

Comparative Study between the Effect of Perineural versus Intravascular Dexmedetomidine in Ultrasound-Guided Supraclavicular Brachial Plexus Block

Abstract

Background: Augmentation of postoperative analgesia with various adjuvants has become a standard in regional anesthesia. There are no studies about dexmedetomidine multiple approaches in supraclavicular brachial plexus block (BPB) was contrasted. We compare perineural dexmedetomidine and intravenous dexmedetomidine Bupivacaine as adjuvant in supraclavicular brachial plexus block.

Materials and Methods: This prospective randomized controlled double-blind study was conducted on 120 patients with age between 20 and 60 years, both sexes, scheduled for elective upper limb surgery. Patients were randomly allocated into 3 groups, 40 patients in each received plain bupivacaine 0.5% (20ml) in supraclavicular BPB; group I (Control group): add 1mL normal saline perineural, group II: Bupivacaine with perineural dexmedetomidine (BDP) add 1 $\mu\text{g.kg}^{-1}$ dexmedetomidine perineurally. group III: Bupivacaine with intravenous dexmedetomidine (BDV) add 0.5 $\mu\text{g.kg}^{-1}$ dexmedetomidine in 50 mL of normal saline administered as infusion over 10 min. Onset and duration of sensory and motor blocks, hemodynamic variables, adverse effects, and duration of analgesia were assessed.

Results: Heart rate and mean arterial pressure was significantly decrease in group III & group II compared to group I were compared by ANOVA (F) test. onset of sensory & motor block was statistically significant shorter in group II compared to group I & III. Duration of sensory & motor block was statistically significant longer in group II compared to group I & III. there was statistically significant decrease VAS in group II were analysed using Kruskal-Wallis test between three groups. There was statistically significant increase RSS in group II & III. The first time of analgesic request was statistically significant prolonged in duration in group II.

Conclusion: Perineural dexmedetomidine (1 µg/ kg) as an adjuvant to bupivacaine is significantly high than IV dexmedetomidine (0.5 µg/ kg) and bupivacaine alone in supraclavicular BPB as regards to the onset and the duration of sensory block, so Increasing postoperative analgesia.

Keywords: Dexmedetomidine, bupivacaine, Perineural, supraclavicular plexus block, Intravascular.

Introduction:

Ultrasound(US) guidance for Brachial plexus block(BPB) may raise success and complication rates ^[1] particularly for the supraclavicular approach due to the risk of pneumothorax ^[2].

BPB has evolved as an important tool in the regimen of the anesthesiologist as a safer option for upper limb surgery and peri - operative pain control to general anesthesia. Its continued growth is due to improvements in regional anesthesia approaches in LA drugs, new adjuvant drugs, and US usage for safe and effective block actions. It significantly minimizes hospitalization^[3].

Several LA additives such as morphine, clonidine, neostigmine and tramadol, etc., are often used to maximize block length, enhance postoperative pain relief, and reduce the need for regular LA medication infusion through catheter.^[3]

Dexmedetomidine is a recent addition to the alpha-2 agonist class that has many favorable impacts when used with supraclavicular BPB perineural injection. It increases LA 's effects without **increasing** side effects ^[4]. α_2 -Adrenergic receptor (AR) agonists **has** sedative, analgesic, perioperative, anesthetic and hemodynamic-stabilizing effects. ^[5].

Analgesic effects of α_2 dexmedetomidine agonists in peripheral nerves, including regional vasoconstriction, by intravascular systemic effects ^[6] so α_2 -adrenoceptor agonists as dexmedetomidine improve LA action ^[7, 24].

The aim of the research is to analyze the impact on the onset and length of sensory, motor and postoperative analgesia of perineural dexmedetomidine versus intravascular dexmedetomidine in US, supraclavicular BPB.

Subjects and Methods:

This prospective randomized controlled double-blind research was carried out on one hundred and twenty subjects with age between 20 and 60 years, both sexes, planned for elective upper limb surgery admitted to General Surgery and orthopedic department from November 2017 to November 2019.

Exclusion criteria were: Patient refusal, Infection at insertion site, coagulation disorders, Peripheral neuropathy and allergy to LA.

For each patient, medical and surgical history was evaluated, and clinical examination was performed. Routine laboratory investigations as CBC, prothrombin time and activity and liver and renal function tests.

An intravenous (IV) line was established with 18G cannula. Monitoring of heart rate (HR) with five leads ECG, blood pressure with **Non-Invasive Blood Pressure (NIBP)** and peripheral oxygen saturation (SpO₂) with pulse oximetry. Crystalloid fluid was administered.

