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Original Article

Effect on Onset and Duration of Sensory and Motor Block with Single Bolus Dose of Intravenous Dexmedetomidine as an Adjuvant on Spinal Anesthesia with 0.5% Hyperbaric Bupivacaine in Lower Limb Surgery

Rupak Bhattarai*, Parasmani Shah, Prabin Sharma

Department of Anesthesiology, Critical Care and Pain Management, Nobel Medical College Teaching Hospital, Biratnagar, Nepal

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Abstract

Background

The hyperbaric bupivacaine is being widely used for spinal anesthesia in lower limb surgeries. Dexmedetomidine can be used intravenously as well as an intrathecal injection along with spinal anesthesia for surgery below the umbilicus.

Materials and Methods

This was a prospective, randomized double blinded study, where 100 patients posted for elective lower limb surgery under spinal anesthesia were divided into two groups. Group A received 0.5% hyperbaric bupivacaine as spinal anesthesia along with intravenous infusion of 0.5 µg /kg/hour of dexmedetomidine over a period of ten minutes. Group B received 0.5% hyperbaric bupivacaine as spinal anesthesia along with intravenous normal saline over a period of ten minutes.

Results

The onset of sensory block was 3.19 ± 0.31 minutes in group A whereas 4.5 ± 0.22 minutes in group B. The onset of motor block was 4.28 ± 1.02 minutes in group A whereas 7.12 ± 0.87 in group B. The onset and duration of sensory and motor block were statistically significant. Regarding duration of sensory block, group A had 186.5 ± 14.04 minutes whereas group B had 148.2 ± 11.31 minutes with p value <0.001. The duration of motor block was 142 ± 11.42 minutes in group A whereas 122.4 ± 8.28 minutes in group B with p value <0.001. The duration of postoperative analgesia was prolonged in group A when compared with group B.

Conclusion

Dexmedetomidine used as a single intravenous injection along with spinal anesthesia with 0.5% bupivacaine tends to shorten the onset of both sensory and motor blocks and increases the duration of sensory and motor blocks. It also prolongs the duration of analgesia with minimal or no changes in hemodynamic parameters.

Keywords: *Bupivacaine, Dexmedetomidine, Spinal anesthesia*

***Corresponding Author:**
Dr. Rupak Bhattarai
Associate Professor
Email:bhattarairupak@hotmail.com
ORCID: https://orcid.org/0000-0002-5521-081X

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Introduction

Postoperative pain generally produces a detrimental acute and chronic effects in terms of quality of life, functional recovery leading to post- surgical complications and thus complicates the risk of resistant post-surgical pain [1]. Therefore, attenuation of post operative pain with multiple types of analgesics decreases the morbidity and mortality of the patients [2]. It is an utmost responsible of an anesthesiologist regarding uneventful postoperative pain relief thus making comfortable preposition for surgical patients.

Subarachnoid block, commonly known as spinal anesthesia is one of preferred technique in operation theatre employed for lower limb surgeries [3]. It thereby produces sympathetic blockage, sensory analgesia and also motor blockage in association on dosage, concentration or volume of local anesthetics used [4]. Bupivacaine is one of the commonly used local anesthetics for spinal anesthesia in our hospital. The addition of opioids like morphine and fentanyl improves the quality of blocks and also provides prolong post operative pain relief [5]. However, non- opioids like dexmedetomidine and clonidine may also be used for prolongation of blocks [6].

Dexmedetomidine has been found more appropriate adjuvant to spinal anesthesia compared to clonidine, as it has more sedative as well as analgesic effects due to its selective 2A receptor agonist activities [11]. There are few studies which has shown efficacy of Dexmedetomidine and clonidine are being used as intravenously to prolong the duration of spinal anesthesia these days [7,8]. It has been used to produce sedation and anxiolysis by binding to presynaptic alpha 2 receptors in locus ceruleus [9]. The stimulation of alpha 2 receptors at the substantia gelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of the release of substance P thus by leading to analgesic effects [10].

Dexmedetomidine has been found more appropriate adjuvant to spinal anesthesia compared to clonidine, as it has more sedative as well as analgesic effects due to its selective 2A receptor agonist activities [11]. There are few studies which has shown efficacy of intravenous dexmedetomidine for prolongation of duration of action of prilocaine, bupivacaine, ropivacaine during spinal anesthesia to provide sedation and post operative analgesia [12,13]

Thus, we thought to study the effect of single bolus dose of intravenous dexmedetomidine with spinal anesthesia in terms of time of onset and duration of sensory and motor block, hemodynamic changes, duration of post operative analgesiain our hospital.

