

ORIGINAL ARTICLE

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A comparative study between the effect of verapamil versus nalbuphine as an adjuvant in supraclavicular brachial plexus block

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Abstract

Background: Brachial plexus block has substituted general anesthesia in the majority of patients planned for upper limb surgeries as it avoids the undesired effects of the medications used in general anesthesia as well as the stress response associated with airway manipulation. Opioid agonist–antagonists such as nalbuphine are used as adjuvant to improve the anesthetic properties of bupivacaine. Verapamil has an additive effect in brachial plexus blockade in the form of decreasing the consumption of analgesics in the postoperative period with reducing onset time and extending the duration of motor and sensory blockade. The aim of this study is to investigate the adjuvant effect of verapamil versus nalbuphine to 0.5% bupivacaine in brachial plexus block as regards onset, duration of sensory and motor blockade and postoperative analgesic augmentation. The study is randomized, prospective, double-blinded, comparative study where 90 patients subjected to arm, forearm and hand surgeries were randomized into three groups, group A received 30 ml of plain bupivacaine 0.5% plus 2 ml of normal saline, group B received 30 ml of bupivacaine 0.5% plus 2 ml verapamil equivalent to 5 mg, group C received 30 ml of bupivacaine 0.5% plus 10 mg of nalbuphine diluted in 2 ml of normal saline.

Results: Results of this study showed that group C and group B sensory block time onset was 7.25 ± 1.5 vs. 10.92 ± 3.84 min, $P < 0.001$ and was shorter than that in group A (13.2 ± 2.66 min). In addition, the motor block onset was (11.10 ± 1.24 vs. 13.50 ± 3.77 min, $P < 0.001$) shorter than group A (17.16 ± 1.30 min). In group C and group B, sensory block duration was 396 ± 32.17 vs. 355.83 ± 18.48 min, $P < 0.001$, respectively and was longer than that in group A (321.13 ± 25.08 min). Also, there was prolonged motor block duration in group C and group B recording (338.92 ± 25.2 vs. 302.93 ± 15.24 min, $P < 0.001$) and was longer than that in group A (280.70 ± 32.35 min). Time of demand of rescue analgesia dose was significantly long in group C and group B (449.53 ± 52.45 vs. 418.13 ± 41.12 min, $P < 0.001$) and was longer than group A (361.31 ± 21.42 min). Both verapamil and nalbuphine have additive effect to bupivacaine improving the all anesthetic parameters of the block.

Conclusion: Both drugs produce favorable enhancement of time onset and effective prolongation of duration of sensory and motor blockade and extend the period of postoperative analgesia with superiority to nalbuphine over verapamil.

Keywords: Brachial plexus block, Nalbuphine, Verapamil, Upper limb surgeries

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Background

Brachial plexus block is considered favorable anesthetic technique for achieving ideal circumstances for surgical interventions of upper limb as it induces full muscle relaxation, maintains stable hemodynamic parameters, and provides a good coverage of postoperative analgesia with minimal side effects (Baloda et al. 2016).

The anesthesiologist's goal is always to improve the local anesthetics efficiency through augmenting the block length and reducing the occurrence of complications of local anesthetic such as systemic toxicity. Several drugs had been successfully added for example, opioid agonists including fentanyl, morphine, tramadol, Alfa2-agonists such as clonidine and dexmedetomidine, and calcium channel blockers such as Verapamil (Sarma et al. 2015).

Nalbuphine is structurally related to 14-hydroxymorphine opioid. Nalbuphine has an agonistic effect at kappa opioid receptors and an antagonistic effect at mu opioid receptors. Its analgesic strength is same as morphine on milligram basis. Nalbuphine is considered safer than pure agonist opioid as it has ceiling effect on respiration such that increasing the dose above 30 mg does not produce further depression of respiratory drive. Nalbuphine has the ability to sustain or even boost the analgesic efficacy of μ -opioid receptor while alleviating its side effects (Gupta et al. 2016).

Verapamil is a non-dihydropyridine calcium channel blocker which can potentiate analgesic action of local anesthetics, prolongs postoperative analgesia, and decreases analgesic consumption. Calcium has a fundamental role in pain signals formation and processing. The stimulation of NMDA receptor results in calcium entry into cells and potentiation of spinal cord and plays a role in pain processing. Hence, central sensitization can be prevented by voltage-gated calcium channel blockers and provide better sensory motor block characteristics (Routray et al. 2017).

