Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 09, 2024

Dexmedetomidine and clonidine as adjuvants to intrathecal 0.75% isobaric ropivacaine in lower limb orthopedic surgery.

Authors: Dr Debasis Sahoo[1], Dr Laxmi Narayan Dash[2], Dr Rupa Pradhan[3], Dr Bimal Prasad Sahu[4], Prof Debadas Biswal[5]

1. Assistant Professor, Department of Anesthesiology, Bhimo Bhoi Medical College and Hospital, Balangir.
2. Assistant Professor, Department of Anesthesiology, SRM Medical College and Hospital, Bhawanipatna, Kalahandi.
3. Assistant Professor, Department of General Medicine, MKCG Medical College and Hospital, Berhampur.
4. Associate Professor, Department of Anesthesiology, MKCG Medical College and Hospital, Berhampur.
5. Professor, Department of Anaesthesiology, SCB Medical College and Hospital, Cuttack.

Corresponding Author: Dr Bimal Prasad Sahu, Associate Professor, Department of Anesthesiology, MKCG Medical College and Hospital, Berhampur. Email. mkcgmcbimal@gmail.com

Abstract:

Introduction: Adjuvants are added to local anesthetics used intrathecally to potentiate and prolong the duration of anesthesia. α-2 agonist clonidine has an established use as additive to local anesthetics in subarachnoid block. Dexmedetomidine is a highly selective α-2 agonist has a wide application during sedation, general anesthesia and intravenous analgesia, but very limited use in intrathecal anesthesia.

Materials and methods: 90 patients posted for lower limb orthopedic surgery were divided into three groups. Group R- received isobaric ropivacaine 0.75%, Group D- isobaric ropivacaine 3 mcg of dexmedetomidine and Group C- isobaric ropivacaine 30 mcg of clonidine through the subarachnoid route. Onset of sensory block, motor block, level of sensory block, degree of motor block were noted for inter group comparison.

Observation: In our study the mean time taken for onset of sensory block was 3.4±0.372 mins in the control group, 2.56±0.379 mins in the clonidine group and 2.24±0.197 mins in the dexmedetomidine group. The time taken for regression of sensory block by two segments in the present study was 81.33±6.47 mins in the control group, 122.13±8.46 mins in the clonidine group and 109.4±7.95 mins in dexmedetomidine group. The mean duration of analgesia in our study was 191±22.9 mins in control group, 342.33±28.12 mins in clonidine group and 369.33±34.13 mins in dexmedetomidine group.

Conclusion: From the present study it was concluded that intrathecal dexmedetomidine in the dose of 3µg or intrathecal clonidine in the dose of 30 µg along with 3 ml 0.75% isobaric ropivacaine, in patients undergoing elective lower limb orthopaedic surgeries had decreased onset time for sensory block and motor block and higher level of sensory block, postoperative analgesia, sensory block, motor block. Since there was no clinically significant difference between clonidine and

dexmedetomidine on spinal block characteristics, dexmedetomidine could be an attractive alternative for prolonging spinal analgesia.

Key Words: Intrathecal drug, Clonidine, Dexmedetomidine, Ropivacaine.

INTRODUCTION

Subarachnoid block is widely used in lower extremity surgeries for its simplicity, safety as well as the shorter time period for completion[1,2]. It produces intense sensory, motor and sympathetic blockade. Ropivacaine a long acting anaesthetic structurally related to bupivacaine has a high pKa and low lipid solubility. The efficacy and tolerability of ropivacaine for spinal anaesthesia in orthopedic surgery has been demonstrated in several studies[3]. It produces surgical anaesthesia and analgesia. Many adjuvants have been added to ropivacaine intrathecally to potentiate the effect of local anaesthetics and allow a decrease in the required doses[4,5].

The efficacy and safety of Clonidine, a partial α-2 adrenorecptor agonist and its intrathecal use is well established[6]. Its addition to local anaesthetic prolongs the duration of both motor and sensory spinal blockade[7]. Dexmedetomidine, a highly selective α-2 adrenergic agonist has evolved as a panacea for various procedures in the perioperative and critical care settings[8].

