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Intrathecal Clonidine as an Adjuvant to Isobaric Levobupivacaine in Gynaecological Surgeries: A Randomized Control Trial

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Abstract

Postoperative pain management is one of the vital duty of an anaesthesiologist apart from managing the patient intraoperatively. Patients presenting for gynaecological surgeries receive subarachnoid block with hyperbaric bupivacaine. Levobupivacaine the pure S-enantiomer of racemic bupivacaine, is a new long-acting local anesthetic that has recently been introduced in the clinical practice with predominant sensory analgesia. By and large opioids are used as adjuvants intrathecally, but their complications at times lead to few unwanted side effects. Intrathecal clonidine has been evaluated as an alternate to neuroaxial opoid for control of pain and has proven to be a potent analgesic This prospective, randomized, double-blind study compared the clinical efficacy, motor block and haemodynamic effects and postoperative analgesia of using 3mL of 0.5% isobaric levobupivacaine plus 0.2ml of 0.9% normal saline (Group LB) Vs 3 mL of 0.5% levobupivacaine with clonidine 30 micrograms (Group LC) for spinal anaesthesia in gynaecological surgery. *Results:* Sensory onset time, (5.12±1.92min) was faster in group LC but no difference in the motor block onset time was found between the groups. Duration of sensory and motor blockade and two segment regression time were significantly lower in levobupivacaine (LB) compared to Levobupivacaine clonidine (LC) group. In group LC, mean arterial pressure was lower than group LB, starting from 10 min until 30 min after injection ($p < 0.05$). Bradycardia was noted in 27% of group LC whereas 3% in LB group. Anaesthesia was adequate and patient satisfaction was good in all cases. Side-effects were minor and infrequent in both groups. *Conclusion:* We conclude that 3 mL of 0.5% levobupivacaine with clonidine 30 micrograms is more effective than 3 mL of 0.5% levobupivacaine alone in spinal anaesthesia for gynaecological surgeries.

Keywords: Levobupivacaine; Spinal Anaesthesia; Clonidine; Postop Pain.

Introduction

Gynaecological surgeries are preferably done under sub-arachnoid block. Bupivacaine is the standard local anaesthetic agent for neuraxial block for these surgeries,and for prolongation of regional anaesthesia, adjuvants like opoids, alpha agonists, epinephrine are added. Clonidine is an alpha – 2 adrenergic agonist, has been extensively used in central neuroaxial and regional blocks acts by increasing the duration and intensity of pain relief, and decreasing the systemic and local inflammatory stress response [1,2].

Levobupivacaine S-enantiomer of racemic bupivacaine has an excellent pharmacodynamic property with significantly decreased cardiovascular [3] and central nervous system [4] toxicity, it seems to be a pleasing substitute for bupivacaine. Comparative clinical studies are available for epidural anesthesia [5,6] peripheral blocks [7,8] obstertrics [9] but none for gynaecological surgeries. This prompted us to undertake a research on levobupivacaine and clonidine.

This was a prospective, randomized control study initiated after the Institutional Ethical Committee approval. Pre-operative evaluation included

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thorough clinical history and examination as well as required investigations. Eighty women of ASA (American Society of Anesthesiologist) status I or II scheduled for gynaecological surgeries were included in the study after obtaining informed written consent. Patients belonging to ASA physical status III and above, height less than 150 cm, any contraindication to regional anaesthesia and any known drug allergy were excluded from the study. Patients were explained about Ten Point visual analogue scale (VAS) prior to the procedure. Randomization was done by computer generated number and randomly allocated in to two groups of 40 each to receive either 3ml of isobaric 0.5% levobupivacaine + 0.2ml Normal Saline (Group LB) or 3ml of 0.5% isobaric levobupivacaine (3ml) + 0.2 ml injection Clonidine 30 μg (Group LC) . All patients were premedicated with T. Ranitidine 150 mg and T. Ondansetron 4 mg two hours prior to surgery. In the operation theatre, patients' baseline hemodynamic and respiratory parameters were noted.

In a sitting position, under all aseptic precautions and using midline approach, subarachnoid block was achieved in L3-L4 space with 25G Quincke's spinal needle and study drug was injected as per the assigned group,over a period of 15-20 seconds without barbotage or aspiration. Patients were immediately placed in the supine position and end of the injection __time was taken as time zero. The patient, the anesthesiologist responsible for intraoperative care, and the individual who performed the postoperative evaluations were blinded to group assignment.

The onset of sensory analgesia and motor blockade were tested. The level of sensory anaesthesia, defined as the loss of sharp sensation by using a pinprick test (20 gauge hypodermic needle), was recorded bilaterally at the mid-clavicular line. The onset of adequate sensory block was defined as the achievement of a sensory block level of T8 dermatome. Surgery was started once the level of sensory block had reached T8.