Patient was made to lay supine with pillow under the shoulder to make the subclavian artery more prominent with the head turned to the opposite direction with the ipsilateral arm adducted. The skin was disinfected by povidone iodine 10% with a linear probe (6- 12 MHz) was placed firmly over the supraclavicular fossa above the midpoint of the clavicle. The needle for infiltration of LA was advanced along the long axis of the probe in the same plane as the US beam. The needle was advanced from lateral to medial in the long axis of the US beam with constant visualization.

Patients were allocated randomly into three groups, 40 subjects in each. Randomization was by sealed envelope technique. Group I: Control group (C): received plain bupivacaine

0.5% (20ml) + 1 mL normal saline in supraclavicular block. Group II: Bupivacaine with perineural dexmedetomidine (BDP) received 20 mL of 0.5% bupivacaine plus 1 µg.kg-1

dexmedetomidine perineurally. Group III: Bupivacaine with intravenous dexmedetomidine (BDV) received 20 mL of 0.5% bupivacaine plus 0.5 µg.kg⁻¹ dexmedetomidine in 50 mL of normal saline administered as infusion over 10 min and given 10 min before start of the supraclavicular block.

Patients were evaluated the following measurements: HR and mean arterial pressure (MAP): Recorded before the block and at 15, 30 min, 1, 2, 4, 6, 12 hrs. after injection. Onset and duration of sensory and motor block, Postoperative pain assessed at 1, 2, 4, 6, 12hr. after operation using **Visual Analogue Scale (VAS)**, Sedation score assessed By Ramsay sedation scale was assessed during the operative time, Time of 1st analgesia request and adverse effects were assessed.

Statistical analysis:

Statistical analysis was analyzed by SPSS v20 (IBM[®], Chicago, IL, USA). Quantitative data were presented as mean and standard deviation (SD) and were compared by ANOVA (F) test. Non- parametric variables (e.g. VAS) were demonstrated as median and interquartile range (IQR) and were analyzed using Kruskal-Wallis test between three groups. Qualitative data were conveyed as number and percent and were compared by the Chi-square (X²) test when appropriate. A P value <0.05 was **considered** statistically significant.

Results

As regard demographic data (age, weight and duration of surgery) among study group was comparable. [Figure (1)] **[Table (1)]**

As regards HR, there was significantly decrease in group III p value <0.01 **with mean ±SD (63.7±4.6 ,55.9±4.42,61.7±5.64,67.3±4.71)respectively** &group II p value <0.01 **with mean ±SD (64.1.5±6.25,59.7±5.37,62.9±4.18,65.6±3.39)respectively** compared to group I at 15, 30min, 1, 2 hr. **with mean ±SD (76.5±5.6,75.5±7.2,75±8.54,76.9±7.75)respectively** and significantly increase in group III p value <0.01 **with mean ±SD (85.7±6.65,86.25±4.50,86.03±5.9)respectively**

and group I p value <0.01 with mean \pm SD (85.53 \pm 6.72,85.30 \pm 4.66,85.23 \pm 5.27)respectively compared to group II with mean \pm SD (81.48 \pm 3.6,81.18 \pm 3.57,81.48 \pm 4.44)respectively at 4,6,12 hr. [Figure (2)]

As regards MAP, there was significantly decrease in group II p value <0.01 with mean \pm SD (70.7 \pm 4.40,71.8 \pm 3.51,72.9 \pm 3.40,74.2 \pm 3.85)respectively & group III p value <0.01 with mean \pm SD (69.6 \pm 4.07,72.6 \pm 5.00,73.8 \pm 4.81,73.9 \pm 4.65)respectively compared to group I with mean \pm SD (81.9 \pm 3.45,83.4 \pm 2.16,84.7 \pm 3.33,86.9 \pm 3.75)respectively at 15, 30min, 1, 2 hr. and significantly increase in group III with mean \pm SD (88.33 \pm 4.89,88.98 \pm 3.70,87.98 \pm 4.80)respectively p value <0.01 and group I with mean \pm SD (88.83 \pm 4.38,88.25 \pm 3.2,89.75 \pm 4.03)respectively p value <0.01 compared to group II with mean \pm SD (82.5 \pm 3.46,83.35 \pm 3.99,84.93 \pm 3.20)respectively at 4,6,12 hr. [Table (2)]

According the onset of sensory & motor block was statistically significant earlier in group II p value <0.01 with mean \pm SD(11.4 \pm 1.56, 14.67 \pm 1.17 respectively)compared to group I mean \pm SD (20.01 \pm 1.67, 22.3 \pm 1.61 respectively)& III mean \pm SD (19.8 \pm 2.44, 22.27 \pm 1.58 respectively) . As regard the duration of sensory & motor block was statistically significant longer in group II p value <0.01 with mean \pm SD (687.12 \pm 33.78, 692.75 \pm 35.93) respectively compared to group I mean \pm SD (214.25 \pm 28.11, 205 \pm 20.18respectively) & III. mean \pm SD (222.25 \pm 29.97, 209.125 \pm 13.64respectively) [Figure (3)]

