

Efficacy of Dexmedetomidine in Supraclavicular Brachial Plexus Block with 0.5% Ropivacaine hydrochloride

Patil BM¹, Shewata G Khatri², karande TK³, Jamadar NP⁴, Deshpande SG⁵

¹Associate Professor, ²Junior Resident III, ³Professor and Head, ⁴Professor and Dean, MIMSR Medical College, Latur, 413512, India, ⁵Professor, Department of Anesthesiology, Government Medical college, Latur (MS), Maharashtra 413512, India.

How to cite this article:

Patil BM, Shewata G Khatri, karande TK. Efficacy of Dexmedetomidine in Supraclavicular Brachial Plexus Block with 0.5% Ropivacaine hydrochloride. Indian J Anesth Analg. 2020;7(4):923-929.

Abstract

In the present study, 100 patients of ASA Grade I and II between age group of 20-65 years of weight range 40-70 kg were included. These 100 patients were divided into 2 equal groups of 50 patients each according to the drugs administered for brachial plexus block. Group A control group received 30 ml of Ropivacaine 0.5% with 0.5 ml of normal saline and Group B patients received 30 ml Ropivacaine 0.5% with Dexmedetomidine 50 µgm 0.5 ml for brachial plexus block. Intravenous infusion line was set up and all patients were monitored throughout intraoperative period and observed for changes in pulse rate, blood pressure, respiration and any untoward effects.

It was observed that, the onset of motor and sensory block was significantly quicker in Group B (study group) as compared to Group A (control group). The duration of motor blockade and sensory blockade was significantly longer in Group B patients as compared to Group A patients. The quality of sensory blockade was excellent in Group B patients and satisfactory in Group A patients. The duration of postoperative analgesia was significantly more prolonged in Group B patients as compared to Group A patients. There were no significant changes in mean pulse rate and mean arterial pressure at various time intervals in both groups during intraoperative and postoperative period. There were no dreadful complications in any patients during intraoperative and postoperative period in both groups.

Keywords: Dexmedetomidine; Supraclavicular; 0.5% Ropivacaine hydrochloride.

Introduction

Many times peripheral nerve blocks provide ideal operative conditions and desired prolonged postoperative analgesia without any significant systemic side effects. These techniques offer an excellent alternative for patients with compromised hemodynamic status or where general anesthesia is relatively at greater risk.

Most of the upper limb orthopaedic and plastic reconstructive surgeries are being performed under regional blocks. Brachial plexus block provide

adequate intraoperative anesthesia, prevents untoward side effects of endotracheal anesthesia, preserves mental functions and provides better intraoperative profile, uneventful recovery and effective postoperative analgesia.

Brachial plexus is usually approached by interscalene, supraclavicular, infraclavicular and axillary routes. Supraclavicular approach is associated with a rapid onset of action, easy technique and higher success rate. The first supraclavicular brachial plexus block was performed by Kulenkampff in 1920. Ultrasound

Corresponding Author: Shewata G Khatri, Junior Resident III, Department of Anesthesiology, MIMSR Medical College, Latur, 413512, India.

E-mail: satdeshpande@rediffmail.com

guided brachial plexus block is safest in recent era.^{22,45,33,9,10}

Lignocaine hydrochloride had been common local anesthetic agent, now almost not in practice due to its side effects of central neuraxial complications. Bupivacaine hydrochloride being most commonly accepted local anesthetic agent for regional techniques of anesthesia Bupivacaine has prolonged duration of action combined with its high quality sensory block relative to motor block. Some cardiac toxicity compelled for better choice of local anesthetic agent. Levo Bupivacaine was also tried in between for some years^{3,8,9,15,48}. Ropivacaine hydrochloride is newer local anesthetic with longer duration of action, with many similarities with Bupivacaine, wider safety margin and with less cardio-toxicity.^{41,33,27,40}

Various adjuvants have been tried with local anesthetic agents to potentiate the action, to prolong the duration of action in view of reducing the side effects of each other. Adrenaline, Neostigmine, Ketamine, opioids, clonidine and new one Dexmedetomidine.^{3,5,8,13,29,27} These are commonly used adjuvants along with local anesthetic agents.

