A study to compare using 0.5% of hyperbaric bupivacaine with clonidine and dexmedetomidine low dose for the lower limb surgeries in a tertiary care hospital

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Abstract

Introduction: Pain relief after Operation is one of the most common growing concern for an anesthesiologist as an uneventful postoperative period makes surgery a comfortable proposition for surgical patients. Perkins and co-workers provided an insight into the reality that poorly managed acute pain like postoperative pain can lead to the occurrence of chronic pain.

Objective: To compare the effect, onset and degree of sensory and motor blockade of using Hyperbaric Bupivacaine Hydrochloride of 0.5% with clonidine along with dexmedetomidine.

Materials and Methods: A Comparative study was carried out by the Department of Anesthesiology, G. R. Medical College and J. A. Group of Hospitals, Gwalior (M.P.). This study was done on 120 patients who were undergoing lower limb surgery belonging to either sex with age group 18-60 years. 40 Patients were allocated into different groups by randomization technique.

Results: The time of onset of sensory blockade was found to be Quicker in Group 2 & 3 when compared with Group 1 where the time was 5.78 ± 0.97 mins, 2.88 ± 0.85 mins and 2.90 ± 0.81 mins in Group 1, Group 2 and Group 3 respectively. The Onset of motor blockade was found to be earlier in Group 2 & 3 as compared to Group 1 i.e. 8.38 ± 1.25 mins in Group 1, 5.28 ± 0.64 mins in Group 2 & 5.38 ± 0.63 in Group 3.

Conclusion: From the study we concluded that there is no additional benefits by adding either clonidine or dexmedetomidine to hyperbaric bupivacaine resulted in increasing the action of sensory and motor blockade.

Keywords: Pain, Clonidine, Subarachnoid block, Sensory block, Motor block.

Introduction

"Pain is perfect misery, worst of all evils, and when excessive, overturns all patience.

The task of medicine is to preserve, restore health and to relieve pain. Understanding pain is essential to both these goals.¹ Pain is derived from the Latin word plena which means penalty or punishment.²

Postoperative pain relief is a growing concern for the anesthesiologist and making the procedure the uneventful during the postoperative period and making the surgery a sucess.³ Perkins and co-workers provided an insight into the reality that poorly managed acute pain like postoperative pain can lead to the occurrence of chronic pain.⁴

Opioid acting on the central neural system which are given either intrathecal or epidurals had given the better benefit of selective pain relief without affecting sensory or motor Blockade.

The complication of respiratory depression seen among the patients was one of the major reason to prompted further research for the development of non-opioid analgesics which has lesser side effects when compared to opioid analgesica.⁵

Intrathecal adreno receptor which are alpha 2 receptor sensitive acting as a to agonist clonidine is being extensively evaluated as an alternative to the neuraxial opioids in the reduction of the pain. Further it has been also proved to be a potent analgesic which has lesser side effects when compared to opioids drugs.⁶

The alpha 2 receptor agonist drug along with the clonidine presented wide range of actions and also it has the ability to potentiate the functions of local Anesthesia. When

compared to the opioids drugs the central acting drug like clonidine will not be producing complications like pruritus and depression of respiratory centers. Clonidine has other benefits also like prolonging the necessary blockade and reducing the amount of local anesthesia which was required to produce analgesia after the surgery.⁷⁻¹⁰

Another alpha 2 adrenergic agonist drug namely Dexmedetomidine, has a benefit of increasing the duration of motor and sensory blockade and reduction of onset of motor blockade when combined with intrathecal bupivacaine for urological procedures. ¹¹ One of the major advantage of using dexmedetomidine is that it has high selectivity when compared to the action of clonidine for $\alpha 2A$ receptors which are responsible for the hypnotic and analgesic effects.

Hence, this study was designed to compare the effects of using clonidine and dexmedetomidine on characteristics of spinal anesthesia produced by Hyperbaric Bupivacaine hydrochloride 0.5%.

Objective

To compare the effect of using 0.5% Hyperbaric Bupivacaine Hydrochloride with clonidine $(30\mu g)$ and dexmedetomidine $(5\mu g)$ in the onset and degree of sensory and motor blockade.