There was significant lower VAS in group II compared to group I & group III at 2, 4, 6,12hr. with p value <0.01 [Table (3)]

There was statistically significant increase RSS in group II & III compared to group I. with p value <0.01 [Table (4)]

The first time of analgesic request was statistically significant prolonged in duration in group II with p value <0.01 mean \pm SD (751.75 \pm 50.16 min) compared to group III, mean \pm SD (232.125 \pm 30.06 min); & group I. mean \pm SD (240.75 \pm 22.29 min) [Figure (4)]

Regarding adverse events among comparable groups was comparable as in group II showed hypotension in one patient and bradycardia in one patient while in group III there was hypotension in 3 patients and bradycardia in 4 patients. There was no significant difference among the three groups regarding adverse events with p-value > 0.05. [Table (5)]

Discussion

Dexmedetomidine is a new addition to the class of alpha-2 agonist which has got numerous beneficial effects when used through perineural injection with supraclavicular BPB. It enhances the effects of LA without increasing the incidence of side effects. Usage of US intraoperatively is becoming more common and much easier. The use in these blocks improves the performance rate and reduces the complications. Regional BPB approaches gained popularity in integrative pain control for surgical and therapeutic reasons. [8]. Adjuvants are medications for peripheral nerve blocks (PNBs) applied to the LA to improve the onset and increase the duration of analgesia. [9] Dexmedetomidine is an α_2 adrenoceptor agonist highly special and selective, with α_2 : α_1 selectivity binding ratio [10, 23]

As regards to hemodynamic changes HR & MAP was significantly decrease in MAP when decreased more than 20% from the base line or MAP less than 65 while bradycardia occurs when HR less than 50 bpm between group II and III comparison compared to group I at 15, 30min, 1, 2 hr. and significantly increase in group I & group III compared to group II at 4,6,12 hr.

Our results in agreement with, Schnabel et al (2018) [11], evaluated the combination of perineural dexmedetomidine to LA compared with LA sole or LA with systemic administration of dexmedetomidine, they showed intraoperative decrease in HR &MAP in systemic and perineural dexmedetomidine groups more than controlled group. Also, Dai et al (2018) [12], showed decreased changes in the heart rate and mean blood pressure. Moreover,

Jung et al (2018) ^[13], showed decrease in HR &MAP in perineural dexmedetomidine groups. Additionally, similar finding was reported by Vorobeichik et al (2017) ^[14], found that dexmedetomidine increase incidence of bradycardia and hypotension. Moreover, Agarwal et al (2014) ^[15], showed that HR &BP in dexmedetomidine group were significantly decrease than in control group.

In controversy to this study, He et al (2018) ^[16], showed no significant changes in HR and MAP. **However, the difference between this study and our study that they had lower sample size (30 patients) and lower perineural dose 50 µg as they used in their study.**

Our results showed that the onset of sensory and motor block was statistically significant earlier in group II in comparison with group III & I.

Our results in agreement with, Dai et al (2018) ^[12], showed shorten onset for both sensory and motor blocks and increased duration of sensory and motor blocks in dexmedetomidine groups. Also, Chinnappa et al(2017) ^[17], found that Perineural dexmedetomidine prolong postoperative analgesia, hastens the onset of sensory and motor block. In addition, Vorobeichik et al (2017) ^[14], found that dexmedetomidine shorten onset for both sensory and motor blocks with increased duration of sensory and motor blocks in perineural group. Also, Singh et al (2016) ^[18], found that dexmedetomidine decrease onset time for sensory and motor block significantly and increase duration of sensory and motor blocks.

In controversy to this study, He W-s et al (2018) ^[16]. Consider that sensory and motor block starting times between the 2 groups were not significantly different. Also, Abdallah et al (2016) ^[19], found both perineural and intravenous dexmedetomidine can effectively increase BPB analgesic duration and no prolongation of motor block duration. Additionally, Gandhi et al(2012) ^[20], showed that onset of both motor and sensory block in control group is

earlier than in dexmedetomidine group. However, the difference between this study and our study that they had blind technique as they used in groups. But in agreement with our results, the duration of sensory and motor block was longer in dexmedetomidine group.

As regards to Visual analogue scale (VAS) our result showed that the VAS was statistically significant lower with perineural dexmedetomidine in group II compared with group I&III after 4 hr. from the block. And no statistically significant between group I&III.

