, the data were analysed for the 60 patients [Table/Fig-1].



[Table/Fig-1]: Patient flowchart, according to Consolidated Standards of Reporting Trials (CONSORT).

Regarding haemodynamic parameters and demographic factors like age, weight, height, BMI, gender, ASA status, and length of surgery, patients in the two groups were comparable [Table/Fig-2].

Demographical variables	Group A (n=30)	Group B (n=30)	p-value (Unpaired t-test)
Age (years)	41.27±9.51	41.10±8.15	0.942
BMI (kg/m^2)	25.19±1.90	25.55±1.94	0.463
Gender (Male/Female)	15/15	16/14	0.796
ASA status (I/II)	11/19 (36.7%/63.3%)	14/16 (46.7%/53.3%)	0.432

[Table/Fig-2]: Demographic variables.
Values are expressed as the mean±SD or the number of patients.
ASA: American society of anaesthesiologists; SD: Standard deviation; BMI: Body mass index

Onset of sensory block and motor blockade were significantly faster group B as compared to group A. The duration of analgesia and the duration of sensory and motor blockade were also significantly prolonged in group B. The difference was found to be statistically very significant (p-value <0.001) [Table/Fig-3].

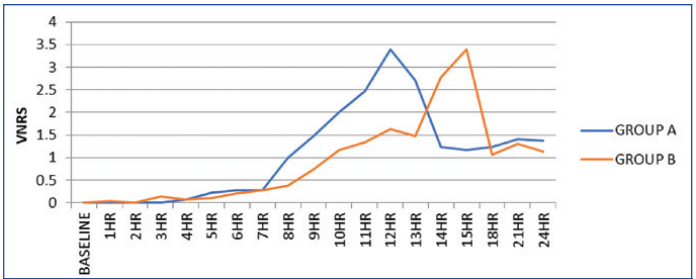
The postoperative mean VNRS score were lower in group B as compared to group A from 5th hour to 24th hour intervals (except at time intervals 14th hour and 15th hour), and the differences were statistically significant [Table/Fig-4a,b].

Time	Group A (n=30)	Group B (n=30)	p-value
Onset of sensory block (min)	10.10±0.80	8.42±0.35	<0.001
Onset of motor block (min)	11.02±0.84	9.72±0.55	<0.001
Duration of sensory block (min)	595.17±17.29	653.83±16.17	<0.001
Duration of motor block (min)	487.33±21.04	582.83±14.18	<0.001
Mean duration of analgesia (min)	743.00±23.22	854.67±10.08	<0.001

[Table/Fig-3]: Block characteristics and duration of analgesia between groups. Values are expressed as the mean±SD, Group A=Levobupivacaine+saline group, Group B=Levobupivacaine+dexamethasone group, SD: Standard deviation

VNRS (hours)	Group A (n=30)		Group B (n=30)		p-value (Unpaired t-test)
	Mean	SD	Mean	SD	
Baseline	0.00	0.00	0.00	0.00	NA
1	0.00	0.00	0.03	0.18	0.321
2	0.00	0.00	0.00	0.00	NA
3	0.00	0.00	0.13	0.35	0.039
4	0.07	0.25	0.07	0.25	1.000
5	0.23	0.43	0.10	0.31	0.171
6	0.27	0.45	0.20	0.41	0.549
7	0.27	0.45	0.27	0.45	1.000
8	1.00	0.00	0.37	0.56	<0.001
9	1.47	0.51	0.73	0.78	<0.001
10	2.00	0.00	1.17	1.18	<0.001
11	2.47	0.51	1.33	1.21	<0.001
12	3.40	0.56	1.63	1.45	<0.001
13	2.70	1.51	1.47	1.38	0.002
14	1.23	0.43	2.77	0.77	<0.001
15	1.17	0.38	3.40	1.22	<0.001
18	1.23	0.43	1.07	0.37	0.111
21	1.40	0.50	1.30	0.60	0.484
24	1.37	0.49	1.13	0.51	0.075

[Table/Fig-4a]: Comparison of postoperative Verbal Numeric Rating Score (VNRS) at different time interval.



[Table/Fig-4b]: Verbal Numerical Rating Scale (VNRS) in both the groups.

Regarding operating conditions, there was no statistically significant difference between the groups. Throughout the perioperative period, there were no side-effects.