Seema partani.A.K. Chhabra et al[9] in a dose-response study investigating the effects of adding clonidine 30 µg and dexmedetomidine 5 µg to a fixed dose of 0.5% hyperbaric bupivacaine (12.5 mg) for lower abdominal surgeries found a significant faster onset of sensory and motor block. Dexmedetomidine provided longer duration of sensory and motor block and post-operative analgesia as compared to clonidine with minimal hemodynamic alterations. Shweta Kujur, K. K. Arora et al[10] investigated the effects of adding clonidine 30 µg and dexmedetomidine 3 µg to a fixed dose of 0.75% isobaric ropivacaine (22.5 mg) for lower limb orthopaedic surgery and found that intrathecal Dexmedetomidine or Clonidine added with isobaric ropivacaine did not produce any significant hemodynamic instability or sedation. Mean time for onset of sensory and motor block was quite low in dexmedetomidine group whereas mean duration of sensory and motor block was also quite prolonged ($p<0.001$). Hence, the present study was being undertaken to evaluate and compare the effects of dexmedetomidine and clonidine as intrathecal adjuvants to ropivacaine.

AIM AND OBJECTIVE

To evaluate the effects of dexmedetomidine and clonidine as intrathecal adjuvant to ropivacaine on the duration and quality of anaesthesia with regards to time taken for onset of sensory block, level of sensory blockade attained and time taken for the same, maximum grade of motor blockade attained and time taken for the same, time taken for sensory block regression by two segments, duration of analgesia and adverse effects.

MATERIALS AND METHODS

A prospective randomized comparative study was conducted in SCB Medical College, Cuttack after obtaining ethical permission from hospital ethical committee. The study was conducted on 90 hospital inpatients of ASA grade I and II after taking informed consent scheduled for lower limb orthopedic surgeries between September 2022 to October 2023. Patients having no risk factors like IHD, diabetes or hypertension were included in the study. Patients with preexisting neurological or

spinal deformities, allergic to local anesthetics, pregnant women or lactating mother, taking ACE Inhibitors, calcium channel blocker, α-2 receptor blocker or anticoagulants were excluded from the study. Group R- Received 3.5 ml of 22.5mg of isobaric ropivacaine 0.75%, Group D- Received 3.5ml of 22.5mg of isobaric ropivacaine 0.75% with 3 mcg of dexmedetomidine and Group C- Received 3.5ml of 22.5mg of isobaric ropivacaine 0.75% with 30 mcg of clonidine.

Stardard fasting guidelines of eight hours was followed for all patients and in the operating room preloading was done with 500ml of ringer lactate solution. Lumbar puncture was performed in sitting position with 25-gauge Quincke's spinal needle under aseptic precautions and 3.5 ml of study drug was injected. The anaesthesiologist who administered anaesthesia was blinded to the group allocation. Vitals were recorded every 2 minutes up to the 10 minutes and every 5 minutes thereafter up to 20 minutes and beyond 20 minutes the vitals were recorded every 20 minutes till the discharge from PACU (Post Anaesthesia Care Unit). Onset of sensory block, motor block, level of sensory block, degree of motor block were noted for inter group comparison.

The sensory dermatome level was assessed by pin prick method. The motor dermatome level was assessed according to the modified Bromage Scale. Time to reach T-10 dermatome and to reach the Bromage 3 level was noted after which the surgical procedure was initiated. Time to regress to dermatome L-1 and time to reach Bromage 0 was noted in the post-operative care unit. All durations were calculated taking the spinal injection time as time zero. The pain score was recorded by using visual analog pain scale (VAS) between 0 and 10 (0 = no pain, 10 = severe pain). Diclofenac Sodium was used as rescue analgesia when VAS was greater than 4. Sedation was assessed by using Modified Ramsay sedation scale. Hypotension was defined as a decrease in systolic blood pressure more than 30% from baseline or SBP less than 90mmHg which was treated by Ephedrine 6 mg. Bradycardia was defined as heart rate less than 60/min and atropine 0.6mg was used when heart rate falls below 50/min. Side effects including nausea, vomiting, bradycardia, hypotension, respiratory depression, urinary retention, shivering were assessed intra-operatively as well as post-operatively.