Dexmedetomidine, a pharmacologically active dextroisomer of medetomidine is a sedative α_2 adreno-receptor agonist used as an adjuvant during regional and local anesthesia techniques. It has an α_2 and α_1 selectivity ratio which is eight times more potent than clonidine.^{9,10} It has shorter half life of 2-3 hours as compared to 12-14 hours of clonidine¹¹. It has desired sedative action without respiratory depression. It has potent analgesia sparing effect, reducing the opioid requirement perioperatively.^{15,20,38,42,11}

The present study was undertaken to evaluate the efficacy of Dexmedetomidine when given along with Ropivacaine in supraclavicular brachial plexus block in respect to onset of sensory and motor block, duration of motor and sensory block, quality of block, total duration of postoperative analgesia, hemodynamic stability and intra and postoperative complications.

Material and Methods

In the present study, 100 patients of either sex with age range of 20-65 years, weighing 40-70 kg of ASA grade I and II posted for upper limb surgeries were selected. The patients with neuromuscular disorders, coagulopathy, extremes of age, pregnancy, etc were excluded from the study. These 100 patients were divided into 2 equal groups of 50 patients each. Group A patients received Ropivacaine 0.5% 30 ml with 0.5 ml normal saline

and group B received Ropivacaine 0.5% 30 ml with Dexmedetomidine 50 μ gm in 0.5 ml for brachial plexus block. All patients were preanesthetically evaluated for fitness of anesthesia and necessary investigations were carried out. After college ethical committee approval, informed valid consent was obtained from every patient.

After securing intravenous infusion line on opposite side of block, all standard monitoring devices were attached. Under all aseptic precautions, after cleaning and draping, supraclavicular brachial plexus block was instituted and mixture of Ropivacaine was infiltrated by fan like in supraclavicular region. All the patients were monitored throughout the procedure for development of any complications related to technique of block or drugs administered. Intraoperatively the changes in pulse arte blood pressure, oxygen saturation were recorded at regular interval intraoperatively as well up to 12-18 hours postoperatively.

In all patients, the onset motor block, onset of sensory block, duration of motor and sensory block, quality of sensory block, muscle relaxation, total duration of surgery, duration of postoperative analgesia, intraoperatively changes in mean pulse rate, mean arterial pressure were monitored and noted. All patients were observed for intraoperative and postoperative complications. All observations were statistically evaluated for its significance.

Observations

Out of 100 patients, there were about 75-76% male patients and 24-25% female patients in both groups. Mean age range was 35.88 \pm 10.74 years in Group B and 35.78 \pm 9.47 years in group a patients. The weight range was 57.0 \pm 6.11 kg in Group B and 56.24 \pm 5.22 kg in Group B patients. These patients were posted for various operative procedures as shown in Table 1.

Table 1: Showing various operative procedures

Diagnosis	Group A		Group B	
	Number	Percentage	Number	Percentage
# Both bones	23	46%	25	50%
# Galezzi	13	26%	14	28%
# Radius	8	16%	6	12%
# Ulna	4	8%	3	6%
P/O/C # Radius	2	4%	2	4%
Total	50	100%	50	100%

There were maximum number of patients having # both bones in both groups followed by # Galezzi, # radius and # ulna.

These patients were posted for following operative procedures as shown in Table 2.

Table 2: Showing Operative Procedures

Operative procedures	Group A	Group B
C & IF with nailing	27	25
Implant Removal	2	2
ORIF plating	21	20
Total	50	50

Mean onset of sensory was assessed by pin prick test at each minute after the completion of block in dermal areas of median nerve, ulnar, radial and musculo-cutaneous nerves. It was assessed as 0 – normal sensation, 1 as loss of sensation (analgesia) and 2s loss of touch sensation (anesthesia). Mean onset of sensory block was noted as shown in Table 3.

Table 3: Showing Mean Onset of Sensory Block

	Group B	Group A
Onset of Sensory block in minutes	16.47 ± 3.0	10.12 ± 2.83
	t = 10.788, p < 0.002 HS	

The mean onset of sensory block was 10.12±2.83 minutes in Group A patients and 16.42±3.0 minutes in Group B patients. The onset of sensory block was significantly quicker in Group B as compared to Group A patients.