Materials and Methods

This is the prospective, randomized, double blinded study done at routine operation theatre, Nobel Medical College Teaching Hospital, Biratnagar, Nepal over a period of one and half years from December 2021 to June 2023 after ethical clearance received for institutional review committee. Informed consent was taken for enrollment. The inclusion criteria include ASA physical status I and II, age between 18 to 60 years, patient scheduled for elective lower limb surgeries. The exclusion criteria include patient refusal, patients on any sedation, hypnotics, opioids or antidepressants or any contraindications for spinal anesthesia.

Sample size was calculated using a formula n= $\underline{(Za + Zb)^2 \times \sigma^2}/d^2$ [where standard deviation $\underline{\sigma}$=2.52as per previous study [14] and desirable error (d) =1, Confidence interval of 95 %=0.84 and Power of test at 80%= 1.96, thus sample size in each group calculated at 49.14, thus taken as 50 in each group, therefore the total size for the study is 100. A total of 100 patients using a sealed envelope method was divided into two groups, dexmedetomidine group (Group A) and Control group (Group B), thus considering 50 patients in each group. The routine pre-anesthetic checkup was done one day prior to surgery and patients were explained about the technique of anesthesia. A written informed consent was taken, and all patients were kept nil per oral for at least 8 hours prior to surgery. On the day of surgery once the patient is on operation table, an intravenous line was secured with 18G cannula in non-dominant hand and injection Ringer lactate was infused at the rate of 30ml/kg. All standard monitors for monitoring heart rate, systolic and diastolic blood pressure, oxygen saturation and ECG was attached and baseline recording were recorded. The anesthesiologist who was not part of this study prepared the drugs in an identical syringe. GroupA (Dexmedetomidine) received:Single bolus intravenous dose of 0.5ug/kg of Dexmedetomidine. Group B (Control) received: Single bolus intravenous Normal Saline

The study drugs were premixed to a total volume of 30 ml and were given intravenously slowly over 10 minutes as a single dose by anesthesiologist who was not involved in this study. Thereafter, position for a spinal anesthesia was made. Spinal anesthesia was given under aseptic con-

ditions with 25gauge needle at L3-L4 or L4-L5 interspace using 3ml of 0.5% Bupivacaine Heavy. All patients were kept on simple face mask with 5 L/min of oxygen. Heart rate, Systolic and Diastolic blood pressure were recorded soon after spinal anesthesia, every 2 minutes interval for 10 minutes and then every 5 minutes till the end of surgery and then every 15 minutes in recovery room. Hypotension was defined a decrease in systolic blood pressure below 90 mmHg and was treated with injection Mephentermine of 6mg intravenously. Heart rate below 50 beats/minutes was considered as Bradycardia and was treated with 0.6mg of atropine intravenously.

Onset of sensory block was considered as time taken from injecting bupivacaine into subarachnoid space till the patient did not feel cold sensation at T10 level. Sensory recovery was considered as regression to S1 level. Sensory blockage was assessed on every 2 minutes for the first 10 minutes and thereafter every 15 minutes during surgery and post operatively by using alcohol swab.

Motor blockage were assessed on every 2 minutes before the onset of surgery and every 15 minutes in Recovery room by modified Bromage scale (0= able to move hip, knee and ankle; 1= unable to move hip and knee but able to move ankle; 3= unable to move hip, knee and ankle)[7]. Onset of motor blockage was considered as time taken for motor block to reach modified bromage scale of 3. Recovery from motor blockage was considered as regression of modified bromage scale to 0. From the onset of sensory block to time of administration of first rescue analgesia with visual analogue score (VAS) of less than 3 was considered as duration of analgesia. Injection Paracetamol 15mg/kg intravenous was given as rescue analgesia. Patient were discharged from recovery room after sensory regression to S1 and Modified bromage scale to zero.

