



Int. J. Modn. Res. Revs.

Volume 3, Issue 10, pp 795-798, October, 2015

ISSN: 2347-8314

ORIGINAL ARTICLE

**COMPARATIVE CLINICAL STUDY OF EFFECT OF ADDING 5µg DEXMEDETOMIDINE
VERSUS 50µg CLONIDINE TO INTRATHECAL 12.5 mg OF 0.5% HYPERBARIC
BUPIVACAINE ON SPINAL BLOCK IN PATIENTS SCHEDULED FOR ELECTIVE LOWER
ABDOMINAL SURGERIES**

¹Dr. C.S. Prakash and ^{*2}Dr. G. Gangadhar Chowdary

¹Professor, Division of Anaesthesia, Rajah Muthiah Medical College & Hospital, Annamalai University,
Annamalainagar – 608 002

^{*2}Post Graduate, Division of Anaesthesia, Rajah Muthiah Medical College & Hospital, Annamalai
University, Annamalainagar – 608 002

Article History: Received 14th September, 2015, Accepted 9th October, 2015, Published 10th October, 2015

ABSTRACT

BACKGROUND AND OBJECTIVES: Uncontrolled postoperative pain may produce a range of detrimental acute and chronic effects. Spinal anaesthesia provided by bupivacaine may be too short for providing postoperative analgesia. This study is conducted to evaluate the efficacy of intrathecal dexmedetomidine or intrathecal clonidine as an adjuvant to hyperbaric bupivacaine with regards to the onset and duration of sensory and motor blockade, as well as postoperative analgesia and adverse effects. **METHODOLOGY:** Ninety patients aged 20-60 years were randomly divided into three groups each group consisting of 30 patients of either sex belonging to ASA class I and II posted for elective lower abdominal surgeries were given spinal anaesthesia using bupivacaine 0.5%, heavy 2.5 ml with either normal saline 0.5 ml (group B) or 50 µg of preservative free clonidine (group C) or 5µg of preservative free dexmedetomidine (group D). Assessment of the sensory and motor blockade were done at the end of each minute till the maximum level achieved. Measurement of blood pressure, pulse rate, respiratory rate and arterial oxygen saturation were obtained. Postoperatively the patients were observed for the duration of analgesia, time taken for complete regression of sensory blockade to S1 and time taken for complete recovery of motor power. **RESULTS:** Our results showed a statistically highly significant prolongation of sensory and motor blockade, time taken for sensory regression by two segments and postoperative analgesia in the dexmedetomidine and clonidine group compared to the control group. **INTERPRETATION AND CONCLUSION:** Hence, it is concluded from our study that dexmedetomidine in the dose of 5 µg or clonidine in the dose of 50 µg when added to the bupivacaine 0.5% heavy prolongs the duration of sensory and motor blockade, time taken for sensory regression by two segments and duration of post operative analgesia.

Keywords: Sensory blockade and motor blockade, Bupivacaine heavy; intrathecal clonidine; intrathecal dexmedetomidine; spinal anaesthesia;

1. INTRODUCTION

Intrathecal α_2 agonist clonidine or dexmedetomidine [DXM] have become very popular among surgeons and anaesthesiologists as an adjuvant to bupivacaine. Results of the previous studies show that addition of either of these two agents intrathecally significantly prolongs the duration of both sensory and motor analgesia of hyperbaric bupivacaine. Clonidine has been used extensively and studied as an

adjuvant to bupivacaine in almost all the types of nerve blocks. The mechanism of action of dexmedetomidine differs from clonidine as it possesses selective α_2 -adrenoceptor agonistic activity especially for the 2A subtype of this receptor, which causes it to be a much more effective sedative and analgesic agent than clonidine. While clonidine has been in use as an adjuvant to bupivacaine in subarachnoid block, there are only a few studies available on human upon intrathecal uses of dexmedetomidine. Therefore we designed this study to compare the effect and side effects of addition of clonidine and dexmedetomidine to intrathecal hyperbaric bupivacaine.