Statistical analysis- Data was represented as Mean +/- Standard deviation. Categorical variables were analyzed using Chi-square test. For comparison of three groups Anova test was used. P value <0.05 was taken as statistically significant. Power of study was represented as β, which will be equal to 0.80. To calculate the sample size a two sided α error of 0.05 and a power of 0.80was taken.

OBSERVATION

Demographic Data

	Group R	Group D	Group C	P value
Age (Years)	39.13±10.05	43.53±10.41	41.63±9.85	0.244
Male:Female	20:10	19:11	16:14	0.543
ASA I& II Ratio	21:9	18:12	20:10	0.708
Weight (Kg)	66.87±7.20	66±7.82	64.83±7.50	0.572
Height (cm)	166.47±6.40	164.43±5.92	163.6±5.62	0.205

Duration of surgery (Min)	81.7±22.18	82.83±19.4	83.33±20.9	0.599

Block characteristics

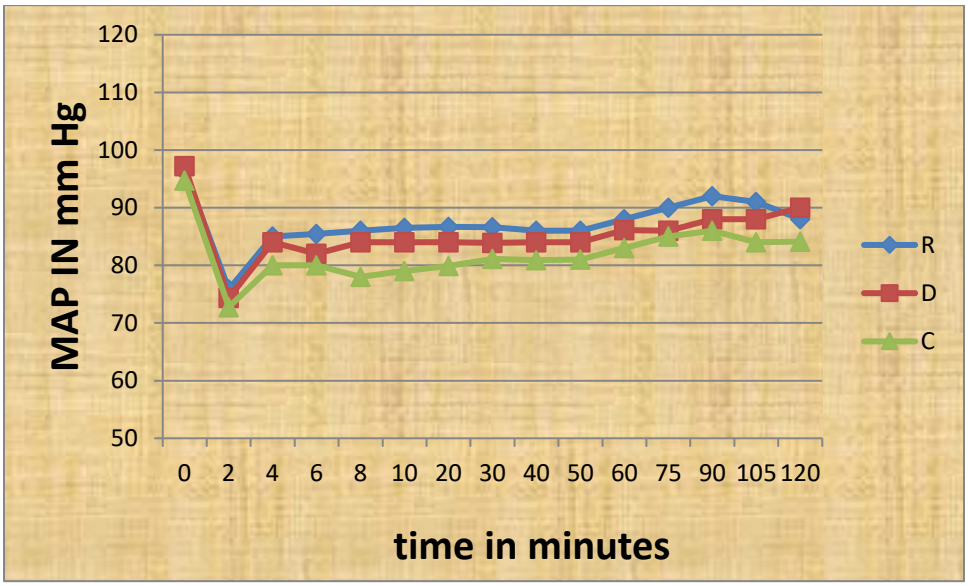
Parameters	Group R	Group D	Group C	P value
Time to achive T10 sensory block	3.44±0.372	2.24±0.197	2.56±0.379	<0.001
Time from injection to highest sensory level (Min)	12.86±0.633	11.65±0.447	12.34±0.3	<0.001
Time for regression of sensory block by two segments (Min)	81.33±6.47	122.13±8.46	109.4±20.93	<0.001
Time taken for sensory blockade regression to S2	172.2±33.50	286.6±50.21	265.83±20.93	<0.001
Time taken from injection to 1st dose of rescue analgesia	192.66±18.18	339.5±28.80	287.16±14.60	<0.001
Time for onset of motor block	4.06±0.38	2.89±0.24	3.34±0.30	<0.001
Time taken for motor blockade regression to bromage 0	156.66±10.28	232.76±23.10	214.43±21.82	<0.001

Bonferroni post hoc analysis of block quality between groups

P value	Group R Vs Group D	Group R Vs Group C	Group D Vs Group C
Time to achive T10 sensory block	<0.001	<0.001	<0.001
Time from injection to highest sensory level	<0.001	<0.001	0.0025
Time for regression of sensory block by two segments	<0.001	<0.001	>0.01
Time taken for sensory blockade regression to S2	<0.001	<0.001	>0.05