The statistical analysis was done once collected data were entered in Microsoft Excel 2010, and converted to statistical Package for social science (SPSS) for windows version 22.0. All descriptive date were calculated as percentage, Mean and standard deviation(SD). All inferential statistics were calculated using Chi square test and independent t test to find out significant differences between groups and other selected variables at 95% confidence interval where p considered as < 0.05.

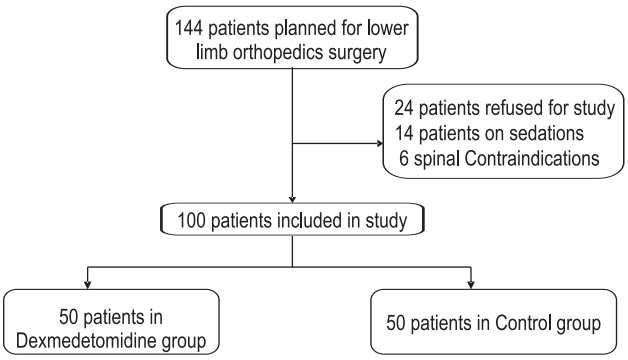

Figure 1: Flow chart of patient's selection

Results

A total of 100 patients were included in our study. The mean age of the patients in dexmedetomidine group was 36.38± 11.32 years, whereas in control group was 35.48 ± 10.44 years. In regards of gender distribution, 80% of patients were male and 20 % were female in dexmedeto-midine group whereas 72% of patients were male and 28% were female in Control group. In dexmedetomidine group, mean patient's weight was 56.84 ± 4.42 kg whereas in Control group, patient's mean weight was 56.64 ± 5.48 kg. Regarding ASA physical status, in Dexmedeto-midine group 70% patient were ASA I and 30 % were ASA II whereas in Control group 70% patients were ASA I and 22 % patients were ASA II.

Table 1: Mean Heart Rate at various time after SAB

Time	Group A Mean ± SD	Group B Mean ± SD	p-value
Baseline	79.32 ± 10.12	79.42 ± 8.21	0.957
2 minutes	75.2 ± 9.98	78.4 ± 8.48	0.087
4 minutes	68.88 ± 9.31	75.62 ± 9.39	0.013
6 minutes	67.2 ± 10.62	71.06 ± 8.37	0.046
8 minutes	67.38 ± 11.29	69.62 ± 7.97	0.255
10 minutes	67.64 ± 12.12	67.46 ± 8.03	0.930
15 minutes	68.42 ± 13.81	67.44 ± 7.52	0.693
20 minutes	66.08 ± 13.17	68.28 ± 6.81	0.569
25 minutes	66.16 ± 10.77	67.46 ± 7.12	0.478
30 minutes	66.66 ± 10.62	67.64 ± 8.11	0.642
35 minutes	66.76 ± 11.26	66.54 ± 7.59	0.926
40 minutes	66.16 ± 10.44	66.62 ± 7.17	0.755
45 minutes	66.14 ± 10.55	66.8 ± 6.52	0.707
50 minutes	66.24 ± 10.28	67.08 ± 6.03	0.619
55 minutes	66.12 ± 9.53	66.28 ± 6.16	0.968
60 minutes	66.52 ± 9.25	66.05 ± 6.91	0.961
65 minutes	66.06 ± 8.71	67.12 ± 6.81	0.499
70 minutes	65.86 ± 7.86	67.35 ± 7.35	0.183
75 minutes	65.82 ± 8.28	68.36 ± 6.52	0.092
80 minutes	66.24 ± 8.13	67.64 ± 6.24	0.372
85 minutes	66.56 ± 8.09	67.42 ± 6.58	0.395
90 minutes	66.12 ± 7.38	67.14 ± 5.95	0.593
95 minutes	67.82 ± 8.36	68.42 ± 5.98	0.732
100 minutes	68.52 ± 8.01	68.34 ± 6.77	0.989
105 minutes	69.32 ± 8.74	68.66 ± 5.61	0.754
110 minutes	69.26 ± 7.95	69.36 ± 4.76	0.970
115 minutes	70.24 ± 9.18	70.85 ± 5.41	0.997
120 minutes	70.83 ± 8.81	70.79 ± 5.32	0.983