Materials and Methods

A Comparative study was done by the Department of Anesthesia at G. R. Medical College and J. A. Group of Hospitals, Gwalior (M.P.).

A total of 120 patients who were posted for the lower limb surgeries of both the gender within the age group of 18-60 years were included in the study.

Out of the selected patients were blinded by sealed envelope technique and observer anesthesiologist was kept unaware of which drug was injected to which patient thus avoiding observer bias. The anesthesiologist who performed the spinal anesthesia took no further part in the study.

Selected 120 patients were divided randomly in three groups depending upon the drug given.

Group 1 (n=40)	Hyperbaric bupivacaine 0.5% (3 ml) + Normal saline (0.5%) injected through intrathecal.				
Group 2	Hyperbaric bupivacaine 0.5% (3 ml) + 30 μg				
(n=40)	clonidine (0.5 ml) Given intrathecal.				
Group 3	Hyperbaric bupivacaine 0.5% (3 ml) + 5 μg				
(n=40)	dexmedetomidine (0.5 ml) Given intrathecal.				

A predefined criterion was establishing for Respiratory depression Bradycardia and hypotension. Onset time for Sensory Blockade was checked by pin prick for every 5 seconds in any dermatome up to T10 level. The sensory blockade duration was obtained from the time of onset of sensory block to sensory regression below the level of L1.

Motor blockade onset was calculated from the time taken when the intrathecal drug injection till the development of Motor blockade, where the person was unable to move the legs and feet. The total time duration of Motor blockade was measured from the onset of complete motor blockade till the time taken when the patient was just able to flex the knee along with the free movement of feet.

The effect of analgesia was calculated from the onset of sensory blockage to the first request for additional analgesia. Visual analogue scale (VAS) was used for the measurement of the pain among the subjects.

Patients were closely observed in the intraoperative and postoperative period for the adverse effects seen among the subjects like vomiting, dyspnoea, nausea, chest pain, respiratory depression, sedation, dysrhythmia, shivering, bradycardia, hypotension and any other.

The observations were recorded, tabulated and statistical analysis carried out by using appropriate statistical software. Student "t" test was used for the inter group analysis. The association was found to statistically significant when the p value was < 0.05.

Results

Out of the total 120 study subjects, 40 subjects were chosen in each of the groups 1, 2 and 3.

All the parameters were compared between the Group 1 and 2, Group 1 and 3, Group 2 and 3.

Table 1: Study participants demographic profile

Variable	Group 1	Group 2	Group 3	
Age(yrs.) (mean \pm SD)	41.83 <u>+</u> 10.24	41.18 <u>+</u> 10.68	41.15 <u>+</u> 10.45	
Weight (in Kg)	60.60 <u>+</u> 9.14	60.43 <u>+</u> 10.44	61.30 <u>+</u> 9.64	
Height (in cm)	162.40 <u>+</u> 3.00	161.03 <u>+</u> 3.68	161.93 <u>+</u> 3.78	
Sex(M:F)	18:22	19:21	18:22	

The mean age in our study was 41.83 ± 10.24 , 41.18 ± 10.68 and 41.15 ± 10.45 years among Group 1, Group 2 and Group 3. The percentage of the female participants was much higher than the male participants in the study.

The association between the Group 1 Vs 2, Group 1 Vs 3, Group 2 Vs 3 was found to not significant statistically for all the demographic variables like age, weight and height.

Table 2: Onset and duration of sensory and motor blockade with analgesia duration and VAS score between three groups

Parameters	Group 1		Group 2		Group 3	
Farameters	Mean	SD	Mean	SD	Mean	SD
Sensory blockade onset time in minutes	5.78	0.97	2.88	0.85	2.90	0.81
Motor blockade onset time in minutes	8.38	1.25	5.28	0.64	5.38	0.63
Sensory blockade Duration in minutes	165.25	24.70	208.08	11.79	209.03	11.07
Motor blockade Duration in minutes	123.75	7.19	170.45	19.28	171.08	20.23
Analgesia Duration (mins)	179.98	21.46	346.10	58.48	350.10	56.40
VAS at time of first analgesia request	62.25	10.97	35.50	9.86	35.00	8.47
Sedation score	1.18	0.38	2.15	0.36	2.10	0.30

In the above table shows the (mean \pm SD), time taken for the onset of sensory blockade was 5.78 \pm 0.97 mins, 2.88 \pm 0.85 mins and 2.90 \pm 0.81 mins among the Group 1, Group 2 and Group 3 respectively.