Methods

The study is randomized, prospective, double-blinded, comparative study conducted from December 2018 to November 2019. Following the approval of the departmental ethical committee and written informed consent of the patients, 90 patients aged between 18 and 60 years of age, American Society of Anesthesiologists (ASA) physical status I and II underwent upper limb surgeries. Patients were allocated by computer generated randomized number into three equal groups of 30 each and received one of the following:

- Group A: patients received 30 ml of plain bupivacaine 0.5% plus 2 ml of normal saline.
- Group B: patients received 30 ml of bupivacaine 0.5% plus 2 ml verapamil equivalent to 5 mg.

- Group C: patients received 30 ml of bupivacaine 0.5% plus 10 mg of nalbuphine diluted in 2 ml of normal saline.

Exclusion criteria included patients having abnormal coagulation profile, skin infection at the injection site, allergy to bupivacaine and other drugs involved in the study, polytrauma patients having pneumothorax or any contraindication to perform the procedure, inability to visualize the brachial plexus with ultrasound guidance or failure of block, and patients taking medications for psychiatric illness.

Study interventions

- All patients were admitted after fasting for 6 h. On arrival in the operation theatre, intravenous access was established and lactated Ringer solution was infused and patient received .05 mg per kg midazolam intravenously as sedation. Standard monitoring equipment were attached (non-invasive blood pressure monitor, electrocardiogram (ECG), and pulse oximetry) and vital data were recorded.
- The block was accomplished by the most experienced doctor. The block was performed using a portable ultrasound system with linear high-frequency transducer (HFL-38) to get the sonographic anatomy of brachial plexus in the transverse and longitudinal planes.
- Under aseptic conditions, the ultrasound probe was situated parallel to the clavicle in the supraclavicular area to show the plexus as a "bunch of grapes" or as having a "honeycomb" appearance. The block was done with a short beveled echogenic needle 5 cm, 22 G for optimal control and visibility. The predetermined volume of 32 ml was injected around the brachial plexus after negative aspiration to avoid inadvertent intravascular injection. Distension of brachial plexus sheath was regarded as an indication of successful block. A massage for 5 min was applied to aid an equal volume distribution.
- The sensory block onset was evaluated by pinprick method using a 3-point scale for pain (0 for no pain, 1 for blunt pain, 2 for sharp pain) and contrasted to equivalent stimulus on opposite arm. The sensory block onset was the time between the end of the local anesthetic (LA) injection to first disappearance of pinprick sensation in any dermatome (C5-T1), and duration of analgesia in the postoperative period was the time interval from end of LA administration till the patient request for the rescue analgesia.
- Motor block was assessed by adduction of the thumb (ulnar nerve), or abduction of the thumb (radial nerve), opposition of thumb (median nerve),

and elbow flexion (musculocutaneous nerve) using modified Bromage scale. Grade 1: patient can perform elbow flexion and fingers movement but unable to raise the extended arm. Grade 2: patient cannot perform elbow flexion but can move the fingers. Grade 3: complete motor paralysis. The interval between the injection and grade 3 weakness was considered as the onset of the motor block. Duration of motor block was recorded from beginning of motor block to full recovery of muscle power and was confirmed by asking the patients to determine the time when they were able to first move the fingers of the anesthetized arm.

- Patients were examined for onset of sensory and motor blockade at 2 min interval till complete loss of sensation and complete paralysis which was achieved at the point of grade 3 weakness and 0 point for pain.
- Intraoperative vital data of heart rate, blood pressure, oxygen saturation and respiratory rate, were checked every 5 min till 30 min and every 10 min until the end of the procedure.
- All patients were observed for complications either associated with the technique, e.g., pneumothorax or related to drugs used in the study for example hypotension, bradycardia, oxygen desaturation, nausea, vomiting, pruritus, pain, or any other adverse effect.
- Pain in the postoperative phase was assessed via visual analogue scale (VAS) from 0 to 10 cm in which 0 signified that the patient had no pain and 10 cm signified that the patient was in maximal pain at 1 h interval till demand of rescue analgesia (VAS \geq 3). Injection of tramadol 100 mg with Ondansetron 4 mg will be given intravenously as rescue analgesic.