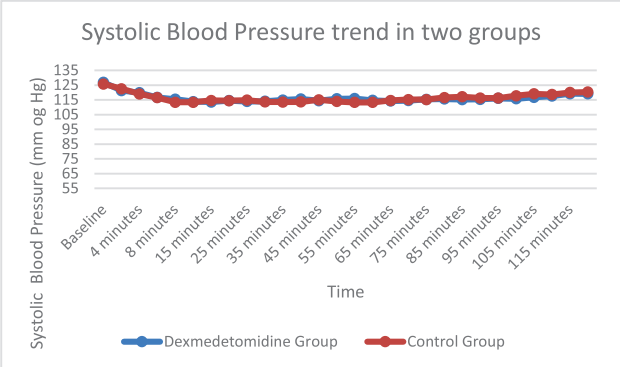

Figure 2: Systolic Blood Pressure trend between two groups

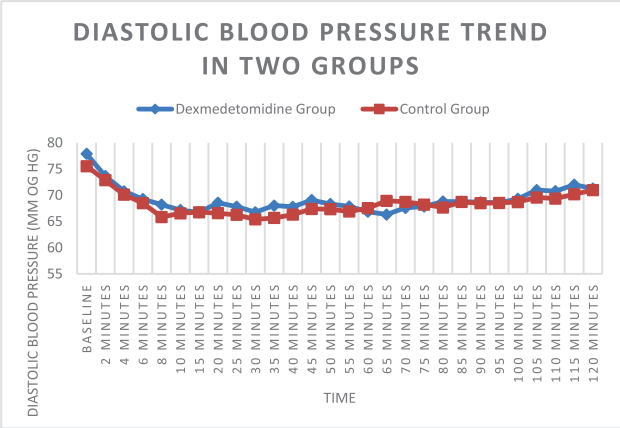

Figure 3: Diastolic Blood Pressure trend between two groups

Table 2: Onset of Sensory and Motor block

Blocks (in minutes)	Group A	Group B	p-value
Sensory Block (Mean ± SD)	3.19 ± 0.31	4.5 ± 0.22	<0.001
Motor Block (Mean ± SD)	4.28 ± 1.02	7.12 ± 0.87	<0.001

Table 3: Duration of Sensory and Motor Block

Blocks in minutes	Group A	Group B	p-value
Sensory Block(Mean ± SD)	186.5 ± 14.04	148.2 ± 11.31	<0.001
Motor Block(Mean ± SD)	142.4 ± 11.42	122.4 ± 8.28	<0.001

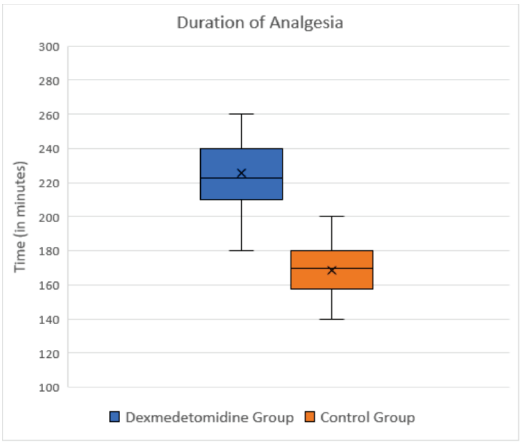

Figure 4: Analgesia duration between two groups

Table 4: Side effects in two groups

Side effects	Group A	Group B	p-value
Bradycardian (%)	5 (10)	1 (2)	0.140
Hypotensionn (%)	2 (4)	3 (6)	0.695

Discussion

The alpha-2 adrenoreceptor agonist was synthesized and used as nasal decongestant in early 1960's. The complete anesthesia was posible by using new adjuvant alpha-2 agonist such as medetomidine and its stereoisomer, dexmedetomidine [15]. Dexmedetomidine is a superior highly selective alpha-2 agonist and has significant sympatholytic and possess stable hemodynamic properties. Therefore, there is a dose dependent decrease in heart rate and blood pressure [15]. In our study the dose of dexmedetomidine was taken as 0.5 ug/kg. This was taken by the study done by Jaakola ML et al [11], where an evaluation of the analgesic effects of different doses of intravenous dexmedetomidine on ischemic pain in healthy workers demonstrated moderate analgesia with a ceiling effect 0.5ug/kg. The dexmedetomidine should be administer over no less than 10 minutes as rapid administration causes tachycardia, bradycardia and hypertension [16]