The mean onset of motor block was noted as the time from administration of drug to time required for complete motor block (Grade II) where motor block was assessed as 0 – normal motor functions, 1 – ability to move only fingers and 2 – inability to move elbow joint. It was as shown in Table 4.

Table 4: Showing Mean Onset of Motor Block

	Group A	Group B
Onset of Motor block in minutes	23.22 ± 2.54	17.14 ± 3.49
	t = - 9.962, p < 0.001 HS	

The mean onset of motor block was 23.22±2.54 minutes in group A and 17.14±3.49 minutes in Group B patients. The mean onset of motor block was significantly quicker in Group B patients as compared to Group A patients.

Mean duration sensory block was noted as the time from administration of drug to time required to complete resolution of local anesthetic drug action. It was as shown in Table 5.

Table 5: Showing Mean Duration of Sensory Block

	Group A	Group B
Mean Duration of Sensory Block in minutes	531.5 ± 37.45	700.8 ± 20.39
	t = - 28.077, p < 0.001 HS	

Mean duration of sensory block was 700.8 ± 20.39 minutes in Group B patients as compared to 531.5 ± 37.45 minutes in Group A patients. The duration of sensory block was significantly longer in Group B patients as compared to Group A patients.

Mean duration of motor block was assessed as the time from administration of drug to time required for complete recovery of motor function. It was noted as shown in Table 6.

Table 6: Showing Mean Duration of Motor Block

	Group A	Group B
Mean Duration of Motor Block in minutes	441.8 ± 40.04	612.1 ± 14.95
	t = - 28.178, p < 0.001 HS	

Mean duration of motor block was 441.8 ± 40.04 minutes in group A and 612.1 ± 14.95 minutes in group B patients. The mean duration of motor block was significantly more in group B patients as compared to group A patients.

The mean duration of sensory block was significantly more in both groups as compared to mean duration of motor block. Thus in group B there is prolonged duration of postoperative analgesia than group B patients.

Mean duration of operative procedure was noted as the time from surgical incision to time taken up to skin closure, It was as shown in Table 7.

Table 7: Showing Mean Duration of Operative Procedure

	Group A	Group B
Mean Duration of Operative procedure in minutes	105.8 ± 18.93	105.9 ± 17.22
	t = - 0.228, p < 0.05 NS	

Mean duration of operative procedure was approximately identical in both groups and there was no statistical significant difference.

The quality of supraclavicular plexus block was assessed and noted in both groups. Quality of block was assessed as 0 – complete failure, 1 – unsatisfactory block and 2 – satisfactory block. It was as shown in Table 8.

Table 8: Showing Quality of Block

	Group A	Group B
Quality of Block	1.91 ± 0.3	1.96 ± 0.2
	t = - 28.178, p < 0.001 HS	

The quality of block was satisfactory in both groups and failure of block patients were not included in the study. So the findings were not statistically significant.

The adequacy of the block or postoperative analgesia was assessed with visual analogue scale

(0-10) in both groups. 0 – No pain, 2 – annoying (mild pain), 4 – uncomfortable (moderate pain), 6 – dreadful (severe pain), 8 – horrible (very severe pain) and 10 – agonizing (not able to perform surgery).

Table 9: Showing Visual analogue scale

	Group A	Group B
Mean Duration of Motor Block in minutes	2.68 ± 0.47	2.7 ± 0.46
	t = - 0.214, p < 0.05 HS	

Most of the patients were having either no pain or very mild pain in both groups. The findings were not statistically significant.

In all patients, mean pulse rate was monitored and was noted as preoperative, every 5-10 minutes up to 30 minutes, at 15, 30 and 60 minutes intervals intraoperatively and postoperatively for 6 hours. Throughout intraoperative period, mean pulse rate was almost stable in both groups at various time intervals.

In both groups, mean arterial pressure at above time intervals during intraoperative postoperative period was noted. There was no statistically significant difference in mean arterial pressure at various time intervals intraoperatively as well as postoperatively in both groups. Thus hemodynamic stability was noted in both groups intraoperative and postoperative period. Respiratory rate and arterial oxygen saturation were maintained in both group patients throughout intra and postoperative period.

There were no any intraoperative or postoperative complications during administration of block or drugs administered in any patients.

