

Effect of Intravenous Dexamethasone on the Duration of Analgesia Provided by Supraclavicular Brachial Plexus Block for Upper Limb Surgery

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ABSTRACT

Background: Pain is associated with increased sympathetic activity leads to tachycardia, elevated blood pressure and myocardial insults so pain control is necessary during the surgery and in the postoperative period. Aim of the study was to study the effect of intravenous dexamethasone on the duration of analgesia provided by supraclavicular block (SCB) for upper limb surgery.

Methods: 75 patients, age between 18 to 70 years of either sex, ASA class I and II, who were undergoing upper limb surgery randomized into three groups of 25 patients each by computer generated random number. Group S - 25 patients were given 5ml of normal saline intravenously along with ultrasound-guided SCB with 25ml 0.5% bupivacaine. Group DF - 25 patients were given 4mg intravenous dexamethasone in 5ml normal saline along with ultrasound-guided SCB with 25ml 0.5% bupivacaine. Group DE - 25 patients were given 8mg intravenous dexamethasone in 5ml normal saline along with ultrasound-guided SCB with 25ml 0.5% bupivacaine.

Results: The demographic data were comparable in all groups. The VAS score was significantly lower in Group DF and DE compared to Group S at 3,4,6,8,10,12 and 24 hours, with p values < 0.0001 at 3,4,5,6,8,10 and 12 hours and p value 0.0002 at 24 hours. The VAS scores between the groups DF and DE were comparable at 3,4,5,6,8,10,12 and 24 hours without any significant difference. The time for first rescue analgesia was significantly in Group DF and DE compared to Group S (p value < 0.0001). There was no significant difference between the groups DF and DE in the time for first rescue analgesia (p value 0.75).

Conclusion: We conclude that dexamethasone used intravenously even in lower doses as 4mg along with supraclavicular brachial plexus block effectively increases the duration of analgesia and motor blockade, shortens the onset of sensory and motor blockade, reduces the total analgesic requirement in the first 24 hours after surgery.

General Pain has been defined by the International Association for the Study of Pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”[1]. Providing good pain relief during the surgery and in the postoperative period is one of the main components of anaesthesia. Pain

is associated with increased sympathetic activity during the postoperative period. This increased sympathetic activity leads to tachycardia, tachypnea, elevated blood pressure, delirium and even myocardial insults so effective postoperative pain control is necessary. Adequate pain relief also improves patient satisfaction and reduces morbidity. To provide this postoperative pain

The authors declare no conflicts of interest.

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relief, Non-Steroidal Anti-Inflammatory Drugs and opioids are being used along with infiltration of local anaesthetic agents at the surgical site.

Regional anaesthesia is a technique in which local anaesthetic drugs are being used to reduce sensations in a part of the body which is to be operated while the patients remain awake and breathe on their own. The advantages of this over general anaesthesia are there is no hemodynamic disturbance or stress response due to laryngoscopy and intubation, no need for mechanical ventilation, faster postoperative recovery, early mobility and faster discharge from hospitals. Due to these advantages, nowadays regional nerve blocks are being used as an effective technique to manage intraoperative and postoperative pain. For upper limb surgeries, the most commonly used technique of regional anaesthesia is the brachial plexus block. Supraclavicular brachial plexus block introduced by Kulenkampff D in 1911, is widely used for elbow, forearm and arm surgeries [2]. In this technique, the brachial plexus is approached from above the clavicle and a local anaesthetic agent is deposited around it. At this site, the structures are arranged compactly which results in the swift onset of a dense and reliable block of the brachial plexus. The procedure achieves blockade at the level of the distal trunk. Although single shot block gives immediate postoperative analgesia, postoperative pain can persist for several days which demands opioids and other analgesics like NSAIDs. Increased opioid usage can lead to respiratory depression apart from pruritus, nausea, vomiting, constipation and urinary retention. Renal dysfunction can occur with NSAIDs. Due to these adverse effects of NSAIDs and opioids, it will be useful to increase the duration of analgesia provided by supraclavicular block by the addition of some drugs so that polypharmacy can be avoided in the postoperative period or by the placement of indwelling catheters which allow prolonged infusion. An indwelling catheter can provide analgesia for several days but its usage is limited by the technical difficulty in placement and removal of catheter or infection.