In the present study heart rate, systolic and diastolic blood pressure were not significant statistically though the hemodynamic parameters were stable in both the group. In relation to our study, the decrease in heart rate was seen more in the dexmedetomidine group (5 patients) when compared with the control group (1 patient). Therefore, the bradycardia was observed more in dexmedetomidine group when compared with the control group in our study, this was similar with the study done by Whizar-Lugo V et al [17],Tekin M et al [12] and Kubre J et al [18]. But there was contradictory to all above studies done by Al Mustafa MM et al [19], where he reported that there was no difference in terms of bradycardia and requirements of atropine in between dexmedetomidine and control groups. The post- synaptic activation of alpha 2 adrenoreceptors in central nervous system may lead to lowering of sympathetic actions, the levels of catecholamines in circulation and this may be the reason of decrease in heart rate in our study.

In our study, the systolic and diastolic blood pressure were comparable between the two groups but was not statistically significant. The incidence of hypotension was seen in 4 % of patients in dexmedetomidine group whereas seen in 6 % of

patients in control group. There was no such difference in terms of hypotension in both the groups. This finding was similar to the study done by Kubre J et al [18], Reddy VS et al [20]. The study done by Hong JY et al [21] reported more incidence of hypotension in dexmedetomidine group, the reason behind it may be due to the elderly patients undergoing transurethral resection of prostrate (TURP) which was contrary to our study. In terms of mean onset of sensory block, the dexmedetomidine group (3.19±0.31 minutes) when compared with control group (4.5 ±0.22 minutes), which was statistically significant in present study. These findings states that the dexmedetomidine group had shorter time for onset of sensory block when compared with control group. This was consistent and similar with the study done by Harsoor SS et al [22]. The Kolarkar P et al [23] did similar study and found the onset of sensory block to be less when compared with the control group. The reason behind this may be due to the activation of alpha-2 receptor which in turn inhibits the effects of nociceptive transmission of impulses. To the contrary of above studies Tekin M et al [12] and Elcickek K et al [23] did similar studies and resulted that there was no difference in between the onset of sensory block between the two group.

In the present study the mean duration of sensory block was significantly prolonged in dexmedetomidine group (186.5 ±14.04 minutes) when compared with control group (148.2 ±11.31minutes). This was consistent with the study done by Kaya FN et al [24], who proposed that dexmedetomidine when used intravenously prolongs the effects of spinal anaesthesia with bupivacaine. The present study also equivalents with the study done by Kubre J et al [18], Al Mustafa MM et al [19] and Whizar – Iugo V et al [17]. The mean onset of motor block was found to be shorter in dexmedetomidine group (4.28 ±1.02 minutes) compared with control group (7.12 ±0.87) and this was statistically significant. The similar study done by Al Mustafa MM et al [18], Kanazi GE et al [25] also demonstrated that dexmedetomidine group had similar findings regarding onset of motor block. The similar study done by Kaya FN et al [24] resulted that the mean onset of motor block was not statically significant and comparable between two groups. The mean duration of motor block was longer in dexmedetomidine group (142.4 ±11.42 minutes) compared to control group (122.4 ±8.28). This was statistically significant and similar findings were reported by various authors like Whizar-Lugo V et al [17], Mustafa MM et al [19], Tekin M et al [12] and Hong et al [21]. Though some of the authors used both loading and infusion dose of dexmedetomidine but still were consistent with our study where dexmedetomidine had prolongation of mean duration of motor block.

In our study, the time for request first analgesia in the post operative period was longer in dexmedetomidine group when compared with control group. This resembled with the reports by various authors like Al-Mustafa MM et al (19), Kubre J et al (18), Hong JY et al (21) and Reddy M et al [26]. The effects of dexmedetomidine and bupivacaine at supra- spinal, analgesics, spinal, constrictions of blood vessels may be the reason for above mentioned effects. The effects of these drugs to produce sedation and analgesia may attribute the above findings. The effects of these drugs to produce sedation and analgesia may attribute the above results and these findings also correlates well with the study done by Paudel B et al [27].

Conclusion

The single bolus infusion dose of intravenous dexmedetomidine 0.5µg /kg shortens the onset of sensory and motor block, increases the duration of sensory and motor block, prolongs the analgesics requirements post operatively by prolonging the duration of analgesia with lesser incidence of bradycardia and hypotension when given as an adjuvant to Bupivacaine in Spinal Anesthesia.