Discussion

Supraclavicular brachial plexus block is being accepted regional anesthesia technique for upper limb orthopaedic or general surgery operative procedures in recent era.^{12,21,47,44,33} For regional anesthesia Lignocaine hydrochloride, Bupivacaine hydrochloride, levoBupivacaine and now Ropivacaine are usually preferred. Lignocaine hydrochloride being blamed for transient neurotoxicity and bupivacaine having cardiotoxicity⁶ hence not in common practice. Ropivacaine with less cardiovascular and neurotoxicity as compared to Lignocaine and bupivacaine is being tried in regional anesthesia techniques.^{7,6,16} Ropivacaine is less potent than bupivacaine and levobupivacaine at lower doses. Ropivacaine 0.75% has significantly faster sensory and motor onset of action than 0.5% bupivacaine.^{8,16,26,30,20} In 0.5% concentration in dose

of 30 ml has less toxicity and efficient early sensory and motor onset of action in various regional blocks.^{2,3}

McGlade et al.¹⁰⁷, Casali et al.¹⁰⁸, Riazi et al.¹⁰⁹ have tried Ropivacaine 0.5% for brachial plexus block in their studies. As like these authors we have also used 0.5% Ropivacaine for brachial plexus block. For improved quality of block and prolonged postoperative analgesia was obtained by adding various pharmacological agents to local anesthetic solutions noted by Damin B Murphy, Colin J L, M C Carter and Vincent W S (2000).^{22,23,46,37,33} They emphasized the efficacy of adding analgesic adjuvants as opioids, clonidine neostigmine, Tramadol to brachial plexus block. They noted that analgesic benefits of opioids adjuvants remain equivocal. Dexmedetomidine acts as a selective α_2 adrenoreceptor agonist. There is increased ratio of α_2 and α_1 activity of 1620:1 with Dexmedetomidine as compared to 220:1 with clonidine. In dose of 1 $\mu\text{gm/kg}$ it is equipotent and beneficial⁹⁷ Brummett^{20,21,22} showed that Dexmedetomidine prolonged the duration of nerve block when added to Ropivacaine in dose dependent manner. Obayhand et al. (2000)¹¹, Marhofer et al. (2012)⁴⁸, Rancourt et al. (2012)¹¹ many other authors have used Dexmedetomidine 0.5-1 $\mu\text{gm/kg}$ as adjuvant to local anesthetic agent Bupivacaine, Levo Bupivacaine or Ropivacaine in regional blocks. Many of these authors have observed early onset of action (sensory and motor) and prolonged duration of analgesia and complete sensory and motor blocks in their studies. As compared to these authors, we have also noted significantly quicker onset of sensory and motor blockade in Dexmedetomidine group as compared to plane group in brachial plexus block. Our observations coincide with Esmaoglu et al.², Ohayag et al.¹¹, K Kaygusuz et al.¹⁰, A S Ammare et al.⁴⁹, Sandhya Agrewal^{4,2}, A P Singh¹⁴, etc. There were similar findings as quicker onset of sensory and motor block.

In the present study, the duration of sensory blockade was 700±20.39 minutes in study group and 531.50±37.45 minutes in plane group. There was statistically significant prolonged duration of sensory block in study group as compared to control or plane group. The duration of motor blockade was also significantly longer in study group as compared to control group. These observations were similar to the observations of many above authors in their respective studies. As like Rachana Gandhi et al.¹⁰ we have noted prolonged duration of sensory and motor blockade. It was on the basis that larger fibers require higher concentration

of local anesthetic agents than small fibers. The minimum effective concentration of local anesthetic required for large motor fibers was greater than small sensory fibers.^{35,42,44} So motor functions return before pain perception and duration of motor block was shorter than sensory block.^{20,43,37} It is particularly beneficial in lower extremity blocks for day care surgery so that early ambulation and early discharge of the patient from hospital.