Many adjuncts have been added to local anaesthetics to lengthen the blockade duration by inducing vasoconstriction or delaying diffusion of local anaesthetic from the injection site. An ideal adjunct of local anaesthetic should increase the duration of blockade with no/minimal adverse effects. Some of the additives used with local anaesthetics include adrenaline, clonidine, morphine, pethidine, tramadol, butorphanol, dexmedetomidine, ketamine, midazolam and glucocorticoids [3-12]. Steroids relieve pain by reducing inflammation and blocking pain transmission by C-fibers. So steroids can be given systemically or perineurally to increase the block efficacy.

Dexamethasone is a long-acting glucocorticoid that is being used in the treatment of neuropathic pain and

complex regional pain syndrome. Postoperative pain is shown to be reduced by dexamethasone even in the absence of any nerve bloc [13]. Many studies are being done to increase the analgesic duration of peripheral nerve blocks by adding dexamethasone to local anaesthetics [14-16]. Perineural dexamethasone is shown to prolong the analgesic duration in many studies. This is mediated by attenuation of the inflammatory mediators release, reduction of ectopic neural discharge and inhibition of potassium channel mediated discharge of nociceptive C-fibers. Using perineural dexamethasone has raised concerns of neural toxicity, but the evidence remains inconclusive [17]. Use of perineural dexamethasone is not approved by FDA, EU or any regulatory body as in vitro studies have demonstrated an increased peripheral neurotoxicity risk. Studies are being done to use intravenous dexamethasone instead of perineural dexamethasone as a method to increase analgesic duration [18-20]. We hypothesise that Intravenous dexamethasone alters the duration of analgesia provided by supraclavicular brachial plexus block for upper limb surgeries. Hence, we aim to study the effect of intravenous dexamethasone on the duration of analgesia provided by supraclavicular brachial plexus block for upper limb surgery.

Methods

This prospective Randomised Study was conducted after approval from institutional ethics committee and registration with clinical trial registry of India (CTRI/2021/03/031910) between 1st November 2019 to 31st March, 2021. 75 patients age between 18 to 70 years of either sex, ASA class I and II, BMI up to 30 kg/m². duration of surgery within 180 minutes, who were undergoing elective upper limb surgeries were included for the study. Patients with pre-existing neurological deficit, neuropathy involving surgical limb, any allergy to local anaesthetic drugs, pregnancy, Coagulopathy and bleeding disorder, Local site infection, were excluded.

The sample size calculation was based on a study of Mathew R et al in 2019 observed that the duration of analgesia in the group receiving intravenous (IV) dexamethasone was 858 ± 86.168 min [17]. Taking these values as a reference for sample size calculation using G power 3.1 software for three groups with an effect size of 0.5 (moderate effect size) at a confidence level of 95% and 80% power, the total sample size was calculated as 74, rounded off to 75 subjects. So, 25 subjects will be taken in each of the groups.

Written informed consent was taken from all the patients. After careful pre-anaesthetic examination and investigation, patients meeting the inclusion criteria were taken for the study. 75 patients were randomly divided into three groups of 25 patients each by computer generated random number. Group S - 25 patients were given 5ml of normal saline intravenously along with ultrasound-guided supraclavicular brachial plexus block

with 25ml 0.5% bupivacaine. Group DF - 25 patients were given 4mg intravenous dexamethasone in 5ml normal saline along with ultrasound-guided supraclavicular brachial plexus block with 25ml 0.5% bupivacaine. Group DE - 25 patients were given 8mg intravenous dexamethasone in 5ml normal saline along with ultrasound-guided supraclavicular brachial plexus block with 25ml 0.5% bupivacaine.

After a thorough preoperative evaluation, the enrolled patients have been explained about supraclavicular brachial plexus block on the day of the surgery in the preoperative area. After shifting the patient to the operating table standard monitoring in the form of ECG, heart rate, non-invasive BP, Pulse oximetry were attached. Baseline vitals were recorded. A wide bore intravenous cannula was secured and IV fluids infusion was started. Supplemental oxygen was administered at the rate of 6 litres per minute. The patient was sedated with intravenous midazolam 0.03 – 0.04 mg/kg and the neck was turned away from the side in which block was to be given. Skin preparation was done in and around the site with chlorhexidine based solution then draping was done.