Our results In agreement with, He W-s et al(2018)^[16], demonstrated that VAS decreased in dexmedetomidine group. In addition, Jung et al(2018)^[13], demonstrated that numeric pain rating scale (NRS) was significantly increased in control group.

As regards to sedation score (RSS) our results showed that the RSS was statistically significant high in group II&III in compare with group I and no statistically significant between group II&III.

In agreement with the present study, Agarwal et al (2014)^[15], they showed that patients received perineural dexmedetomidine were adequately sedated.

In controversy to this study, Jung et al (2018)^[13], found that sedation score between the study groups was comparable. Also, Kang et al (2018)^[21], demonstrated that the sedation score between groups were comparable.

As regards to duration of analgesia, our results showed that duration of analgesia was statistically significant increase in group II in compare with group I&III and no statistically significance between group I & III.

Our results In agreement with, He W-s et al (2018)^[16], concluded duration of analgesia was increased in group dexmedetomidine as compared with control group. Moreover, Vorobeichik et al (2017)^[14], demonstrated that dexmedetomidine prolong analgesic duration. Dexmedetomidine also reduced postoperative oral morphine consumption. Also, Kang et al (2018)^[21], demonstrated that IV dexmedetomidine at a dose of

2.0 µg/kg significantly expand the duration of BPB analgesia. In addition, Schnabel et al (2018) ^[11], showed that the duration of analgesia associated with systemic or perineural dexmedetomidine was comparable.

In addition, Swami et al (2012)^[22], concluded that dexmedetomidine when added to local anesthetic in supraclavicular BPB prolong the duration of analgesia.

In agreement with the present study , Vorobeichik et al (2017)^[14] , demonstrated no adverse effects in comparison between groups.

Conclusion

Perineural dexmedetomidine (1 µg/ kg) as an adjuvant to bupivacaine is better than IV dexmedetomidine (0.5 µg/ kg) and bupivacaine alone in supraclavicular BPB due to longer duration of sensory block, so improving postoperative analgesia.

Ethic and consent:

Approval taken from Tanta Faculty of Medicine Ethics Committee (number 31288/12/16) and a written informed consent obtained from every participant in this research.

References

1. Biradar PA, Kaimar P, Gopalakrishna K (2013): Effect of dexamethasone added to lidocaine in supraclavicular brachial plexus block: A prospective, randomised, double-blind study. *Indian J Anaesth* 57: 180.
2. Honnannavar KA, Mudakanagoudar MS (2017): Comparison between Conventional and Ultrasound-Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries. *Anesthesia, essays and researches* 11: 467-71.
3. Rutkowska K, Knapik P, Misiolok H (2009): The effect of dexmedetomidine sedation on brachial plexus block in patients with end-stage renal disease. *Eur J Anaesthesiol* 26: 851-5.
4. Mantz J, Josserand J, Hamada S (2011): Dexmedetomidine: new insights. *Eur J Anaesthesiol* 28: 3-6.
5. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R (2013): A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. *J Anaesthesiol Clin Pharmacol* 29: 496.
6. Weerink MAS, Struys M, Hannivoort LN, Barends CRM, Absalom AR, Colin P (2017): Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine. *Clin Pharmacokinet* 56: 893-913.
7. Emelife PI, Eng MR, Menard BL, Myers AS, Cornett EM, Urman RD, et al. (2018): Adjunct medications for peripheral and neuraxial anesthesia. *Best practice & research Clinical anaesthesiology* 32: 83-99.
8. Gamo K, Kuriyama K, Higuchi H, Uesugi A, Nakase T, Hamada M, et al. (2014): Ultrasound-guided supraclavicular brachial plexus block in upper limb surgery: outcomes and patient satisfaction. *Bone Joint J* 96-b: 795-9.

9. Albrecht E, Vorobeichik L, Jacot-Guillarmod A, Fournier N, Abdallah FW (2019): Dexamethasone Is Superior to Dexmedetomidine as a Perineural Adjunct for Supraclavicular Brachial Plexus Block: Systematic Review and Indirect Meta-analysis. *Anesthesia and analgesia* 128: 543-54.
10. Helal SM, Eskandr AM, Gaballah KM, Gaarour IS (2016): Effects of perineural administration of dexmedetomidine in combination with bupivacaine in a femoral-sciatic nerve block. *Saudi journal of anaesthesia* 10: 18-24.
11. Schnabel A, Reichl SU, Weibel S, Kranke P, Zahn PK, Pogatzki-Zahn EM, et al. (2018): Efficacy and safety of dexmedetomidine in peripheral nerve blocks: A meta-analysis and trial sequential analysis. *European Journal of Anaesthesiology* 35: 745-58.
12. Dai W, Tang M, He K (2018): The effect and safety of dexmedetomidine added to ropivacaine in brachial plexus block: A meta-analysis of randomized controlled trials. *Medicine* 97: 125-73.
13. Jung HS, Seo KH, Kang JH, Jeong J-Y, Kim Y-S, Han N-R (2018): Optimal dose of perineural dexmedetomidine for interscalene brachial plexus block to control postoperative pain in patients undergoing arthroscopic shoulder surgery: A prospective, double-blind, randomized controlled study. *Medicine* 97 561-6.
14. Vorobeichik L, Brull R, Abdallah F (2017): Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and meta-analysis of randomized controlled trials. *British journal of anaesthesia* 118: 167-81.
15. Agarwal S, Aggarwal R, Gupta P (2014): Dexmedetomidine prolongs the effect of bupivacaine in supraclavicular brachial plexus block. *J Anaesthesiol Clin Pharmacol* 30: 36.