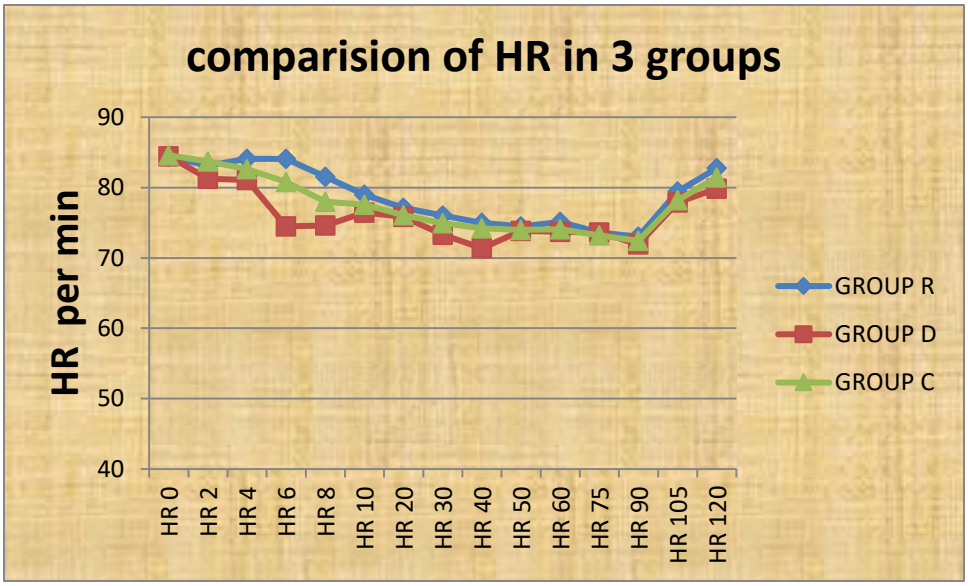
Time taken from injection to 1st dose of rescue analgesia	<0.001	<0.001	0.001
Time for onset of motor block	<0.01	<0.01	<0.01
Time taken for motor blockade regression to bromage 0	<0.001	<0.001	0.004

Mean blood pressure:



Mean blood pressure was comparable in all three groups and was statistically not significant.

Comparison of Heart rate among the groups



Side effects in each group

Side effects	No. of patients			Kruskal wallis P value
	R	D	C	
Hypotension	3(10%)	3(10%)	4(13.33%)	0.895
Bradycardia	2(6.66%)	4(13.33%)	3(10%)	0.693
Resp. depression	0	0	0	1
Nausea, vomiting	1(3.33%)	3(10%)	2(6.66%)	0.589
Shivering	4(13.33%)	1(3.33%)	2(6.66%)	0.342

DISCUSSION

Clonidine is a selective partial alpha-2 adrenergic agonist. The analgesic effect of clonidine is mediated spinally through activation of post synaptic alpha-2 receptors in substantia gelantinosa of spinal cord. It also activates the descending inhibitory pathways (medullospinal pathways) and there by decreases the release of nociceptive substances from substantia gelatinosa. Clonidine has found a definitive place as an adjuvant to ropivacaine to prolong the duration of analgesia.

Dexmedetomidine an α-2adrenergic agonist is pharmacologically related to clonidine and is the most recent agent in this group approved by FDA in 1999 for the use in humans as short term medication (<24 hrs) for analgesia and sedation in intensive care unit. Dexmedetomidine is a highly selective alpha 2 agonist with 8 times more affinity for alpha 2 receptors than clonidine. The ratio of alpha 1:alpha 2 receptor affinity for dexmetomidine is 1:1620 and for clonidine is 1:220. It is commonly used for premedication and as an adjunct to general anaesthesia. It reduces opioid and inhalational anaesthetic requirements.

The groups were comparable with respect to age, sex, height and body weight. The types of surgeries performed were identical in both the groups. The parameters were kept identical in both the groups to avoid variations in the intraoperative and postoperative outcome of the patients.

In our study the mean time taken for onset of sensory block was 3.4±0.372 mins in the control group, 2.56±0.379 mins in the clonidine group and 2.24±0.197 mins in the dexmedetomidine group. Significant decrease in the onset of sensory blockade in clonidine group and in the dexmedetomidine group compared to the control ropivacaine group. The onset was shorter in group D than group C which was statistically significant P<0.001.