**Corresponding author: Dr. G. Gangadhar Chowdary, Department of Anaesthesia, Rajah Muthiah Medical College Hospital, Annamalai University, Chidambaram*

2. MATERIALS & METHODOLOGY

After approval of institutional ethical committee, prospective, controlled double blind study was carried out in 90 normotensive adult patients of ASA grade I and II undergoing surgeries below the level of umbilicus. Ninety patients in the age group between 20 years and 60 years of either sex belonging to ASA Grade-I and Grade-II posted for elective lower abdominal surgeries without any co-morbid diseases were grouped randomly into three groups (n=30). Randomization was done using simple sealed envelope technique:

Group B (control group): received 12.5mg of 0.5% hyperbaric bupivacaine with 0.5ml normal saline.

Group C (clonidine group): received 12.5mg of 0.5% hyperbaric bupivacaine with 50µg clonidine.

Group D (dexmedetomidine group): received 12.5mg of 0.5% hyperbaric bupivacaine with 5µg dexmedetomidine.

The doses of dexmedetomidine and clonidine were chosen according to a 1:10 ratio found to be equipotent and would produce similar effects on the characteristics of bupivacaine spinal anaesthesia. Preoperative assessment will be done for each patient and written informed consent is taken. Patients will be kept NPO for solids 6hrs and clear fluids 2 hrs before surgery. Patients will be premedicated on the night before surgery with Tablet Ranitidine 150mg and Tablet Alprazolam 0.5mg. Intravenous line obtained with 18 gauge cannula and preloaded with Ringer lactate 500ml half an hour before anaesthesia. Monitoring will be done using multiparameter monitor having pulse oximetry, ECG and NIBP

The test drugs are prepared by the senior anaesthesiologist who is not involved in the study, Clonidine (Cloneon; 150 µg/ml of Neon laboratories) is diluted to 1.5 ml with normal saline and 0.5 ml (50 µg) of it will be added to 2.5 ml of 0.5% hyperbaric bupivacaine. Dexmedetomidine (Dexem 50 µg/0.5 ml, of Themes Laboratories) 0.5 ml is diluted to 5 ml with normal saline and 0.5 ml of this is added to 2.5 ml of 0.5% hyperbaric bupivacaine. The observer and the patient are blinded for the study drug.

The following parameters are noted,

- Onset of sensory blockade and motor blockade.
- Maximum level of sensory blockade attained and the time taken for the same will be noted.
- Maximum level of motor blockade attained and the time taken for the same will be noted.
- Two segments sensory regression time will be noted.
- Total duration of analgesia will be noted.
- Total duration of sensory blockade and motor blockade will be noted
- Sensory blockade will be tested using pinprick method with a blunt tipped 27G needle at every minute for first 5 mins and every 5 mins for next 15 mins and every 10 mins for next 30 mins and every

15 mins till the end of surgery and there after every 30 mins until sensory block is resolved.

- Quality of motor blockade will be assessed by modified Bromage scale.

Haemodynamic monitoring will be done during the block every 5 mins for first 15 mins and every 10 mins for next 30 mins and once in 15 mins till the end of surgery and post operatively every hourly employing multi parameter monitor which displays heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure (DBP), mean arterial pressure (MAP), ECG and SpO2 hourly.

STATISTICAL ANALYSIS

A sample size of 25 patients per group was determined through power analysis (a ¼ 0.05; b ¼ 0.80) to detect an increase of 30 min in the time of a two dermatome sensory regression with a standard deviation of 28 min. Considering the drop outs, 30 patients were selected for each group in our study. Results are expressed as the means and standard deviations, medians and ranges, or numbers and percentages. The comparison of normally distributed continuous variables between the groups was performed using one-way analysis of variance (ANOVA) and, if appropriate, followed by the Bonferroni test for post hoc analysis. Nominal categorical data between study groups were compared using the chi-squared test or Fisher's exact test as appropriate. Ordinal categorical variables and non-normal distribution continuous variables were Dexmedetomidine or clonidine for supplementation of spinal bupivacaine compared using the Mann—Whitney U-test. P < 0.05 was considered to be significant

3. RESULTS

Table 1 shows the age distribution of the patients in all the three groups. The minimum age in group B (control group), group C (clonidine group) and group D (dexmedetomidine group) were 20 years. The maximum age in group B is 50 years, in group C is 59 years and in group D is 55 years. The mean age in group B is 31.17 ± 9.75 years, group C is 36.6 ± 11.08 years and group D is 33.07 ± 11.58 years. There is no significant difference in the age of patients between the groups. All the three groups were similar with respect to age distribution (p>0.05).