16. He W-s, Liu Z, Wu Z-y, Sun H-j, Yang X-c, Wang X-l (2018): The effect of dexmedetomidine in coracoid approach brachial plexus block under dual stimulation *Medicine* 97: 122-40.
17. Chinnappa J, Shivanna S, Pujari VS, Anandaswamy TC (2017): Efficacy of dexmedetomidine with ropivacaine in supraclavicular brachial plexus block for upper limb surgeries. *J Anaesthesiol Clin Pharmacol* 33: 81-5.
18. Singh AP, Mahindra M, Gupta R, Bajwa SJ (2016): Dexmedetomidine as an adjuvant to levobupivacaine in supraclavicular brachial plexus block: A novel anesthetic approach. *Anesthesia, essays and researches* 10: 414-9.
19. Abdallah FW, Dwyer T, Chan VW, Niazi AU, Ogilvie-Harris DJ, Oldfield S, et al. (2016): IV and Perineural Dexmedetomidine Similarly Prolong the Duration of Analgesia after Interscalene Brachial Plexus Block: A Randomized, Three-arm, Triple-masked, Placebo-controlled Trial. *Anesthesiology* 124: 683-95.
20. Gandhi R, Shah A, Patel I (2012): Use of dexmedetomidine along with bupivacaine for brachial plexus block. *National Journal of Medical Research* 2: 67-9.
21. Kang R, Jeong JS, Yoo JC, Lee JH, Choi SJ, Gwak MS, et al. (2018): Effective dose of intravenous dexmedetomidine to prolong the analgesic duration of interscalene brachial plexus block: A single-center, prospective, double-blind, randomized controlled trial. *Reg Anesth Pain Med* 43: 488-95.
22. Swami SS, Keniya VM, Ladi SD, Rao R (2012): Comparison of dexmedetomidine and clonidine (α_2 agonist drugs) as an adjuvant to local anaesthesia in supraclavicular brachial plexus block: A randomised double-blind prospective study. *Indian J Anaesth* 56: 243.
23. Dharmarao, P. S., & Holyachi, R. (2018). Comparative study of the efficacy of dexmedetomidine and fentanyl as adjuvants to ropivacaine in ultrasound-guided supraclavicular brachial plexus block. *Turkish Journal of Anaesthesiology and Reanimation*, 46(3), 208.

Palsule, V. S., Shah, A. P., & Kanzariya, H. H. (2017). Dexmedetomidine in supraclavicular block: Effects on quality of block and analgesia. *Indian Journal of Pain*, 31(1), 28.