Motor blockade was assessed with modified Bromage score as follows. Time taken for complete motor blockade was recorded every minute for first 20 minutes.

0 No paralysis, able to flex hips/knees/ankles

1 Able to move knees, unable to raise extended legs

2 Able to flex ankles, unable to flex knees

3 Unable to move any part of the lower limb

The onset time of motor block was defined as the interval between intrathecal administration and to a Bromage score of 3.

In the postanesthesia care unit, the patients were assessed for the following parameters. Status of sensory and motor blockade were monitored every 30 min till the complete recovery of both.

Status of pain, based on a visual analog scale (VAS) ranging from 0 (no pain) to 10 (maximal pain). All tests (i.e., sensory/motor block and VAS) were performed by a staff not involved in the study. Duration of sensory block was defined as the interval between intrathecal administration of the study drug to the point of the VAS score of three.

Duration of motor block was defined as the interval from intrathecal administration to the point in which the Bromage score was back to zero. Hemodynamic alterations like hypotension and bradycardia or any other post-operative events were also noted and treated accordingly. Hypotension was defined as a decrease in the systolic blood pressure of more than 30% from the baseline or less than 90 mmHg. It was treated with infusion of 100ml of ringer lactate solution and/or i.v. boluses of mephentermine 5mg. Bradycardia was defined as a heart rate of less than 50 beats per minute and was treated with i.v. injection of atropine 0.6mg

Sample Size

Assuming an alpha level of 0.05 and a power of 0.80, a minimum of 40 patients in each group were required to detect a mean difference of 30 minutes between groups in duration of sensory analgesia

Statistical analysis: Statistical analysis was performed using the Software SPSS version 17. Data was analysed using one way ANOVA and Bonferroni test was used for "post hoc" comparisons. Categorical variables were analyzed using Chi-square test. A p value less than or equal to 5% was considered as significant. Continuous variables were presented as mean+/-SD or as median (range); categorical data were presented as number.

Results

No significant statistical difference was found in demographic distribution of patients.

Sensory onset time, (5.12±1.92min) was significantly faster in Groups LC but no difference in the onset time of motor block was noted between the groups. Duration of sensory(190.37±12.01)and motor blockade (115±13.15) and two segment regression time (120.50±10.55) were significantly lower in levobupivacaine (LB) compared to

Levobupivacaine clonidine (LC) group. Hypotension was noted in both groups groups (42-50%). In group LC, mean arterial pressure was lower than group LB, starting from 10 min until 30 min after injection ($p < 0.05$) and treated with injection mephentermine 5mg iv in aliquots

Bradycardia was noted in 27% of group LC whereas (3%) in LB ($P < 0.05$) treated with injection atropine 0.5mg iv. Anaesthesia was adequate and patient satisfaction was good in all patients Shivering was more in group LB (20%)

Table 1: Patient characteristics, duration & type of surgery (P value)

Demographic Variables	Group LB	Group LC	P value
Age	42±8	40±6	0.91
Weight	54.±3	56±4	0.92
Height	153±4	152±6	0.86
*ASA 1/2	36/4	35/5	0.68
Duration of surgery	75.5 min	78.5 min	0.95
Type of surgery	Abdominal hysterectomy(32) Ovarian cystectomy(8)	Abdominal hysterectomy(28) Ovarian cystectomy(12)	0.81

* American society of Anesthesiologists (ASA)

Table 2: Study variables studied in both groups

Variables	Group LB	Group LC	P value
Sensory onset time	6.03±1.008	5.12 ±1.923	.035
Motor onset time	6.67±1.47	7.48±2.20	0.175
Two segment regression time	120.50±10.55	190.16±15.25	0.05
Duration of sensory block	190.37 ±12.01	302.05 ±18.65	0.00
Duration of motor block	115±13.15	165±17.25	0.04

Table 3: Statistics for side effects

Side Effects	Group LB	Group LC
Bradycardia	1(4%)	8(27%)
Hypotension	18(42%)	20(50%)
Nausea & vomiting 4(13%)	2(8%)	4(10%)
shivering	8(20%)	1(4%)