Statistical analysis

Data were collected, revised, coded, and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations, and ranges when parametric. Also qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using chi-square test and/or Fisher's exact test when the expected count in any cell found less than 5. The comparison between more than two groups regarding quantitative data and parametric distribution was done by using one-way ANOVA test followed by post hoc analysis using Tukey's test. Level of significance: > 0.05 non-significant, < 0.05* significant, < 0.001** high significant.

Sample size

Using PASS program, setting alpha error at 5% and power at 90% results from previous study Routray et al.

(2017) showed that the mean duration of motor block was 280.7 min and 306.9 for bupivacaine and Verapamil respectively while for nalbuphine 10 mg was 418.4 (Gupta et al. 2016)) based on this, total 90 cases divided to three groups, each group contained 30 patients. The effect size was calculated 0.795.

Results

Demographic data

No statistically significant difference exists between the three groups as regards demographic data as age, gender, ASA, and weight (P value > 0.05) (Table 1).

Onset of sensory and motor block

Onset time of sensory and motor block was assessed and statistically compared in all patients. Results showed that group C had the fastest onset then group B then group A. Regarding motor block onset it was obvious that group C, the nalbuphine group had the fastest onset of both sensory and motor block. A highly significant statistical difference (P < 0.001) existed between the three groups (Table 2).

Duration of sensory and motor blockade

Group C had the longest duration of sensory, then came the group B which was shorter than group C but longer than group A. Concerning motor blockade, group C had the longest duration of motor block and was longer than both verapamil group B and plain bupivacaine group A significant statistical difference (P < 0.001) existed between the three groups (Table 3).

Time for a request for rescue analgesia

Patients were assessed for the severity of postoperative pain at 1 h interval till demand of rescue analgesia (VAS \geq 3). Group C was found to have the longest duration of post-operative pain relief then group B then group A. A significant statistical difference (P < 0.001) existed between the three groups (Table 4).

Discussion

The current study revealed that nalbuphine in group (C) allows sensory and motor components of the block to obtain the fastest onset and longest duration. Verapamil in group (B) was less potent than nalbuphine but it had positive influence on the whole block characters as it initiated faster onset and sustained longer duration of motor and sensory block than the plain bupivacaine group (A). As regards the time for rescue analgesia, nalbuphine was able to maintain the longest post-operative analgesia. Verapamil could also prolong the extent of analgesia but to a lesser degree than nalbuphine.

Verapamil is a non-dihydropyridine L type calcium channel blocker. It is synthetically derived from

Table 1 Comparison between groups A, B, and C as regards demographic data

		Group A No = 30	Group B No = 30	Group C No = 30	P value	Sig.
Gender	Male	19 (63.3%)	22 (73.3%)	20 (66.7%)	0.700	NS
	Female	11(36.7%)	8 (26.7%)	10 (33.3%)		
Age (years)	Mean ± SD	38.70 ± 13.28	39.77 ± 11.81	36.90 ± 11.98	0.664	NS
Weight (kg)	Mean ± SD	76.67 ± 16.22	73.4 ± 14.06	74.67 ± 9.98	0.648	NS
ASA	I	28 (93.3%)	26 (86.7%)	27(90.0%)	0.690	NS
	II	2 (6.7%)	4 (13.3%)	3(10.0%)		

Results are presented as number (%) or mean ± SD. P value > 0.05 non-significant

papaverine. It has the ability to inhibit the fast sodium channels similar to local anesthetics, as a result when verapamil is added to local anesthetics; it can produce potent analgesic effect as well as prolonged sensory and motor blocks in comparison to the unaided use of local anesthetic (Tabaeizavareh et al. 2012).

There are studies showing results compatible with or favoring the result of the current study. For example, Gerges in 2016 performed study that Compared the adjuvant effect of dexmedetomidine versus verapamil when combined with lidocaine in intravenous regional anesthesia (IVRG) in orthopedic surgery of upper limb and the results showed that Verapamil as an adjuvant was as potent as dexmedetomidine in improving the quality of anesthesia in intravenous regional anesthesia (Gerges 2016).