Recommendation

Dexmedetomidine, a selective alpha-2 receptor agonist when used as a bolus intravenous infusion as an adjuvant to bupivacaine for spinal anesthesia is found to be beneficial in patients undergoing lower limb surgery. It is also recommended for its sedative and additional analgesic properties, however its use in children and elderly needs more research in future. The close monitoring by an anesthesiologist is important as bradycardia and hypotension should be promptly managed.

Acknowledgement

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Conflict of interest

There were no any conflicts of Interest.

References

[1] Kehlet H, Jensen TS, Woolf CJ, Persistent post-surgical pain: risk factors and prevention, The Lancet. 13:367 (2016) 1618-25. DOI: 10.1016/S0140-6736(06)68700-X. PMID: 16698416.

[2] Liu S, Carpenter RL, Neal JM, Epidural Anesthesia and Analgesia their role in postoperative outcome, Anesthesiology: The Journal of the American Society of Anesthesiologists. 82:6 (1995) 1474-506. DOI: 10.1097/00000542-199506000-0019.PMID:7793661

[3] Sule AZ, Isamade ES, Ekwempu CC, Spinal anesthesia in lower abdominal and limb surgery research. 7:1 (2005) 226-30. DOI: 10.4314/Njsr.v7i1.12287.

[4] Wulf HF, The centennial of spinal anesthesia, Anesthesiology, The Journal of the American Society of Anesthesiologists. 89:2 (1998) 500-6. DOI: 10.1097/00000542-199808000-00028. PMID: 9710410

[5] Swain A, Nag DS, Sahu S, Samaddar DP, Adjuvants to local anesthetics: Current understanding and future trends, World Journal of clinical cases. 5:8 (2017)307-23. DOI: 10.12998/Wjcc.v5.i8.307. PMID: 28868303.

[6] Ganesh M, Krishnamurthy D, A comparative study of dexmedetomidine and clonidine as an adjuvant to intrathecal bupivacaine in lower abdominal surgeries, Anesthesia: Essays and Researches. 12:2 (2018) 539-45. DOI:10.4103/aer.AER_54_18. PMID: 29962631

[7] Rani HL, Upendranath I, Comparative study of intravenous dexmedetomidine plus intrathecal bupivacaine vs intrathecal bupivacaine alone for prolongation of spinal analgesia, Journal of Evolution of Medical and Dental Sciences. 4:94 (2015) 15952-9. DOI: 10.4103/0970-9185.83678. PMID: 21897504.

[8] Rhee K, Kang K, Kim J, Jeon Y, Intravenous clonidine prolongs bupivacaine spinal anesthesia, Acta anesthesiologicascandinavica.47:8 (2003) 1001-5. DOI:10.1034/j.1399-6576.2003.00158.x: PMID: 12904193.

[9] Yabeck- Karam VG, Aouad MM, Perioperative uses of dexmedetomidine, Middle East Journal of Anesthesiology. 18:6 (2006) 1043-58. PMID: 17263262.

[10] Giovannitti Jr JA, Thoms SM, Crawford JJ, Alpha-2 adrenergic receptor agonists: a review of current clinical applications, Anesthesia progress. 62:1 (2015) 31-8. DOI: 10.2344/0003-30006-62.1.31. PMID: 25849473.

[11] Jaakola ML, Salonen M, Lehtinen R, Scheinin H, The analgesic action of dexmedetomidine- a novel alpha 2 -adrenoceptor agonist-in healthy volunteers, Pain. 46:3 (1991) 281-5. DOI: 10,14260/jemds/2015/1065.

[12] Tekin M, Kati I, Tomak Y, Kisli E, Effect of dexmedetomidine IV on the duration of spinal anesthesia with prilocaine: A double- blind, prospective study in adult surgical patients, Current Therapeutic Research. 68:5 (2007) 313-24. DOI: 10.1016/j.curtheres.2007.10.006. PMID: 24692763.

[13] Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q, Effects of intravenous and Intrathecal Dexmedetomidine in Spinal Anesthesia: A Meta- Analysis, CNS neuroscience & therapeutics. 19:11 (2013) 897-904. DOI:10.1111/cns.12172. PMID:24118775.