This study concurs with the study by Sweta kujur et al[10] but the mean onset of sensory block was significantly prolonged in their study. For group C it was (369±38.3 sec), for group R it was (726±32.06 sec), the mean onset of sensory block for group D was (112±34.2 sec) similar to our study.

The mean time taken for maximum sensory blockade in the present study was 12.86±0.633 mins in the control R group, 12.34±0.3 mins in clonidine group and 11.65±0.447 mins in dexmedetomidine group. There was a statistically significant decrease in the mean time taken for the maximum sensory blockade in the clonidine group and dexmedetomidine group compared to the control group.

In this study the maximum level of sensory blockade achieved was T5. Two out of 30 patients in control R group, 8 out of 30 patients in clonidine group and 12 out of 30 patients in dexmedetomidine group had T5 level of sensory blockade. There was no statistical significant difference in the maximum level of sensory blockade in the clonidine group and dexmedetomidine group compared to the control group. This differed from the study done by Sweta kujur et al[10] where level of sensory block achieved was up to T 10 in group R, T8 in group D and T 7 in group C patients.

The time taken for regression of sensory block by two segments in the present study was 81.33±6.47 mins in the control group, 122.13±8.46 mins in the clonidine group and 109.4±7.95 mins in dexmedetomidine group. There was a statistically significant increase in the mean time taken for regression of sensory block by two segments in clonidine group and dexmedetomidine group compared to the control group. In a study conducted by Kanazi GE et al.[11] it was observed, the time taken for regression of sensory block by two segments to be 80±28 mins in control group, 101±37 mins in clonidine group and 122±37 mins in dexmedetomidine group, with significant prolongation of two segment regression compared to the control group.

The time taken for sensory block to regress to S2 in the present study was 172.2±42.41 mins in the control group, 286.6±24.6 mins in the clonidine group and 265.83±30.61 mins in the dexmedetomidine group. There was a statistically significant increase in the mean time for regression of sensory block to S2 in clonidine group and dexmedetomidine group compared to the control group. This was comparable with the study conducted by Sweta kujur et al[10] where the time taken for regression of sensory block to S2 was less in control group than clonidine and dexmedetomidine.

The mean duration of analgesia in our study was 191±22.9 mins in control group, 342.33±28.12 mins in clonidine group and 369.33±34.13 mins in dexmedetomidine group. There was a statistically significant increase in the duration of analgesia in dexmedetomidine and clonidine group compared to the control group. It was consisted with the study conducted by Grandhe RP et al.[12] where the mean duration of analgesia was 3.8 ±0.7 hours in the control group and 6.3±0.8 hours when using clonidine of 1µg/kg with a mean weight of 60.6±19.4 kg.

The mean time for onset of motor block was 4 ±0.38 mins in control group, 3.34±0.24 mins in clonidine group and 2.89±0.30 mins indexmedetomidine group. There was a statistically significant decrease in the mean time for onset of motor blockade in the dexmedetomidine group and clonidine group compared to the control group. Significant decrease in the mean time for onset of motor blockade in the dexmedetomidine group and clonidine group compared to the control group was similar to study done by Sweta kujur et. al.[10]

The mean duration of motor blockade was 156.66±10.28mins in control group, 214.43±21.82 mins in clonidine group and232.76 ±23.1 mins in dexmedetomidine group. Significant increase in the duration of motor blockade was observed in dexmedetomidine group and clonidine group compared to the control group. Similar results were observed by Sweta kujur et al[10] where the motor block lasted significantly longer in group D (220 ± 35.4 min) & group C (175.4 ± 30 min) as compared to group R (110± 23.8 min) ($P < 0.001$).

There was no statistically significant difference between the groups regarding mean arterial pressue and decrease in the mean heart rate. However it was found that there was a delay in maximum decrease in the mean heart rate in the clonidine group compared to the dexmedetomidine group and the control group. There is higher mean sedation score in D group and C group than R group. Nausea and vomiting and shivering was not statistically significant on analysis ($p>0.05$).