Lalla and his colleagues in 2010 performed a study which concluded that addition Verapamil to local

anesthetic could prolong the sensory blockade duration in brachial plexus block. In contrast to the results of this current study, verapamil had no significant effect on the onset of both sensory and motor block. This discrepancy in the result of the two studies may be due to the difference in the dose of verapamil used, we added 5 mg of verapamil on the other side Lalla and his colleges added only 2.5 mg (Lalla et al. 2010).

A study conducted by Routray and his colleagues in 2017 showed results supporting the outcomes of the present study, that adding 5 mg of verapamil to levobupivacaine in brachial plexus block produced faster onset of sensory and motor block and augmented the duration of both sensory and motor block (Routray et al. 2017).

In another study conducted by Choe and his colleagues in 1998 found that verapamil and bupivacaine in the form of epidural application caused less postoperative analgesic consumption (Choe et al. 1998).

Table 2 Comparison between the three groups as regards onset of sensory and motor block

Onset of sensory block (min)		ANOVA	
Groups (n = 30)	Mean ± SD	F	P value
Group A (n = 30)	13.37 ± 2.53	60.199	< 0.001**
Group B (n = 30)	11.23 ± 2.46		
Group C (n = 30)	7.30 ± 1.32		
Tukey's test			
GA and GB	GA and GC	GB and GC	
< 0.001**	< 0.001**	< 0.001**	
Onset of motor block		ANOVA	
Groups	Mean ± SD	F	P value
Group A (n = 30)	17.33 ± 1.54	69.124	< 0.001**
Group B (n = 30)	13.30 ± 2.78		
Group C(n = 30)	11.37 ± 1.4		
Tukey's test			
GA and GB	GA and GC	GB and GC	
< 0.001**	< 0.001**	< 0.001**	

Results are presented as number (mean ± SD). Table 2 shows statistically significant difference between the three groups regarding the onset of sensory and motor block (P value < 0.001**)

Table 3 Comparison between the three groups as regards duration of sensory and motor blockade

Duration of sensory block		ANOVA	
Groups	Mean ± SD	F	P value
Group A (n = 30)	321.17 ± 18.86	137.430	< 0.001**
Group B (n= 30)	354.60 ± 13.03		
Group C (n = 30)	396.20 ± 19.99		
Tukey's test			
GA and GB	GA and GC	GB and GC	
< 0.001**	< 0.001**	< 0.001**	
Duration of motor block		ANOVA	
Groups	Mean ± SD	F	P value
Group A (n = 30)	300.60 ± 10.26	60.926	< 0.001**
Group B (n = 30)	318.83 ± 7.00		
Group C (n = 30)	338.9 ± 19.69		
Tukey's test			
GA and GB	GA and GC	GB and GC	
< 0.001**	< 0.001**	< 0.001**	

Results are presented as number (mean ± SD). Table 3 shows a statistically significant difference between the three groups regarding the duration of sensory and motor block (P value was < 0.001**)

Table 4 Comparison between the three groups as regards time for request for rescue analgesia (post-operative analgesic duration)

Rescue analgesia		ANOVA	
Groups	Mean \pm SD	F	P value
Group A (n = 30)	361.07 \pm 12.66	120.883	< 0.001**
Group B (n = 30)	395.23 \pm 8.98		
Group C (n = 30)	448.23 \pm 34.57		
Tukey's test			
GA and GB	GA and GC	GB and GC	
< 0.001**	< 0.001**	< 0.001**	

Results are presented as number (mean \pm SD). Table 4 shows a statistically significant difference between the three groups regarding the time for request for rescue analgesia (P value was < 0.001**)

Reuben and Reuben in 2000 performed a study which investigated the additive effect of verapamil to lidocaine in brachial plexus and their results were incompatible with the results of this current study because they showed that verapamil had no effect on 24-h analgesic consumption. The absence of additive analgesic influence may be due to lower dose of Verapamil used 2.5 mg (Reuben and Reuben 2000).

Another case report conducted by Moyano, and Garcia in 2012 regarding the effect of adding verapamil to morphine infusion in severe cancer pain showed that combining low dose verapamil with morphine was able to minimize the dose of opioid, starting at lower dose 2.5 mg verapamil IV every 12 h reaching maximum dose 5 mg IV every 6 h with monitoring of hemodynamics (Moyano and Garcia 2012).

Changing the intravenous route mentioned in this case report and administration of verapamil by subcutaneous route as an additive to subcutaneous lignocaine has no effect on prolonging the duration of anesthesia as stated by Laurito and his colleagues in 1994. (Laurito et al. 1994).