With the patient in the supine position and head turned away from the side in which block was to be given, the linear probe of the ultrasound machine was positioned in a transverse plane superior to the clavicle approximately at its midpoint. Lateral and superficial to subclavian artery the brachial plexus was visualised as hypoechoic oval structures. Skin infiltration was done with 1ml of 2% lignocaine 1cm lateral to the transducer. Then block needle was introduced in-plane towards the brachial plexus from lateral to medial direction. When the tip of the needle reached the brachial plexus, aspiration was done to rule out placement in any blood vessel. Then 25ml of 0.5% bupivacaine was given along with 4mg intravenous dexamethasone in 5ml normal saline in group DF patients, 8mg intravenous dexamethasone in 5ml of normal saline in group DE patients and 5ml normal saline intravenously in group S patients. After giving the block, sensory blockade was assessed by pinprick method. Complete abolition of pinprick response was considered as the onset of sensory blockade. The onset of motor blockade was tested every minute with modified Bromage scale for upper extremities. The onset of motor block was taken as the time duration between the end of block administration and when Grade 2 is achieved in Modified Bromage scale. In the postoperative period, the pain was assessed using the Visual Analogue Scale (VAS) every hourly till VAS score >4. The duration of sensory blockade was taken as the time between the onset of sensory block to the first report of postoperative pain at the surgical site. Injection tramadol 1 mg/kg slow iv was used as a rescue analgesic when VAS >4. The patient was observed hourly after the surgery was over till the motor block got reversed and then at 24 hours. Duration of motor block was taken as the time between the onset of motor block to return of normal motor strength in the operative limb.

Primary objective of the study was to compare the duration of analgesia provided by 4mg and 8 mg intravenous dexamethasone along with 25ml of 0.5% bupivacaine and 25ml of 0.5% bupivacaine alone in supraclavicular brachial plexus block. Secondary objectives of the study were to find the time of onset of sensory blockade, to find the time of onset of motor blockade, to find the duration of motor blockade, to find out the postoperative analgesic requirements in the first 24 hours after surgery

In statistical analysis categorical variables were presented in number and percentage (%) and continuous variables were presented as mean \pm SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected, then a non-parametric test was used. Quantitative variables were compared using ANOVA/Kruskal Wallis Test (when the data sets were not normally distributed) between the three groups and Unpaired t-test/Mann-Whitney Test (when the data sets were not normally distributed) was used for comparison between the two groups. Qualitative variables were compared using Chi-Square test /Fisher's exact test. p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results

All the 3 groups were comparable in age distribution. There is no significant difference between the groups (p value= 0.523). Distribution of gender was comparable between all three groups without any statistically significant difference (p value = 0.662). No significant difference was seen in height(cm) (p value=0.222), weight (kg) (p value= 0.501) and BMI (kg/m²) (p value=0.996) between the groups S, DF and DE. Mean \pm SD of height (cm), weight(kg), BMI (kg/m²) in group S was 167.68 \pm 6.77, 62.72 \pm 9.09, 22.23 \pm 2.31 respectively, in group DF was 164.72 \pm 7.47, 60.48 \pm 8.87, 22.21 \pm 2.22 respectively and in group DE was 164.52 \pm 7.16, 60.12 \pm 7.24, 22.18 \pm 1.92 respectively with no significant difference between them. Duration of surgery was comparable in all three groups without any significant difference (p value = 0.589) (Table 1).

The time for onset of sensory blockade and motor blockade were significantly lower in Group DF and DE compared to Group S (p value <0.0001). Mean \pm SD of time for onset of sensory blockade in group S was 13.44 \pm 1.12 minutes, in group DF was 11.2 \pm 2.14 and in group DE was 10.68 \pm 2.1 minutes. There was no significant difference in the time for onset of sensory blockade (p value =0.332) between the groups DF and DE. Mean \pm SD of time for onset of motor blockade in group S was 17.72 \pm 1.37 minutes, in group DF was 15.36 \pm 2.14 and in group DE was 14.76 \pm 2.42 minutes. There was no significant difference in the time for onset of motor blockade (p value =0.441) between the groups DF and DE (Table 2).