A duration of 8.38 ± 1.25 mins in Group 1 was the time taken for the onset of complete motor blockade, among Group 2 it was 5.28 ± 0.64 mins and 5.38 ± 0.63 in Group 3.

The total time duration of sensory blockade in our study was found to be 165.25 ± 24.70 mins in group 1, Group 2 had

 208.08 ± 11.79 mins and 209.03 ± 11.07 mins in Group 3. The Mean total duration of motor blockade in minutes seen in our study was found to be 123.75 ± 7.19 mins in Group 1, group 2 it was 170.45 ± 19.28 mins & 171.08 ± 20.23 mins in Group 3

The total duration of analgesia in our study among Group 1 was 179.98 \pm 21.46 mins, Group 2 346.10 \pm 58.48 mins and 350.10 \pm 56.40 in Group 3.

The VAS Score at time of first analgesia request was found to be 62.25 ± 10.97 in Group 1, Group 2 it was 35.50 ± 9.86 and Group 3 it was 35.00 ± 8.47 .

The (mean \pm SD), sedation score was 1.18 ± 0.38 mins in Group 1, 2.15 ± 0.36 mins in Group 2 & 2.10 ± 0.30 in Group 3

Maximum sensory level achieved by all groups is T4 and sensory blockade was achieved at Highest level was T6.

Table 3: Inter-group statistical comparison between three groups for different variables

	Group 1 vs 2		Group 1 vs 3		Group 2 vs 3	
Groups	t-value	p-value	t-value	p-value	t-value	p-value
Sensory blockade Onset	14.22	Sig	14.41	Sig	0.10	0.91
Motor blockade Onset	13.96	Sig	13.55	Sig	0.70	0.48
Sensory blockade Duration	9.90	Sig	10.23	Sig	0.37	0.71
Motor blockade Duration	14.35	Sig	13.94	Sig	0.14	0.88
Analgesia Duration	16.87	Sig	17.83	Sig	0.31	0.76
VAS	11.47	Sig	12.44	Sig	0.24	0.81

The sensory Blockade onset was found to be statistically significant between the Groups 1 & 2, Groups 1 & 3 and not significant between the group 2 & 3.

The action of Anesthesia in blocking both the Sensory and Motor Blockade in our study was found to be statistically significant between the Group 1 Vs 2 and Group 1 Vs 3 and was not statistically significant between the Group 2 & 3.

The duration of analgesia was statistically significant between Group 1 & 2 and Group 1 & 3 and between Group 2 & 3 statistically not significant.

The VAS Score at the time of first analgesia request was found to statistically Significant between the Groups 1 & 2 and Groups 1 & 3 and statistically non-significant between Group 2 & 3.

Table 4: Comparison of side effects and complications among the groups

Complications	Group 1 vs 2	Group 1 vs 3	Group 2 vs 3
	p-value	p-value	p-value
Nausea and vomiting	0.69	0.69	1.00
Hypotension	0.21	0.21	1.00
Bradycardia	Sig	0.64	0.10
Shivering	Sig	Sig	Sig
Sedation	Sig	Sig	0.36
Sedation score	Sig	Sig	Sig

The side effects and the complication were found to be significant statistically for the Bradycardia, shivering and sedation score in the Group 1 & 2. Between the Group 1 & 3 only shivering and sedation side effects were found to be statistically significant.

Discussion

In the study done by Saxena et al 12 the mean time duration for the onset of sensory blockade was Quicker among the clonidine group (30 μg) when it was compared with the bupivacaine group 3.95 \pm 1.76 min which was highly significant. The mean time duration taken for the onset of motor blockade was quicker for the clonidine group (30 μg) i.e. 2.30 ± 0.45 min when compared to 7.41 ± 0.55 min among the bupivacaine group, which was also found to be significant.