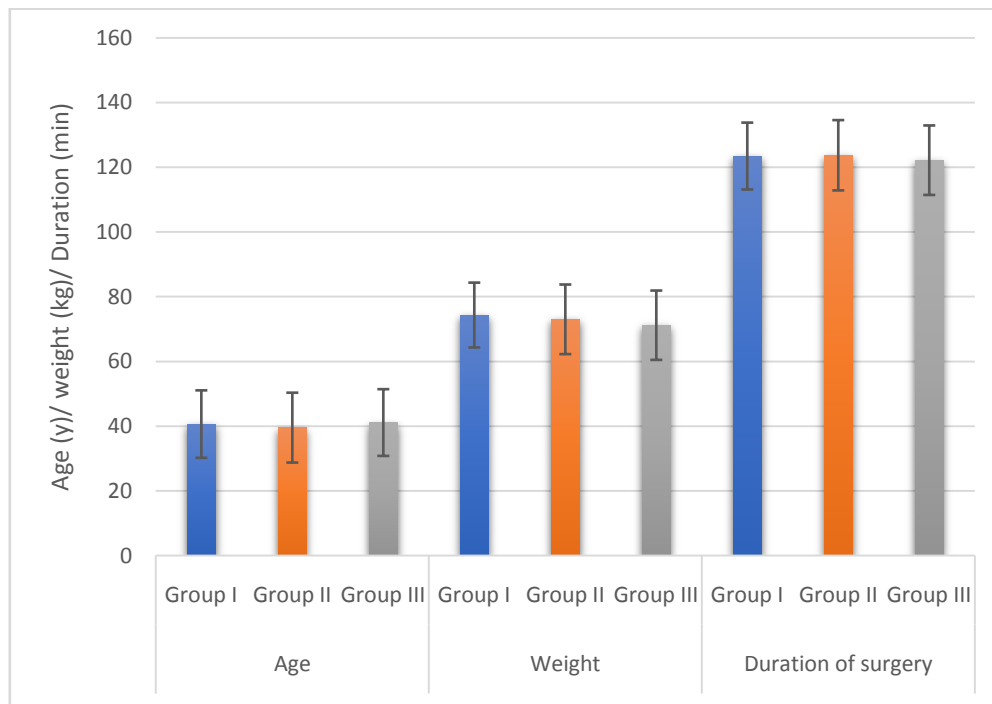


Figure (1): Age (y), weight (Kg) and duration of surgery (min) of the studied patients

Table (1): Demographic data of the studied patients

Variable		Group I N = 40	Group II N = 40	Group III N = 40	P value
Age (y)	Mean ± SD	40.6 ± 10.42	39.6 ± 10.79	41.2 ± 10.31	0.079
	Range	21-59	20-57	23-58	
Weight (Kg)	Mean ± SD	74.4 ± 10.01	73.1 ± 10.75	71.2 ± 10.71	0.416
	Range	55-93	53-92	52-90	
Duration of surgery (min)	Mean ± SD	123.5 ± 10.34	123.8 ± 10.85	122.2 ± 10.74	0.795
	Range	100-150	105-155	100-145	

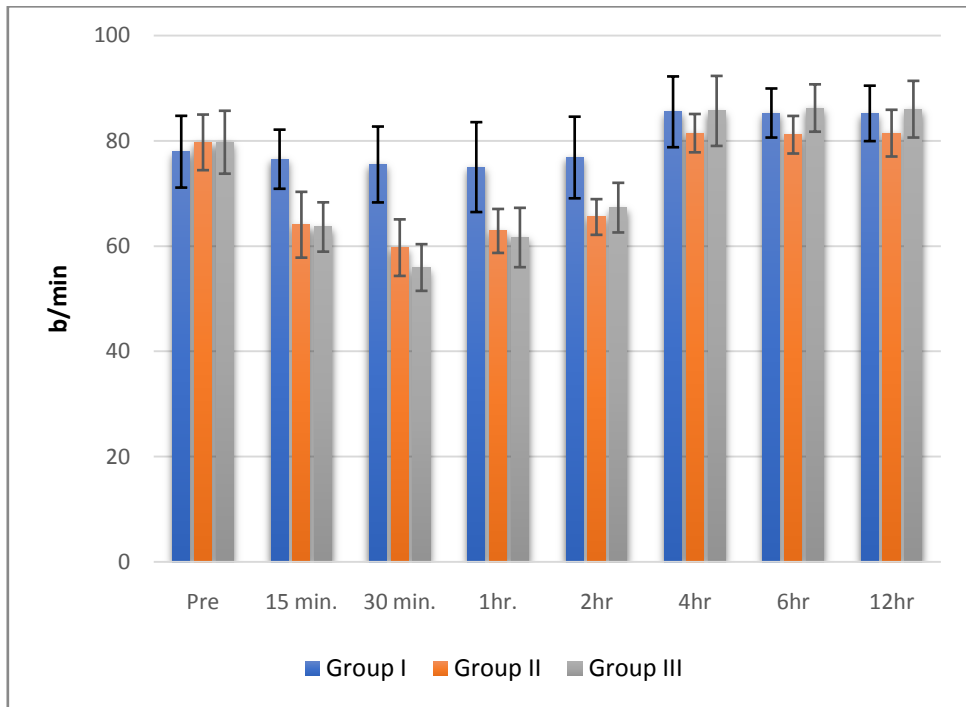


Figure (2): Heart rate (HR) changes (b/min) among the three groups

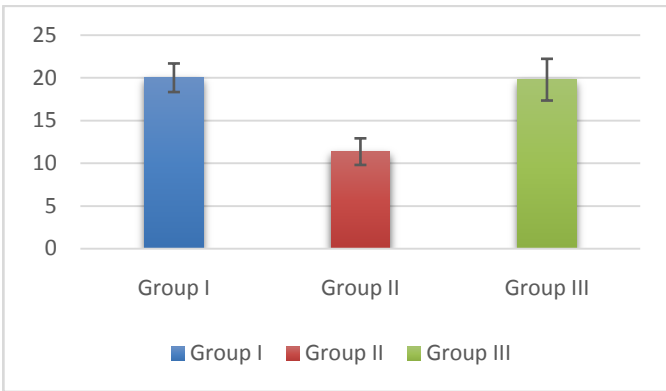
UNDER PEER REVIEW

Table (2): Comparison of Mean arterial pressure (MAP) changes (mmHg) among the three groups.