There were minimum changes in hemodynamic parameters as mean pulse rate, mean arterial pressure at various time intervals intraoperatively as well as postoperatively in both groups. Thus Dexmedetomidine with local anesthetic is safe adjuvant for hemodynamic stability during regional anesthesia techniques. With higher concentration of drugs, there may be decrease in heart rate and mean arterial pressure which may be seen secondary to systemic absorption of Dexmedetomidine.⁹⁻¹¹ Presynaptic activation of α_2 adreno-receptors in central nervous system inhibits release of norepinephrine, terminating prolongation of pain signals and their postsynaptic activation. Para Sympathetic activity reduces heart rate and blood pressure. Transient hypertensive response may be encountered with dose of 1-4 $\mu\text{gm/kg}$ attributed to initial stimulation of β_2 receptors in vascular smooth muscles. Bradycardia is a reflex response to transient response as it persists subsequently due to central sympathetic inhibition.^{49,39} Baroreceptor reflex and heart rate response to pressor agents is well preserved with Dexmedetomidine, which is responsible for hemodynamic stability.^{21,19,28}

There was prolonged and satisfactory duration of postoperative analgesia in both groups and it was more study in study group as compared to control group. The quality of sensory and motor blockade was comparable in both groups and these were in accordance with above many authors. There were no dreadful intraoperative as well as postoperative complications related to the drugs or technique of anesthesia in both groups.

Summary

In the present study, 100 patients of ASA grade I and II between age group of 20-65 years of weight range 40-70 kg were included. All patients were preanesthetically evaluated and investigated for fitness of anesthesia. These 100 patients were divided into 2 equal groups of 50 patients each according to the drugs administered for brachial plexus block. Group A control group received 30 ml of Ropivacaine 0.5% with 0.5 ml of normal saline and group B patients received 30 ml

Ropivacaine 0.5% with Dexmedetomidine 50 μgm 0.5 ml for brachial plexus block. Under all aseptic precautions supraclavicular brachial block by infiltrating the drug was administered according to group allocated. All emergency drugs and trolley was kept ready. Intravenous infusion line was set up and all patients were monitored throughout intraoperative period and observed for changes in pulse rate, blood pressure, respiration and any untoward effects.

After the completion of block, onset of sensory and motor block, duration of sensory and motor block, duration of surgery, quality of sensory block, and total duration of analgesia was noted in all patients of both groups. Intraoperative and postoperative complications related to the technique of anesthesia and drugs were observed in both groups.

It was observed that, the onset of motor and sensory block was significantly quicker in group B (study group) as compared to group A (control group). The duration of motor blockade and sensory blockade was significantly longer in group B patients as compared to group A patients. The quality of sensory blockade was excellent in group B patients and satisfactory in group A patients. The duration of postoperative analgesia was significantly more prolonged in group B patients as compared to group A patients. There were no significant changes in mean pulse rate and mean arterial pressure at various time intervals in both groups during intraoperative and postoperative period. There were no dreadful complications in any patients during intraoperative and postoperative period in both groups.

Conclusions

Supraclavicular brachial plexus block is accepted technique of anesthesia for upper limb orthopaedic or general surgery operative procedures. Ropivacaine hydrochloride 0.5% in dose of 25-30 ml is better alternative for brachial plexus block as replacement for 0.5% Bupivacaine hydrochloride. Addition of adjuvants Dexmedetomidine (50-100 μgm) along with Ropivacaine for brachial plexus block improves the quality of block and significantly prolongs the duration of postoperative analgesia. Ropivacaine 0.5% with Dexmedetomidine 50 μgm provides early onset of sensory and motor block, better quality of sensory block, prolonged duration of intraoperative duration of motor and sensory blockade and also prolongs the duration of postoperative analgesia without significant changes in hemodynamic parameters. There are

less chances of intraoperative and postoperative dreadful complications.

Hence addition of Dexmedetomidine with local anesthetic agent satisfies all the requirements of regional block particularly brachial plexus block in indicated patients. It can be safely administered in regular practice of anesthesia.