Sethi et al¹³ evaluated the effect of low dose intrathecal clonidine which was used as an adjuvant to bupivacaine and found that the onset of action was clinically and statistically

significant with faster onset in clonidine group compared to bupivacaine groups.

In another study conducted by Kanazi et al¹⁴ evaluated the effect of clonidine (Group 2) & dexmedetomidine (Group 3) as an adjuvant to bupivacaine on 60 patients undergoing transurethral resection of prostate or bladder tumor under spinal anesthesia and found that patients in group 2 & 3 had a significantly shorter onset time of motor block than patients in control group.

In our study it was found that combination of intrathecal bupivacaine with dexmedetomidine or clonidine had reduced the onset of sensory and motor Blockade significantly when compared with Bupivacaine alone.

Our study shows that intrathecal clonidine $(30\mu g)$ or dexmedetomidine $(5\mu g)$ does not affect the cephalic extension of sensory blockade. Our results were comparable with the studies done by Kanazi et al¹⁴ who found that the median peak sensory level reached were T6 in group 1 (Bupivacaine) & group 3 (Dexmedetomidine) and T6.5 in group 2 (clonidine $30\mu g$) without significant differences

between the groups (P >0.3). Seah et al 15 found that 150µg intrathecal clonidine didn't not affect the highest sensory level achieved by 3ml 0.5% hyperbaric bupivacaine. Elia et al 16 found that intrathecal usage of clonidine as an adjuvant to local anesthetic does not affect the cephalic extension of sensory blockade.

In our study, $5\mu g$ dexmedetomidine intrathecal was used along with bupivacaine, but there was no significant difference with respect to the duration of sensory and motor block when compared with clonidine group. In studies done by Al-Ghanem et al, ¹⁷ the effect of addition of 5 μg dexmedetomidine or 25 μg fentanyl intrathecal to 10 mg isobaric bupivacaine in vaginal hysterectomy and he also concluded that 5 μg dexmedetomidine produces more prolonged motor and sensory block as compared with 25 μg fentanyl.

In the another study done by Sethi et al 13 found that intrathecal clonidine 1 µg/kg prolonged the duration of sensory and motor blockade produced by 12.5 mg 0.5% bupivacaine. Niemi, ⁸ Seah et al 15 and Kanazi et al 14 also found similar results of prolonged sensory and motor blockade with intrathecal clonidine.

Our study showed that intrathecal clonidine (30µg) & dexmedetomidine (5µg) increases the duration of analgesia which is similar to the findings of Saxena et al 12 found that the mean duration of analgesia was prolonged in clonidine group (30 µg) 264.75 \pm 44.3 min compared to bupivacaine (control group) 99.75 \pm 21.91 min which was highly significant with p value < 0.01. Al-Mustafa et al, 11 Van Tuijl et al, 19 Dobrydnjov et al 20 and Sethi et al 13 also found that intrathecal clonidine as an adjuvant prolong the time to first analgesic request.

The Kanazi et al²⁹ and Saxena et al³⁴ findings with respect to the VAS score at the time of first analgesia request was similar to our study findings.

In the studies done by Kaabachi et al,²¹ Seah et al,¹⁵ Elia et al¹⁶ and Tuijl et al,¹⁹ the side effects and complications were similar to our study findings.

Conclusion

From the findings of our study we could conclude that using either clonidine or dexmedetomidine to hyperbaric bupivacaine results in earlier onset of sensory & motor blockade, prolongs duration of sensory & motor blockade and duration of analgesia without producing significant hemodynamic or respiratory complication. Moreover, dexmedetomidine did not offer significant advantage over clonidine.

Conflict of Interest: None.

References

- Howard L Fields, Joseph B Martin. Pain-Pathophysiology and Management in Harrison's Principles of Internal Medicine, 15th Edition, McGraw-Hill, 2001.
- Larson MD. History of anesthetic practice, Chapter 1 in Millers 'Anesthesia, Sixth Edition, Elsevier Churchill Livingstone, 2004;3-54.