Opioids and their derivatives have been widely used to potentiate local anesthetics in regional anesthesia. In spite of their obvious potentiating effect on the characteristics of the block as shortening the onset time of anesthesia and prolongation of analgesia, opioids have several annoying side effects such as vomiting, sedation, histamine release, and respiratory depression that limit their use. Nalbuphine with mixed μ antagonist and k agonist activity has a potent analgesic activity with less pronounced side effects; so it has been used as an additive to local anesthetic via different routes.

In the current study, the combining of nalbuphine with 0.5% bupivacaine improved the whole block characteristics as well as post-operative analgesia. Nalbuphine had potentiating effect on the nerve block onset. This result comes in agreement with the result of a study performed by Nazir and Jain in 2017 in which 10 mg

nalbuphine of were added to 30 ml bupivacaine 0.375% in brachial plexus block and results showed that nalbuphine accelerated the onset of sensory and motor block significantly (Nazir and Jain 2017).

In harmony with the current study, Bakri and his colleagues, in 2016, tested the impact of nalbuphine when added to lidocaine in hand surgeries performed by IVRG and found that nalbuphine shortened the onset time and prolonged the duration for both sensory and motor blocks with no adverse effects (Bakri et al. 2016).

Augmentation of duration of both motor and sensory was evident in this current study and was supported by other studies for example, a study performed by Das and his colleges in 2017 who tested the addition of 10 mg of nalbuphine to 30 ml of 0.25% levobupivacain in the block of brachial plexus and found considerable prolongation of the duration of sensory and motor blockades, and reduction of the analgesics demand in the postoperative phase. But nalbuphine did not show any positive influence on the onset time of sensory and motor blockades (Das et al. 2017).

Also, Gupta and his colleges in 2016 added 10 mg nalbuphine to 20 ml of 0.5% bupivacaine and found that nalbuphine had no impact on the onset time of block but enhanced the sensory and motor block duration and postoperative analgesia (Gupta et al. 2016).

In contrast to the current study, in the previous two studies, there was inability to demonstrate any significant effect of nalbuphine on the onset of sensory and motor blockade; this can be explained by lower concentration of local anesthetic used in the former and lower volume of local anesthetic in the latter.

Nalbuphine was added to local anesthetics via routes other than perineural, and the additive effect was evident. For example, Kumaresan and his colleges in 2017 performed a study showed that 0.6 mg nalbuphine was effective adjuvant in spinal anesthesia as it delayed the request for analgesics postoperatively (Kumaresan et al. 2017).

Similar results were found in a study performed by Mohamed and his colleges in 2015 found that nalbuphine added to bupivacaine in caudal anesthesia provided longer postoperative analgesia and sedation without respiratory depression (Mohamed et al. 2015).

Conclusion

From the previous data, we concluded that both verapamil and nalbuphine possessed an additive effect to 0.5% bupivacaine in supraclavicular brachial plexus block, but when comparing the two drugs, we deduced that nalbuphine had the upper hand in shortening the onset time of sensory and motor blockade and in prolongation of duration of both sensory and motor blockade as well as in providing longer post-operative analgesia and the difference was statistically significant.

Abbreviations

ASA: American Society of Anesthesiologists; cAMP: Cyclic adenosine monophosphate; IVRG: Intravenous regional anesthesia; LA: Local anesthetics; NS: Non-significant; PACU: Post-anesthesia care unit; SD: Standard deviation; Sig.: Significance; VAS: Visual analog score; VGCC: Voltage-gated calcium channels

Acknowledgements

Not applicable.

Authors' contributions

MI designed the study, revised literature, performed the analysis, followed the patients, measured the onset and duration of sensory and motor block, and time for rescue analgesia, and wrote the manuscript. AS designed the study, performed the analysis, wrote, and critically revised the manuscript. HM revised literature, performed the analysis, and critically reviewed the manuscript. HS and MM revised literature, followed the patients, collected the data, performed the analysis, and critically reviewed the manuscript. All authors read and approved the final version of the manuscript.