References

1. Damini B Murthy, Collin JL, Cartney J, et al. Novel analgesic adjuvants for brachial plexus block: A systematic review. *Anesth Analg* 2000;90:1122-8.
2. Esmaoglu A, Yegenoglu F, Akin A, et al. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. *Anesth. Analg* Dec 2010;111:1548-51.
3. Lee JA, Atkinson R S, Rushman G B et al. Lee's Synopsis of anesthesia. Oxford: Butterworth Heinmann Ltd; 11th Edition 1993:642.
4. Klein SM, Greengrass RA, Steele SM, et al. A comparison of 0.5% bupivacaine, 0.5% ropivacaine and 0.75% ropivacaine for interscalene brachial plexus block. *Anesth Analg* 1998;87:1316-19.
5. Ray M, Mondal SK, Biswas A. Caudal analgesia in paediatric patients, comparison between bupivacaine and ropivacaine. *Ind Jr. of Anesth* 2003;47:275-8.
6. Kuthiala G, Chaudhry G. Ropivacaine - A review of its pharmacology and clinical use. *Ind Jr Anesth* 2011;55:104-10.
7. Conception M, Arthur GR Steele SM. A new local anesthetic - ropivacaine, its epidural effects in humans. *Anesth Analg* 1990;70:80-5.
8. Scott DB, Lee A, Fagan D, et al. Acute toxicity of ropivacaine compared with that of bupivacaine. *Anesth Analg* 1989;69:563-9.
9. Coursin DB, Maccoli GA. Dexmedetomidine. *Curropin Criticare* 2001;7:221-6.
10. Raimo V, Juha M, Veijo S. Characteristics of selectivity, specificity and potency of medetomidine as α_2 .
11. Joseph D Tobias. Dexmedetomidine in trauma anesthesiology and critical care. *International trauma care (ITACCS)* 2007;17(1).
12. Hall JE, Uhrich TD, Braney JA. Sedative, amnestic and analgesic properties of small dose of Dexmedetomidine infusion. *Anesth Analg* 2000; 90:699-705.
13. Ebert TJ, Hall JE, Braney JA. The effects of increasing plasma concentrations of Dexmedetomidine in humans. *Anesthesiology* 2000;93:382-94.
14. Venn RM, hel J, Grounds RM. Respiratory effects of Dexmedetomidine in surgical patients requiring intensive care. *Crit care* 2000;4:302-8.
15. Hoy SM, Keating GM. Dexmedetomidine a review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. *Drugs* 2011;30:1481-501.
16. Herr d l, Sun-Ping STJ, England M. ICU sedation after coronary artery bypass graft surgery. Dexmedetomidine - based versus propofol based sedation regimns. *J Cardiothoracic Vasc Anesth* 2003;17:576-84.
17. Arian SR, Elbert TJ. The efficacy, side effects and recovery characteristics of Dexmedetomidine versus propofol when used for intraoperative sedation. *Anesth Analg* 2002;95:461-6.
18. Berry M, Lawrence H, Susan BM. Standing nervous system. 38th ed chapter 8 In; Gray's Anatomy 1995; 902-1397.
19. Leinberry CF, Wegbe MA. Brachial plexus anatomy. *Hand Clin* 2004 Feb, 20(1):1-5.
20. Mulroy MF. Peripheral nerve blockade, 4th Edi chapter 27, In *Clinical Anesthesia Stoeling BK*, 2001; 723-7.
21. Matuszczak M. Supraclavicular block 2nd Edition chapter 6; *Peripheral nerve blocks Chelly J E ed*; 1999;35-8.
22. WB Saunders BD. Atlas of Regional anesthesia. Upper extremity block anatomy. 2nd edition chapter 2.
23. Brown DL. Upper extremity block anatomy. 2nd ed chapter 2 In: *Atlas of regional anesthesia*. Philadelphia PA; WB Sanders com 1999;16-22.
24. Lamont LA, Tranquilli WJ, Grimm KA. Physiology of pain. *Veterinary clinics of North America small animal practice* 2000;30(4):703-28.
25. Hudspith MJ, Siddall PJ, Mungalani R. Physiology of pain. *Foundations of anesthesia* 2nd ed London UK Mosby 2006;267-285.
26. Chiu TH, Chen MJ, Yang YR. Action of Dexmedetomidine on rat ceruleus neurons: intracellular recording in vitro. *Eur J Pharmacol* 1995;285:261-8.
27. Khan ZP, Ferguson CN, Jones RM. α_2 and imidazoline receptor agonists and their pharmacology and therapeutic role. *Anesthesia* 1999;54:146-65.
28. Scheinin M, Schwinn D. The locus ceruleus. Site of hypnotic action of α_2 adreno receptor agonists. *Anesthesiology* 1992;76:873-5.