DISCUSSION

Many patients report having trouble sleeping the night after upper limb orthopaedic surgery due to pain. The interscalene brachial plexus block is the best method for treating acute pain in these patients [1]. In the present study, the addition of 4 mg of dexamethasone to levobupivacaine increased the duration of block and the early onset of sensory and motor blockade, which may be the result of a synergistic effect between dexamethasone and levobupivacaine. In addition, there were not many studies that combined levobupivacaine and low-dose dexamethasone for interscalene brachial plexus block in the literature. To investigate its impact on the onset and duration of sensory and motor blockade, authors used 4 mg of dexamethasone.

According to a systematic review and meta-analysis of nine randomised controlled trials, adding dexamethasone to local anaesthetic for peripheral nerve blocks prolonged the duration of sensory block and analgesia, which is identical to that in the present study. They also stated that, shorter doses of dexamethasone (4-5 mg) were just as effective as higher doses of the medication and that the absolute effect was greater with long-acting local anaesthetics, as compared to intermediate-acting local anaesthetics (8-10 mg). They did not, however, analyse any studies that combined levobupivacaine and 4 mg of dexamethasone for interscalene brachial plexus block [13].

Sakae TM et al., showed that adding 4 mg of dexamethasone to 0.75% ropivacaine (20 mL) prolonged the duration of sensory and motor blockade, accelerated the onset of block, and decreased VAS, which is similar to the current study [14]. In addition, Chazapi A et al., added 4 mg of dexamethasone to 30 mL of 0.75% ropivacaine for use in below-the-elbow procedures under ultrasound guidance. They discovered that it lessened the intensity of the pain and extended the analgesic duration [15]. Another study found that, combining dexamethasone with local anaesthetic for brachial plexus block reduces postoperative pain, following arthroscopic rotator cuff repair [16-18].

Dexamethasone, rather than clonidine, epinephrine, or midazolam, currently appears to be the most effective way to prolong analgesia, as an adjuvant for brachial plexus nerve block. The study suggests that, nociceptive C-fiber transmission is specifically inhibited by dexamethasone, though it has not yet been fully explained. The prolongation of motor blockade, was similar in magnitude to that of sensory block during the present study [13]. Its vasoconstrictive effect and decreased ability to absorb local anaesthetics, may be the cause of the prolonged analgesia [19]. Dexamethasone has a high lipophilicity, which can increase its solubility in fat, make it easier to combine it with the nerve sheath, and shorten its duration of action [20].

Similar to the presend study, Tandoc MN et al., showed that dexamethasone prolongs the duration of postoperative analgesia and duration of motor blockade by adding different doses of dexamethasone (4 mg and 8 mg) to 0.5% bupivacaine (40 mL) for interscalene brachial plexus block. The onset of sensory and motor blockade did not differ significantly between the groups, though [21]. Another study of dexamethasone with different doses (4-10 mg) found that, dexamethasone delayed the onset of sensory and motor blockade and prolonged the duration of motor block [22]. When used for ultrasound-guided supraclavicular nerve block, the addition of low dose (4 mg) dexamethasone to 0.5% levobupivacaine (25 mL) prolongs postoperative analgesia, duration of sensory and motor blockade, and lower pain level, compared to levobupivacaine alone. Contrary to the present study, it had no impact on the onset of block, though [11].

Dexamethasone has a variety of systemic effects, including lowering postoperative pain, nausea, vomiting, and hyperglycaemia. Neither of the patient groups in the present study displayed any evidence of systemic effects. The choice of a low dose of dexamethasone in the current study may be one explanation. Williams BA et al., showed that ropivacaine and dexamethasone did not increase neurotoxicity at clinically relevant concentrations [23]. However, there is a long history of safe use of corticosteroids in the epidural space for the management of radicular pain brought on by irritation of the nerve roots [24]. Perineural dexamethasone additionally decreased the frequency of sleep disturbances [18]. Dexamethasone is a desirable option, as an adjuvant for the interscalene brachial plexus block due to the absence of side-effects. For both groups, the haemodynamic responses were stable.

Limitation(s)

The present study did not evaluate the long-term side-effects of dexamethasone. The serum level of levobupivacaine was not checked.

CONCLUSION(S)

The addition of dexamethasone at a dose of 4 mg, to levobupivacaine significantly lengthens effective postoperative analgesia in an ultrasound-guided interscalene brachial plexus block. Additionally, it hastens the onset time of sensory and motor blockade and prolongs its duration.

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