It is found from our study that in dexmedetomidine group and clonidine group there is an early onset of both sensory and motor blockade and a higher level of sensory blockade compared to control group and duration of sensory, motor blockade and duration of analgesia is significantly prolonged in the dexmedetomidine group and clonidine group compared to the control group. Haemodynamics were preserved both intraoperatively and postoperatively. However there was a small percentage of patients who developed significant fall in blood pressure and bradycardia which were easily managed. Seven patients each in dexmedetomidine group and clonidine group and two patients in control group developed hypotension requiring treatment. Five patients in dexmedetomidine group, four

patients in clonidine group and one patient in control group developed bradycardia requiring treatment.

TABLE: 1 AGE DISTRIBUTION

AGE OF THE PATIENT	GROUPS					
	GROUP B		GROUP C		GROUP D	
	NO.OF PTS	%	NO.OF PTS	%	NO.OF PTS	%
21-30	16	53.3	14	46.7	18	60
31-40	9	30	6	20	2	6.7
41-50	5	16.7	6	20	8	26.7
51-60	0	0	4	13.3	2	6.7
TOTAL	30	100	30	100	30	100
Mean ± SD	31.17±9.752		36.60±11.082		33.07±11.585	
Minimum age in Years	20		20		20	
Maximum age in Years	50		59		55	

TABLE: 2 SEX DISTRIBUTION

	GROUPS					
	GROUP B		GROUP C		GROUP D	
	NO.OF PTS	%	NO.OF PTS	%	NO.OF PTS	%
MALE	15	50%	20	66.7%	24	80%
FEMALE	15	50%	10	33.3%	6	20%
TOTAL	30	100%	30	100%	30	100%

RESULTS OBTAINED IN OUR STUDY

SPINAL BLOCK CHARACTERISTICS	GROUP B	GROUP C	GROUP D
Time taken for onset of sensory blockade	2.8±0.6 mins	1.43±0.5 mins	1.17±0.379 mins
Time taken for maximum sensory blockade	7.4±1.1 mins	5.9±0.8 mins	5.2±0.71 mins
The time taken for regression of sensory block by two segments	79.46±10.1 mins	136.33±10.9 mins	136.33±11.59 mins
The time taken for sensory block to regress to S1	203.33±42.41 mins	365±24.6 mins	396.16±30.6 mins
Duration of analgesia	191±22.9 mins	342.33±28.12 Mins	369.33±34.13 mins
Onset of motor blockade	4±0.69 mins	1.63±0.49 Mins	1.13±0.346 mins
Time taken for maximum motor blockade	6.57±0.9 mins	6.43±1.04 Mins	5.2±0.88 mins
Duration of motor blockade	166.16±20.95 mins	279±24.68 Mins	303.66±35.95 mins

4.DISCUSSION

The aim of good post operative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. Other method of prolonging analgesia is using a continuous epidural analgesia, which is technically more difficult and more costly.

Hence, an intrathecal additive to these local anaesthetics forms a reliable and reproducible method of prolonged post operative analgesia and to prolong the duration of anaesthesia. This technique being simple and less cumbersome has gained a wide acceptance.

A number of adjuvants to local anaesthetics for spinal anaesthesia like opioids (fentanyl and buprenorphine), benzodiazepines (midazolam), ketamine and neostigmine have been used. The most common agents used are opioids and they have formed a cornerstone option for the treatment of post operative pain. Spinal opiates prolong the duration of analgesia, but they do have drawbacks of late and unpredictable respiratory depression, pruritus, nausea, vomiting and urinary retention which requires constant postoperative monitoring and urinary catheterisation. Hence opioids are not ideally suited for all patients and for ambulant surgeries.