- Vaswani RK, Raiger LK, Purohit R, Bajaj P. The effect of intrathecal midazolam on postoperative pain relief in orthopedic surgery. Hospital Today 2002;7:150-153.
- Rowling JC. Chronic Pain, Chapter 73 in Millers 'Anesthesia, Sixth Edition, Elsevier Churchill Livingstone, 2004;2763-2784.
- Gustafsson LL, Schildt B, Jackobson K. Adverse effects of extradural and intrathecal opiates; Report of a nationwide survey in Sweden. Br J Anaesth 1982; 54:479-486.
- Eisenach JC. Overview; First international symposium on α 2 adrenergic mechanisms of spinal anaesthesia. Reg Anaesth 1993:18(4S):i-vi.
- Dobrydnjov I, Samarutel J. Enhancement of intrathecal lidocaine by addition of local and systemic clonidine. *Acta Anaesthesiol Scand* 1999;43;556-562.
- Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, hemodynamics and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anaesthesiol Scand 1994;38:724-728.
- Dobrydnjov I, Axelsson K, Samarutel J, Holmstrom B. Postoperative pain relief following intrathecal bupicaine combined with intrathecal or oral clonidine. *Acta Anaesthesiol Scand* 2002;46:806-814.
- Park J, Forrest J and Kolesar R. Oral clonidine reduces postoperative PCA morphine requirements. Can J Anaesth 1996;43:900-906.
- Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. Saudi Med J 2009;30:365–370.
- Saxena H, Singh SK and Ghildiyal SK; Low Dose Intrathecal Clonidine with Bupivacaine Improves Onset and Duration of Block with Haemodynamic Stability. *Internet J Anesthesiol* 2010;23(1).
- Sethi BS, Samuel M, Sreevastava D. Efficacy of Analgesic Effects of Low Dose Intrathecal Clonidine as Adjuvant to Bupivacaine. *Indian J Anaesth* 2007;51(5):415-419.
- Kanazi GE, Aouad MT, Khoury SI, Jazzar AL, Alameddine MM, Yaman RL et al., Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006;50:222-227.
- Seah YS, Chen C, Chung KD, Wong CH, Tan PP. Prolongation of hyperbaric bupivacaine spinal anesthesia with clonidine [Clinical Trial, English Abstract, Journal Article, Randomized Controlled Trial] Ma Zui Xue Za Zhi 1991;29(1):533-537.
- Elia N, Culebras X, Mazza C, Schiffer E and Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: systematic review of randomized trials. *Reg Anesth Pain Med* 2008;33(2):159-167.
- Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, Abu-Ali HM. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gynecological Procedures: A Double Blind Controlled Study. Am J Appl Sci 2009;6:882– 887.
- Sethi BS, Samuel M, Sreevastava D. Efficacy of Analgesic Effects of Low Dose Intrathecal Clonidine as Adjuvant to Bupivacaine. *Indian J Anaesth* 2007;51(5):415-419.
- Tuijl IV, Giezeman MJ, Braithwaite SA, Hennis PJ, Kalkman CJ and Klei VA. Intrathecal low-dose hyperbaric bupivacaineclonidine combination in outpatient knee arthroscopy; a randomized controlled trail. *Acta Anaesthesiol Scand* 2008;52(3):343-349.
- Dobrydnjov I, Axelsson K, Thorn SE, Matthiesen P, Klockhoff H, Holmstrom B et al., Clonidine Combined with Small-Dose Bupivacaine During Spinal Anaesthesia for Inguinal

- Herniorrhaphy; A Randomized Double-Blinded Study. *Anaesth Analg* 2003;96:1496-1503.
- 21. Kaabachi O, Ben Rajeb A, Mebazaa M, Safi H, Jelel C, Ben Ghachem M, Ben Ammar M. Spinal anesthesia in children: comparative study of hyperbaric bupivacaine with or without clonidine. *Ann Fr Anesth Reanim* 2002;21(8):617-621.

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