The hemodynamic parameters are as depicted graphically

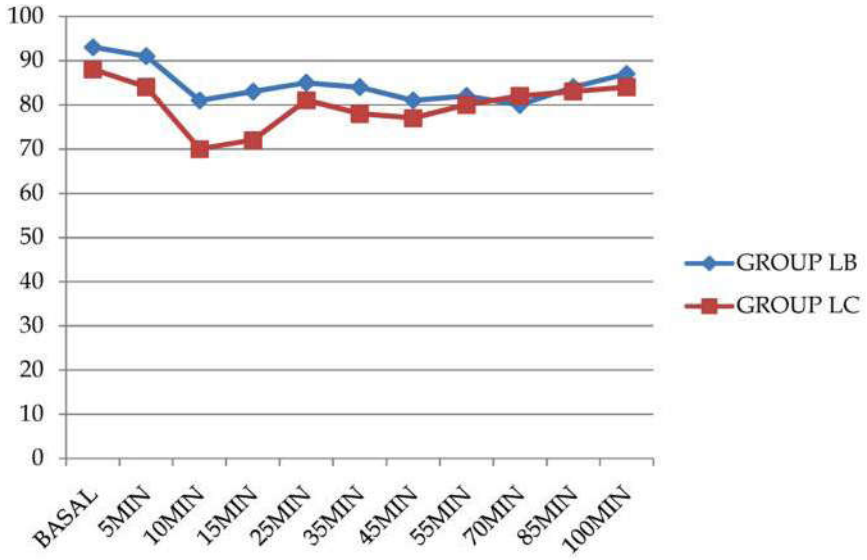

Fig. 1: Mean Arterial Pressure between group

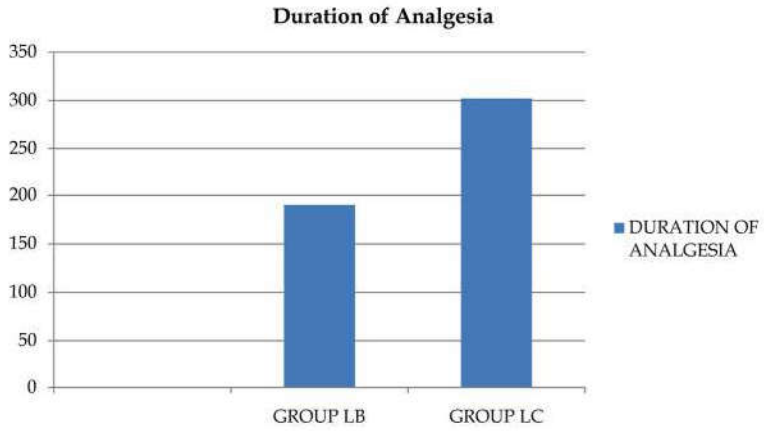

Fig. 2: Duration of sensory block

Discussion

Spinal anaesthesia is usually the technique of choice in gynaecological surgeries because of quick onset , reliability in producing uniform sensory and motor blockade and ease of administration [10]. with short coming of limited duration of action when local anaesthetic alone is used. There are numerous studies comparing bupivacaine with clonidine but only limited studies are available with levobupivacaine and clonidine.

Levobupivacaine has been shown to have less negative inotropic effect and produces less prolongation of the QTc interval than bupivacaine in various studies thus making it as a safer alternative for bupivacaine [11,12,13]. However not many studies have been done to assess the possibility of prolonging the duration of sensory analgesia with either opioids or other adjutants like clonidine.

Clonidine increases acetylcholine concentration in cerebrospinal fluid and activates alpha 2 adrenergic receptors in the dorsal horn of the spinal cord. Alpha 2 adrenoceptors are localised over the primary afferent terminals of neurons in the superficial lamina of the spinal cord and in the nuclei of the brainstem associated with pain. This localisation supports that alpha 2 agonists show their analgesic effects through both peripheral and central pathways [14,15]. Various studies have demonstrated that addition of Clonidine to bupivacaine, even in very small doses, significantly improves the onset and duration of sensory block [16].

In our study sensory onset time was significantly faster in LC group compared with LB. This result was concordant with the study of Jyoti Kulkarni Lodha V, Patil T, et al [17] who compared isobaric bupivacaine with clonidine against isobaric levobupivacaine and found that sensory onset time was faster in levobupivacine and clonidine. But there was no significant difference in the onset of motor block was found between two groups. Earlier studies by Lee Muchhal K, Chan et al [18] also could not elicit any difference in the onset time of motor blockade.

Two segment regression time, duration of motor and sensory blockade were prolonged in group LC and this was inline with the research of Anastassiou, et al [19] who had proved that low dose intrathecal clonidine to levobupivacaine prolongs sensory and duration of motor block time [20].

Bradycardia was noted 27%in LC group and this finding our study was proven in previous studies [21,22].

Shivering was found to be least in group LC (1%) This property of clonidine suppressing the perioperative shivering has been well supported by previous studies but the underlying mechanism of action remains unknown [23].

Conclusion

Clonidine added to levobupivacaine for spinal anaesthesia effectively shortens the sensory onset time and also increases the duration of motor block and postoperative analgesia thus making it as excellent additive of choice with levobupivacaine.

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