The VAS score was significantly lower in Group DF and DE compared to Group S at 3,4,6,8,10,12 and 24 hours with p values < 0.0001 at 3,4,5,6,8,10 and 12 hours and p value 0.0002 at 24 hours. The VAS scores between the groups DF and DE were comparable at 3,4,5,6,8,10,12 and 24 hours without any significant difference (Table 3).

The modified Bromage scale grade was significantly higher in Group DF and DE compared to Group S at 3,4,6,8 and 10 hours with p values < 0.0001 at 3,4,6,8, and 10 hours. The modified Bromage scale grade was comparable in all three groups at 12 hours and 24 hours with p values of 0.315 and 1 respectively. The modified Bromage scale grade between the groups DF and DE were comparable at 6,8,10,12 and 24 hours without any significant difference (Table 4).

The time for first rescue analgesia was significantly in Group DF and DE compared to Group S (p value <0.0001). Mean \pm SD of time for first rescue analgesia in group S was 384 \pm 36.29 minutes, in group DF was

889.24 \pm 67.50 and in group DE was 946 \pm 352.68 minutes. There was no significant difference between the groups DF and DE in the time for first rescue analgesia (p value 0.75). The total drug used for rescue analgesia was significantly lower in Group DF and DE compared to Group S (p value <0.0001). Mean \pm SD of total drug used for rescue analgesia in group S was 123.2 \pm 17.96 mg tramadol, in group DF was 57.6 \pm 7.79 mg tramadol and in group DE was 57.4 \pm 7.79 mg tramadol. There was no significant difference between the groups DF and DE in the total drug used for rescue analgesia (p value 0.952). The duration of motor blockade was significantly higher in Group DF and DE compared to Group S (p value <0.0001). Mean \pm SD of duration of motor blockade in group S was 274.2 \pm 28.82 minutes, in group DF was 653.2 \pm 49.26 and in group DE was 685.4 \pm 235.69 minutes. There was no significant difference between the groups DF and DE in the duration of motor blockade (p value 0.861) (Table 5).

Table 1- Comparison of demographic characteristics between group S, DF and DE.

Demographic characteristics	S (n=25)	DF (n=25)	DE (n=25)	P value
Age(years) (Mean \pm SD)	33.56 \pm 10.56	31.08 \pm 11.33	30.04 \pm 8.69	0.523§
Weight(kg) (Mean \pm SD)	62.72 \pm 9.09	60.48 \pm 8.87	60.12 \pm 7.24	0.501‡
Height(cm) (Mean \pm SD)	167.68 \pm 6.77	164.72 \pm 7.47	164.52 \pm 7.16	0.222‡
Body mass index(kg/m ²) (Mean \pm SD)	22.23 \pm 2.31	22.21 \pm 2.22	22.18 \pm 1.92	0.996‡
Duration of surgery(minutes) (Mean \pm SD)	129.64 \pm 30.78	138.6 \pm 28.28	128.52 \pm 33.96	0.589§

§ Kruskal Wallis test, ‡ ANOVA

Table 2- Comparison of time for onset of sensory blockade and motor blockade (minutes) between group S, DF and DE.

Blockade (minutes)	S (n=25)	DF (n=25)	DE (n=25)	P value
Sensory (Mean \pm SD)	13.44 \pm 1.12	11.2 \pm 2.14	10.68 \pm 2.1	<.0001§
Motor (Mean \pm SD)	17.72 \pm 1.37	15.36 \pm 2.14	14.76 \pm 2.42	<.0001§

§ Kruskal Wallis test

Table 3- Comparison of VAS score between group S, DF and DE.