Hence there is a requirement of an adjuvant to be used along with local anaesthetics which can produce prolonged analgesia without the above said side effects of opioids. Intrathecal alpha 2 agonists are found to have antinociceptive action for both somatic and visceral pain. So in this context alpha 2 agonists may be a very useful drug along with the local anesthetic Bupivacaine 0.5% heavy for spinal anaesthesia.

Clonidine is a selective partial alpha-2 adrenergic agonist. It is known to potentiate both sensory and motor block of local anaesthetics. The analgesic effect of clonidine is mediated spinally through activation of post synaptic alpha-2 receptors in substantia gelatinosa 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 bupivacaine spinal anaesthesia to prolong the duration of analgesia. Dexmedetomidine also an α-2 adrenergic 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 intense care unit. Dexmedetomidine is a highly selective alpha 2 agonist with 8times more affinity for alpha 2 receptors than clonidine.

Randomization was done using simple sealed envelope technique. It was found that a sample size of 25 patients per group was required to detect an increase of 30 min in the time of a two-dermatome sensory regression with a standard deviation of 28 min. Considering the drop outs, 30 patients were selected for each group in our study.

So it is hypothesised that both clonidine and dexmedetomidine will produce a prolonged duration of postoperative analgesia compared to the control. There will be no difference regarding the duration of analgesia between clonidine and dexmedetomidine as equipotent doses are used.

5. CONCLUSION

From the present study it can be concluded that intrathecal dexmedetomidine in the dose of 5µg or intrathecal clonidine in the dose of 50 µg along with 2.5 ml bupivacaine, 0.5% heavy, in patients undergoing elective lower abdominal surgeries,

- Decreases the onset time for sensory blockade
- Decreases the onset time for motor blockade
- Produces higher level of sensory blockade
- Produces prolonged postoperative analgesia
- Produces prolonged sensory blockade
- Produces prolonged motor blockade

It was not associated with side effects like CVS side effects change in rate and rhythm, respiratory depression and hence can be an attractive alternative for opioids for prolonging spinal analgesia.

6. REFERENCES

1. Brown DL. Spinal, epidural and caudal anesthesia. 6th ed. Chapter 43. In: Miller's Anesthesia, Miller RD, ed. Philadelphia: Elsevier Churchill Livingstone; 2005. pp. 1653-60.
2. Corbey MP, Bach AB. Transient radicular irritation (TRI) after spinal anaesthesia in day-care surgery. *Acta Anaesthesiol Scand* 1998;42:425-9.
3. Henderson DJ, Faccenda KA, Morrison LM. Transient radicular irritation with intrathecal plain lignocaine. *Acta Anaesthesiol Scand* 1998;42:376-8.
4. Colin VJ. Spinal anesthesia – principles. 3rd ed. In: Principles of anesthesiology. Philadelphia: Lea & Febiger; 1993. pp. 1445-52.
5. Saxena AK, Arava SK. Current concepts in Neuraxial administration of opioids and non opioids: An overview and future perspectives. *Indian J Anaesth* 2004;48 (1):13-24.
6. Etches RC, Sandler A N, Daley MD. Respiratory depression and spinal opioids. *Can J Anaesth* 1989;36:165-85.
7. Morgan M The rationale use of intrathecal and extradural opioids. *Br J Anaesth* 1989;63:165-88.
8. Crone L-AL, Conly J M, Clark KM. Crichlow AC, Wardell CC, Zbitnew A et al. Recurrent herpes simplex virus labialis and the use of epidural morphine in obstetric patients. *Anesth Analg* 1988;67:318-23.
9. Eisenach James C, De Kock Marc, Klimscha, Walter. Alpha sub 2- adrenergic agonist for regional anesthesia. A clinical review of clonidine. *Anesthesiology* 1996;85 (3):655-74.