Funding

None.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations**Ethics approval and consent to participate**

Approval of research ethical committee of Faculty of Medicine, Ain-Shams University, was obtained (code number: FMASU M D 322/2018) and written informed consent was obtained from patients after description of the procedure and its potential complications.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 26 November 2020 Accepted: 15 March 2021

Published online: 25 March 2021

References

- Bakri MH, Ismail EA, Abd-Elshafy SK (2016) Analgesic effect of nalbuphine when added to intravenous regional anesthesia: a randomized control trial. *Pain Physician* 19(8):575–581
- Baloda R, BhuPAI JPS, Kum ARP, Gandhi GS (2016) Supraclavicular brachial plexus block with or without dexamethasone as an adjuvant to 0.5% levobupivacaine: a comparative study. *J Clin Diagn Res* 10(6):UC09
- Choe H, Kim JS, Ko SH, Kim DC, Han YJ, Song HS (1998) Epidural verapamil reduces analgesic consumption after lower abdominal surgery. *Anesth Analg* 86(4):786–790. <https://doi.org/10.1213/0000539-199804000-00020>
- Das A, RoyBasunia S, Mukherjee A, Biswas H, Biswas R, Mitra T, Mandal SK (2017) Perineural Nalbuphine in ambulatory upper limb surgery: a comparison of effects of levobupivacaine with and without nalbuphine as adjuvant in supraclavicular brachial plexus block—A prospective, double-blinded, randomized controlled study. *Anesth Essays Res* 11(1):40
- Gerges M (2016) Comparison between dexmedetomidine and Verapamil as an adjuvant to local anesthesia in intravenous regional anesthesia in upper limb orthopedic surgery: a randomized double-blind prospective study. *Ain-Shams J Anaesthesiol* 9(4):576. <https://doi.org/10.4103/1687-7934.198261>
- Gupta K, Jain M, Gupta PK, Rastogi B, Pandey MN (2016) Nalbuphine as an adjuvant to 0.5% bupivacaine for ultrasound-guided supraclavicular brachial plexus blockade. *Ind J Pain* 30(3):176
- Kumaresan S, Raj A, Muruga A (2017) Intrathecal nalbuphine as an adjuvant to spinal anaesthesia: what is most optimum dose? *Int J Sci Study* 5(1):57–60
- Lalla RK, Anant S, Nanda HS (2010) Verapamil as an adjunct to local anaesthetic for brachial plexus blocks. *Med J Armed Forces India* 66(1):22–24. [https://doi.org/10.1016/S0377-1237\(10\)80086-3](https://doi.org/10.1016/S0377-1237(10)80086-3)

- Laurito CE, Cohn SJ, Becker GL (1994) Effects of subcutaneous Verapamil on the duration of local anesthetic blockade. *J Clin Anesth* 6(5):414–418. [https://doi.org/10.1016/S0952-8180\(05\)80014-5](https://doi.org/10.1016/S0952-8180(05)80014-5)
- Mohamed MF, Husein RM, El Sonbati MI, Khattab SM (2015) A comparative study of caudal epidural bupivacaine and bupivacaine plus nalbuphine in postoperative analgesia in children. *Ain-Shams J Anaesthesiol* 8(4), 628–629
- Moyano J, Garcia MT (2012) Hydromorphone and verapamil infusion in severe cancer pain. *J Case Rep* 2(2):86–88
- Nazir N, Jain S (2017) Randomized controlled trial for evaluating the analgesic effect of Nalbuphine as an adjuvant to bupivacaine in supraclavicular block under ultrasound guidance. *Anesth Essays Res* 11(2):326
- Reuben SS, Reuben JP (2000) Brachial plexus anesthesia with verapamil and/or morphine. *Anesth Analg* 91(2):379–383. <https://doi.org/10.1097/0000539-200008000-00027>
- Routray SS, Mishra D, Routray D, Nanda K (2017) Effect of Verapamil as an adjuvant to levobupivacaine in supraclavicular brachial plexus block. *Anesth Essays Res* 11(3):656
- Tabaeizavareh MH, Omranifard M, Moalemi A (2012) The effect of verapamil as an adjuvant agent with local anesthetic on sensory block level, hemodynamic and postoperative pain. *Pak J Med Sci* 28(2):259–262
- Sarma BA, Sundari MR, Suman KVJ, Rao DBVM (2015) Low dose dexmedetomidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block. *IOSR J Dent Med Sci (IOSR-JDMS)*

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