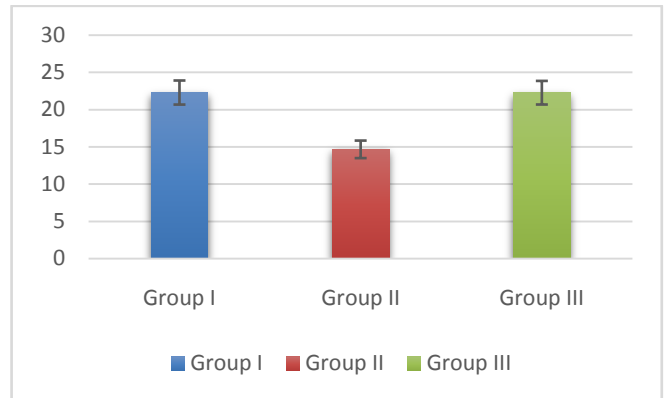
		Pre	15 min	30 min	1 hr.	2 hr.	4 hr.	6 hr.	12 hr.
Group I	Mean	85.3	81.9	83.4	84.7	86.2	88.83	88.25	89.75
	SD	6.74	3.45	2.16	3.33	3.15	4.38	3.18	4.03
Group II	Mean	84.4	70.7	71.8	72.9	74.2	82.90	83.35	84.93
	SD	4.74	4.40	3.51	3.40	3.85	3.46	3.99	3.20
Group III	Mean	84.9	69.6	72.6	73.8	73.9	88.33	88.98	87.98
	SD	6.55	4.07	5.00	4.81	4.65	4.89	3.70	4.80
P value		0.826	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
P1		0.538	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
P2		0.730	<0.01*	<0.01*	<0.01*	0.003*	0.607	0.381	0.056
P3		0.786	0.187	0.378	0.311	0.716	<0.01*	<0.01*	<0.01*

P value: p value for comparing between three group, p₁: p value for comparing between group I and group II, p₂: p value for comparing between group I and group III, p₃: p value for comparing between group II and group III, * statistically significant (p<0.05).

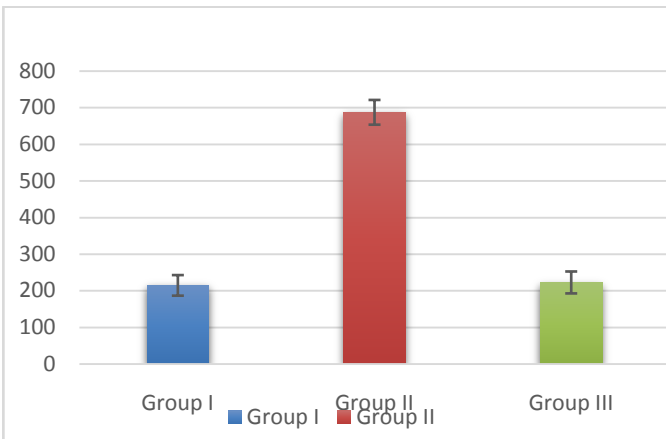
UNDER PEER REVIEW



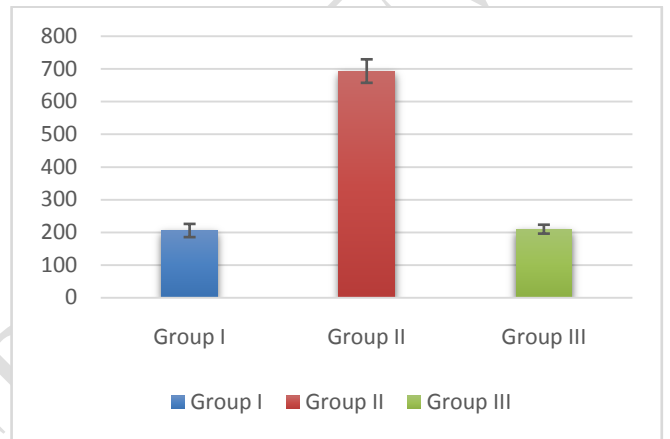
A- Comparison of onset of sensory block(min) among groups



B-Comparison of onset of motor block(min) among groups.



C-Comparison of duration of sensory block(min) among groups.



D-Comparison of duration of motor block (Min) among groups.