[14] Shukry M, Miller JA. Update on dexmedetomidine: use in nonintubated patients requiring sedation for surgical procedures, Therapeutics and Clinical Risk Management.6 (2010)111-21. DOI:10.2147/TCRM. S5374.

[15] Wijeysundera DN, Naik JS, Beattie WS, Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: A meta-analysis, Am J Med. 114 (2003)742–52. DOI: 10.1016/s0002-9343(03)00165-7. PMID:12829201.

[16] Grant SA, Breslin DS, MacLeod DB, Gleason D, Martin G, Dexmedetomidine infusion for sedation during fiberoptic intubation: a report of three cases, J Clin Anesth. 16 (2004) 124–6. DOI:10.1016/j.jclinane.2003.05.010. PMID: 15110375.

[17] Whizar-Lugo V, Gomez- Ramirez IA, Cisneros- Corral R, Martinez-Gallegos N, Intravenous dexmedetomidine vs Intravenous clonidine to prolong bupivacaine spinal anesthesia. A double blind study, Anestesiaen Mexico.19:3 (2007)143-6.DOI: 10.4103/0259-1162.174465.

[18] Kubre J, Sethi A, Mahobia M, Bindal D, Narang N, Saxena A, Single dose intravenous dexmedetomidine prolongs spinal anesthesia with hyperbaric bupivacaine, Anesthesia, essays and researches. 10:2 (2016) 273-7. DOI: 10.4103/0259-1162.174465. PMID: 27212760.

[19] Al- Mustafa MM, Badran IZ, Abu-all HM, Al- Barazangi BA, Massad IM, Al- Ghanem SM, Intravenous dexmedetomidine prolongs bupivacaine spinal analgesia, Middle East J Anesthesiol. 20:2 (2009) 225-31. PMID: 19583070

[20] Reddy SV, Maderdrut JL, Yaksh TL, Spinal cord pharmacology of adrenergic agonist-mediated antinociception, Journal of pharmacology and Experimental Therapeutics. 213:3 (1980) 525-33. PMID: 6110767.

[21] Hong JY, Kim WO, Yoon Y, Choi Y, Kim SH, Kil HK, Effects of intravenous dexmedetomidine on low -dose bupivacaine spinal anesthesia in elderly patients, Acta Anaesthesiologica Scandinavica. 56:3 (2012) 382-7. DOI: 10.1111/j.1399-6576.2011.02614.x.

[22] Harsoor SS, Rani DD, Yalamuru B, Sudheesh K, Nethra SS, Effect of supplementation of low dose intravenous dexmedetomidine on characteristics of spinal anesthesia with hyperbaric bupivacaine, Indian journal of anaesthesia. 57:3 (2013) 265-9. DOI: 10.4103/0019-5049.115616.

[23] Elcicek K, Tekin M, Kati I, The effects of intravenous dexmedetomidine on spinal hyperbaric ropivacaine anesthesia, Journal of anesthesia. 24:4 (2010) 544-8. DOI:10.1007/s00540-010-0939-9. PMID: 20467879.

[24] Kaya FN, Yavascaoglu B, Turker G, Yildirim A, Gurbet A, Mogol EB, Ozcan B, Intravenous dexmedetomidine, but not midazolam, prolongs bupivacaine spinal anesthesia, Canadian Journal of Anesthesia. 57:1 (2010) 39-45. DOI: 10.1007/s12630-009-9231-6.

[25] Kanazi GE, Aouad MT, Jabbour- Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, Bulbul M, Baraka AS, Effects of low- dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block, Acta Anesthesiologica Scandinavica.50:2 (2006) 222-7. DOI: 10.1111/j.1399-6576.2006.00919. PMID: 16430546.

[26] Reddy M, Narayanappa AB, Babu S, Effects of single bolus dose of intravenous Dexmedetomidine on intrathecal hyperbaric Bupivacaine: a randomized double blind placebo controlled trial, Journal of Society of Anesthesiologists of Nepal.3:1 (2016) 8-12. DOI: 10.3126/jsan.v3i1.14652.

[27] Paudel B, Rai P, Tiwari R, Gautam S, Shubham, Evaluation of the Effect of Single Bolus Dose of Intravenous Dexmedetomidine in Spinal Anaesthesia for Lower Limb Surgeries, BJHS. 5:1 (2020) 970-975. DOI: 10.3126/bjhs.v5i1.29636.