29. Gertler R, Brown HC, Mitchell DH. Dexmedetomidine a novel sedative analgesic agent. BUMC proceedings 2001;14:13-21.
30. Bloor BC, Ward DS, Maze M. Effects of intravenous Dexmedetomidine in humans II. Hemodynamic changes. *Anesthesiology* 1992;77:1134-42.
31. Sharma S, Jain P. Dexmedetomidine and anesthesia Ind Jr of clinical practice 2013;24-33.
32. Ishii H, Kohno T, Baba H. Action of Dexmedetomidine on the substantia gelatinosa neurons of rat spinal cord. *Eur J Neurosci* 2008;27(12):3182-90.
33. Roudet C, Mouchet P, Feuerstein C. Normal distribution of α_2 adrenoreceptors in the rat spinal cord and its modification after noradrenergic denervation, a quantitative autoradiographic study. *J Neurosci Res* 1994;39(3):319-29.
34. Stone LS, Broberger C, Reidl MS. Differential distribution of α_2 and α_2c adrenergic receptor immuno reactivity in rat spinal cord. *J Neurosci* 1998;18(15):5928-37.
35. Arain SR, Elbert TJ. The efficacy, side effects and recovery characteristics of Dexmedetomidine versus propofol when used for intraoperative sedation. *Anesth Analg* 2002;95(2):461-6.
36. Candiotti KA, Bergese SD, Bekker AY. MAC study group. Monitored anesthesia care with Dexmedetomidine - a prospective, randomized, double blind, multicenter trial. *Anesth Analg* 2010;111(1):47-56.
37. Panxer O, Moitra V, Sladen RN. Pharmacology of sedative analgesic agents, Dexmedetomidine, remifentanyl, ketamine, volatile anesthetic and the role of peripheral μ antagonists. *Anesthesiology; clinics* 2011;29-34.
38. Mantz J. Dexmedetomidine: *Drugs Today*, 1999 Mar 35(3):151-7.
39. Cunningham FE, Baughman VL, Tonkovich L. Pharmacokinetics of Dexmedetomidine in patients with hepatic failure (abstract). *Clin Pharmacol Ther* 1999 Feb;65:128.
40. Salonen m, Reid K, Maze M. Synergistic interaction between α_2 adrenergic agonists and benzodiazepines in rats. *Anesthesiology* 1992;76:1004-11.
41. Grosu I, Lavand'homme P. Use of Dexmedetomidine for pain control. *Med Rep* 2010;2;90.
42. Robert SB, Coyne PJ, Smith TJ. Dexmedetomidine as an adjuvant analgesic for intractable cancer pain. *J Palliat med* 2011;14(3):371-3.
43. Uger F, Gulcu N, Boycai A. Intrathecal infusion therapy with Dexmedetomidine supplemented morphine in cancer pain. *Acta Anesth Scand* 2007;51(3):388.
44. Bachand R, Scholz J, Ainaud M. The effects of dexmedetomidine in patients in the intensive care setting (abstract no. 622) *Intensive care Med* 1999;25,suppl,1, S160.
45. Martin E, Lehot JJ, Manikis. Dexmedetomidine - a novel agent for patients in the intensive care setting (abstract no.623) *Intensive Care Med* 1999;25 suppl1.
46. Candiotti KA, Bergese SD, Bekker AY. MAC study group. Monitored anesthesia care with Dexmedetomidine - a prospective, randomized, double blind, multicenter trial. *Anesth Analg* 2010;110:47-56.
47. Bergese SD, Zura A, Bekker AY. Dexmedetomidine for sedation during elective awake fiberoptic intubation. A multicenter trial. *Anesthesiology* 2008;109:A-186.
48. Bernardini DJ, Shapiro FE. Dexmedetomidine during TIVA: A unique approach to intraoperative wake up test. *Post graduate Assembly in Anesthesiology, New York*, 2006;P-9021.
49. Mautua MA, Cata JP, Martirena M. Dexmedetomidine for deep brain stimulator placement in a child with primary generalized dystonia, a case report and literature review. *J clin Anesth* 2009;21:213-16.