Figure (3): Comparison of duration and onset of sensory and motor block in minutes among the three groups.

Table (3): Comparison of visual analogue scale (VAS) among the three groups

		1 h	2 h	4 h	6 h	12 h
Group I	Median	1	2	3	4	4
	IQR	0-1	2-3	3-4	3-5	3-5
Group II	Median	0	1	1	1	2
	IQR	0-1	0-1	0-1	1-2	1-2
Group III	Median	1	2	3	4	4
	IQR	0-1	2-3	3-4	3-5	3-5
P value		0.265	<0.01*	<0.01*	<0.01*	<0.01*
P1		0.472	<0.01*	<0.01*	<0.01*	<0.01*
P2		0.106	0.291	0.296	0.057	0.101
P3		0.364	<0.01*	<0.01*	<0.01*	<0.01*

P value: p value for comparing between three group, p_1 : p value for comparing between group I and group II, p_2 : p value for comparing between group I and group III, p_3 : p value for comparing between group II and group III, * statistically significant ($p < 0.05$), IQR: interquartile range.

Table (4): Comparison of sedation score (RSS) among the three groups

		T0	T1	T2	T3	T4	T5	T6
Group I	Median	1	1	1	1	1	1	1
	IQR	1-1	1-1	1-1	1-1	1-1	1-2	1-2
Group II	Median	1	2	2.5	3	2	2	1
	IQR	1-1	2-3	2-3	2-3	2-3	2-2	1-2
Group III	Median	1	2.5	3	3	2	2	1
	IQR	1-1	2-3	2-3	2-3	2-3	1-2	1-2
P value		1.000	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	0.593
P1		1.000	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	0.308
P2		1.000	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	0.559
P3		1.000	0.280	0.176	0.266	0.981	0.369	0.646

P value: p value for comparing between three group, p₁: p value for comparing between group I and group II, p₂: p value for comparing between group I and group III, p₃: p value for comparing between group II and group III, * statistically significant (p<0.05), T0 = baseline time at start of injection, T1 = time after 15 min, T2 = time after 30 min, T3 = time after 45 min, T4 = time after 60 min, T5 = time after 90 min, T6 = time by end of surgery, IQR: interquartile range.

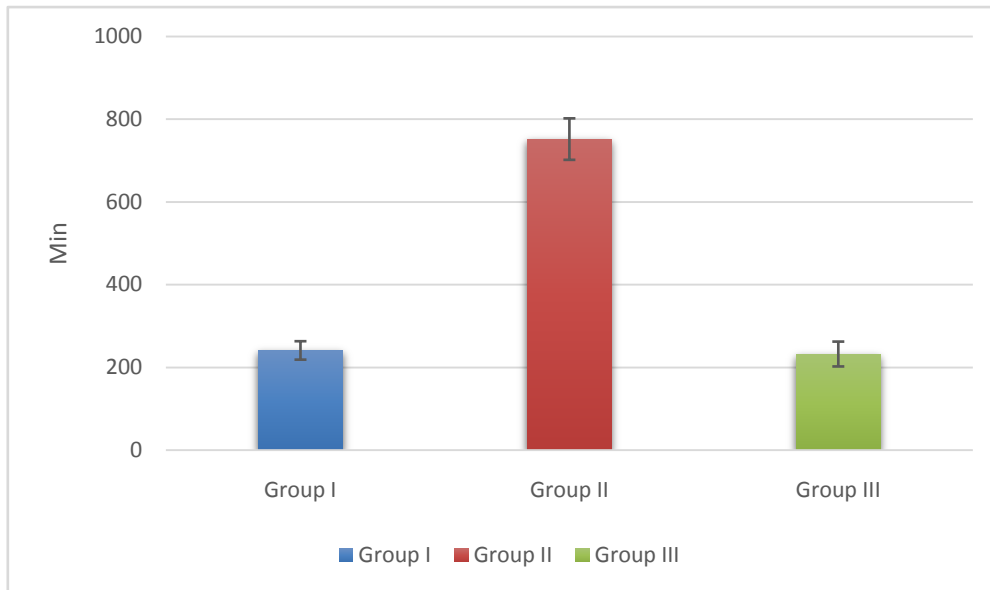


Figure (4): Comparison of time for first request of analgesia among the three groups

UNDER PEER REVIEW

Table (5): adverse events among the three groups.

	Group I	Group II	Group III	Chi-square	P value
Horner's syndrome	0	0	0	—	—
Chest discomfort	0	0	0	—	—
Pneumothorax	0	0	0	—	—
Hypotension	0	1 (3%)	3 (8%)	3.621	0.164
Bradycardia	0	1 (3%)	4 (10%)	5.426	0.066

UNDER PEER REVIEW