VAS score	S(n=25)	DF(n=25)	DE(n=25)	P value
At baseline (Mean \pm SD)	5.56 \pm 1.19	4.04 \pm 2.44	4.16 \pm 1.97	0.016§
At 3 hours (Mean \pm SD)	0.4 \pm 0.5	0 \pm 0	0 \pm 0	<.0001§
At 4 hours (Mean \pm SD)	1.16 \pm 0.75	0 \pm 0	0 \pm 0	<.0001§
At 5 hours (Mean \pm SD)	2.16 \pm 0.75	0 \pm 0	0 \pm 0	<.0001§
At 6 hours (Mean \pm SD)	3.08 \pm 0.81	0 \pm 0	0 \pm 0	<.0001§
At 8 hours (Mean \pm SD)	2.92 \pm 1.47	0.08 \pm 0.28	0.12 \pm 0.33	<.0001§
At 10 hours (Mean \pm SD)	1.36 \pm 0.49	0.44 \pm 0.51	0.52 \pm 0.59	<.0001§
At 12 hours (Mean \pm SD)	2.4 \pm 0.5	1.64 \pm 0.49	1.48 \pm 0.65	<.0001§
At 24 hours (Mean \pm SD)	3 \pm 0.5	2.56 \pm 0.51	2.32 \pm 0.56	0.0002§

§ Kruskal Wallis test

Table 4- Comparison of modified Bromage scale between group S, DF and DE.

Modified Bromage scale	S (n=25)	DF (n=25)	DE (n=25)	P value
At baseline				
Grade 0	25 (100%)	25 (100%)	25 (100%)	No p value
Immediate post-operative				
Grade 2	25 (100%)	25 (100%)	25 (100%)	No p value
At 1 hour				
Grade 2	25 (100%)	25 (100%)	25 (100%)	No p value
At 2 hours				

Grade 1	4 (16%)	0 (0%)	0 (0%)	0.051*
Grade 2	21 (84%)	25 (100%)	25 (100%)	
At 3 hours				
Grade 1	18 (72%)	0 (0%)	0 (0%)	<.0001†
Grade 2	7 (28%)	25 (100%)	25 (100%)	
At 4 hours				
Grade 0	4 (16%)	0 (0%)	0 (0%)	<.0001*
Grade 1	21 (84%)	0 (0%)	0 (0%)	
Grade 2	0 (0%)	25 (100%)	25 (100%)	
At 5 hours				
Grade 0	18 (72%)	0 (0%)	0 (0%)	<.0001*
Grade 1	7 (28%)	0 (0%)	0 (0%)	
Grade 2	0 (0%)	25 (100%)	25 (100%)	
At 6 hours				
Grade 0	25 (100%)	1 (4%)	0 (0%)	<.0001*
Grade 1	0 (0%)	4 (16%)	2 (8%)	
Grade 2	0 (0%)	20 (80%)	23 (92%)	
At 8 hours				
Grade 0	25 (100%)	0 (0%)	0 (0%)	<.0001*
Grade 1	0 (0%)	19 (76%)	21 (84%)	
Grade 2	0 (0%)	6 (24%)	4 (16%)	
At 10 hours				
Grade 0	25 (100%)	4 (16%)	5 (20%)	<.0001*
Grade 1	0 (0%)	21 (84%)	19 (76%)	
Grade 2	0 (0%)	0 (0%)	1 (4%)	
At 12 hours				
Grade 0	25 (100%)	24 (96%)	22 (88%)	0.315*
Grade 1	0 (0%)	1 (4%)	2 (8%)	
Grade 2	0 (0%)	0 (0%)	1 (4%)	
At 24 hours				
Grade 0	25 (100%)	25 (100%)	24 (96%)	1*
Grade 1	0 (0%)	0 (0%)	1 (4%)	

* Fisher's exact test, † Chi square test

Table 5- Comparison of time for first rescue analgesia, total drug used for rescue analgesia and duration of motor blockade (minutes) between group S, DF and DE.