CONCLUSION

From the present study it was concluded that intrathecal dexmedetomidine in the dose of 3µg or intrathecal clonidine in the dose of 30 µg along with 3 ml 0.75% isobaric ropivacaine, in patients undergoing elective lower limb orthopaedic surgeries had decreased onset time for sensory block and motor block and higher level of sensory block, postoperative analgesia, sensory block, motor block. Since there was no clinically significant difference between clonidine and dexmedetomidine on spinal block characteristics, dexmedetomidine could be an attractive alternative for prolonging spinal analgesia.

BIBLIOGRAPHY

1. Mauermann WJ, Shilling AM, Zuo Z. A Comparison of Neuraxial Block Versus General Anesthesia for Elective Total Hip Replacement: A Meta-Analysis. Anesth Analg [Internet]. 2006 Oct [cited 2017 Dec 2];103(4):1018.
2. Valentin N, Lomholt B, Jensen JS, Hejgaard N, Kreiner S. SPINAL OR GENERAL ANAESTHESIA FOR SURGERY OF THE FRACTURED HIP? A Prospective Study of Moratality in 578 Patients. BJA Br J Anaesth. 1986;58(3):284–291.
3. McNamee DA, McClelland AM, Scott S, Milligan KR, Westman L, Gustafsson U. Spinal anaesthesia: comparison of plain ropivacaine 5 mg ml–1 with bupivacaine 5 mg ml–1 for major orthopaedic surgery. BJA Br J Anaesth [Internet]. 2002 Nov 1 [cited 2017 Nov 27];89(5):702–6.
4. Gautier P, De Kock M, Huberty L, Demir T, Izydorczic M, Vanderick B. Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section. BJA Br J Anaesth [Internet]. 2003 Nov 1 [cited 2017 Nov 27];91(5):684–9.
5. Gautier PE, Kock MD, Steenberge AV, Poth N, Lahaye-Goffart B, Fanard L, et al. Intrathecal Ropivacaine for Ambulatory Surgery A Comparison between Intrathecal Bupivacaine and

Intrathecal Ropivacaine for Knee Arthroscopy. Anesthesiol J Am Soc Anesthesiol [Internet]. 1999 Nov 1 [cited 2017 Nov 27];91(5):1239–1239.

6. Gordh T, Post C, Olsson Y. Evaluation of the Toxicity of Subarachnoid Clonidine, Guanfacine, and a Substance P-Antagonist on Rat Spinal Cord and Nerve Roots: Light and Electron Microscopic Observations after Chronic Intrathecal Administration. Anesth Analg [Internet]. 1986 Dec [cited 2017 Nov 27];65(12):1303.
7. Yaksh TL, Reddy SV. Studies in the primate on the analgetic effects associated with intrathecal actions of opiates, alpha-adrenergic agonists and baclofen. Anesthesiology [Internet]. 1981 Jun [cited 2017 Nov 27];54(6):451–67.
8. Grewal A. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol [Internet]. 2011 [cited 2017 Nov 27];27(3):297–302.
9. Partani S, Chhabra AK, Goyal S, Sharma NP, Bhateja S, Gupta S. Comparative analysis of injection clonidine and injection dexmedetomidine added to injection bupivacaine for spinal anaesthesia in lower abdominal surgeries. Int J Res Med Sci [Internet]. 2017 Jan 3 [cited 2017 Dec 6];4(7):2967–71.
10. Kujur S, Arora KK, Murthy MG, Ekka JPS. A comparative study on effects of intrathecal ropivacaine plus dexmedetomidine versus ropivacaine plus clonidine. Int J Res Med Sci [Internet]. 2017 Jan 9 [cited 2017 Dec 2];3(6):1478–83.
11. Scheinin H, Aantaa R, Anttila M, Hakola P, Helminen A, Karhuvaara S.Reversal of the sedative and sympatholytic effects of dexmedetomidine with specific alpha-2 receptor antagonist atipamazole; pharmacodynamioc and kinetic study in healthy volunteers. Anaesthesiology 1998;89:574-84.
12. Ghai, B., Grandhe, R.P., Kumar, A., et al. (2005) Comparative Evaluation of Midazolam and Ketamine with Midazolam Alone as Oral Premedication. Pediatric Anesthesia,15,554-559.https://doi.org/10.1111/j.1460-9592.2004.01523.x