	S (n=25)	DF (n=25)	DE (n=25)	P value
Time for first rescue analgesia(minutes)(Mean ± SD)	384 ± 36.29	889.24 ± 67.50	946 ± 352.68	<.0001§
Total drug used for rescue analgesia(Tramadol) (Mean ± SD)	123.2 ± 17.96	57.6 ± 7.79	57.4 ± 7.79	<.0001§
Duration of motor blockade(minutes)(Mean ± SD)	274.2 ± 28.82	653.2 ± 49.26	685.4 ± 235.69	<.0001§

§ Kruskal Wallis test

Discussion

Postoperative pain causes discomfort and limits early mobilization thereby leading to increased morbidity. Numerous drugs are being used to manage postoperative pain but usage of those drugs are associated with their respective side effects and the analgesic intensity produced by them varies between patients.

The time for onset of sensory blockade was significantly lower in Group DF and DE compared to Group S (p value <0.0001). The study done by Parveen et al which showed that the mean time to sensory onset was earlier in those who received intravenous dexamethasone along with 0.5% ropivacaine in

supraclavicular block than in those who didn't receive dexamethasone but it was not statistically significant [19].

The time for onset of motor blockade was significantly lower in Group DF and DE compared to Group S (p value <0.0001). The study done by Parveen et al which showed that the mean time for motor onset was earlier in those who received intravenous dexamethasone along with 0.5% ropivacaine in supraclavicular block than in those who didn't receive dexamethasone but it was not statistically significant [19].

The VAS score was significantly lower in Group DF and DE compared to Group S at 3,4,6,8,10,12 and 24 hours with p values < 0.0001 at 3,4,5,6,8,10 and 12 hours

and p value 0.0002 at 24 hours. The VAS scores between the groups DF and DE were comparable at 3,4,5,6,8,10,12 and 24 hours without any significant difference. The study by Parveen et al which showed that the pain scores were less in those who received intravenous dexamethasone along with 0.5% ropivacaine in supraclavicular block than in those who didn't receive dexamethasone [19]. This result was similar to the study by Abdallah et al which showed 8mg of intravenous dexamethasone reduced the pain scores in the postoperative period [18].

The time for first rescue analgesia was significantly in Group DF and DE compared to Group S (p value <0.0001). When the mean time for first rescue analgesia was compared in group DF and DE there is a mean difference of 56.76 minutes with a p value of 0.75. It indicates that there is no significant difference in the duration of analgesia between groups that received 4mg dexamethasone intravenously and 8mg dexamethasone intravenously. This result is similar to the study by Parveen et al which showed that the duration of analgesia was prolonged in those who received intravenous dexamethasone along with 0.5% ropivacaine in supraclavicular block than in those who didn't receive dexamethasone [19].

The total drug used for rescue analgesia was significantly lower in Group DF and DE compared to Group S (p value <0.0001). When the mean total drug used for rescue analgesia was compared in group DF and DE there is a mean difference of 0.2mg with a p value of 0.952. It indicates that there is no significant difference in the total rescue analgesic requirement between groups that received 4mg dexamethasone intravenously and 8mg dexamethasone intravenously.

The modified Bromage scale grade was significantly higher in Group DF and DE compared to Group S at 3,4,6,8 and 10 hours with p values < 0.0001 at 3,4,6,8 and 10 hours. The modified Bromage scale grade between the groups DF and DE were comparable at 6,8,10,12 and 24 hours without any significant difference. This shows that the modified Bromage scale is significantly higher till 12 hours in patients who received intravenous dexamethasone along with the block than in those who received intravenous saline along with the block.

The duration of motor blockade was significantly higher in Group DF and DE compared to Group S (p value <0.0001). When the mean duration of motor blockade was compared in group DF and DE there is a mean difference of 32.2 minutes with a p value of 0.861. It indicates that there is no significant difference in the duration of motor blockade between groups that received 4mg dexamethasone intravenously and 8mg dexamethasone intravenously. This result is similar to the study by Parveen et al which showed that the duration of motor blockade was prolonged in those who received intravenous dexamethasone along with 0.5% ropivacaine

in supraclavicular block than in those who didn't receive dexamethasone [19].

There are some limitations to our study. It includes relatively smaller sample size and single institutional study.

Conclusion

We conclude that dexamethasone used intravenously even in lower doses as 4mg along with supraclavicular brachial plexus block effectively increases the duration of analgesia and motor blockade, shortens the onset of sensory and motor blockade, reduces the total analgesic requirement in the first 24 hours after surgery.

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