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Original Research Paper

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A COMPARATIVE STUDY OF EPIDURAL ROPIVACAINE 0.75% ALONE VERSUS EPIDURAL ROPIVACAINE 0.75% WITH PRESERVATIVE FREE MIDAZOLAM IN VAGINAL HYSTERECTOMIES

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ABSTRACT

A randomized prospective comparative double blind study was conducted on ASA I and II patients of female sex, aged between 30-60 years posted for vaginal hysterectomies. They are divided into two groups of 30 each.

Aims and objectives: To Assess and compare the efficacy of epidural Ropivacaine 0.75% Vs epidural Ropivacaine 0.75% and preservative free Midazolam in terms of onset, duration of sensory and motor blockade, duration of analgesia and to evaluate the incidence of adverse effects and complications associated with vaginal hysterectomies.

After preloading, under aseptic precautions epidural catheter was placed in L3-4 space. In Group A – 18 ml of 0.75% Ropivacaine + 2ml Normal saline injected into epidural space. In Group B 18ml of 0.75% Ropivacaine + 2ml preservative free Midazolam (2mg) injected into epidural space.

The various parameters studied and the results and observations of the two groups were compared. With regard to age, height, the mean sensory level achieved, duration of motor blockade, respiratory rate and oxygen saturation, the difference is considered to be statistically not significant. There was significant difference with regard to duration of analgesia and sedation (Group A 304.33±25.15 min, Group B 318.00±25.78 with P value 0.0421). It can be concluded that addition of preservative free Midazolam 2mg to 18 ml of 0.75% Ropivacaine by epidural route, causes definite prolongation of analgesia together with optimum sedation and without significant side effects.

KEYWORDS :

INTRODUCTION

Regional anaesthesia for gynaecological surgeries is generally safer than general anaesthesia. It avoids general anaesthesia related problems such as polypharmacy, airway manipulation, misplacement of endo tracheal tube, hypo or hyper ventilation, vomiting and pulmonary aspiration. It reduces surgical stress and attenuates increase in plasma catecholamine and other hormones. Regional anaesthesia gives intra and post operative pain relief with full preservation of mental status and normal reflexes.

The popularity of epidural anesthesia is increasing widely. Single shot epidural anaesthesia using local anaesthetics alone provides a relatively short duration of post operative analgesia. Placement of catheter into epidural space to administer repeated doses or running of local anaesthetic solution infusion may increase the risk of infection and delay early mobilization and hence explains its unpopularity.

Therefore adjuvants are needed in order to prolong the analgesic effects of local anaesthetics. The addition of opiods significantly prolongs the duration of epidural analgesia but is associated with a number of unpleasant side effects such as nausea, vomiting, pruritus and urinary retention as well as the risk of respiratory depression. In an attempt to avoid these problems, other non opioid adjuvants such as Clonidine, Ketamine and Neostigmine, were investigated with a variable degree of success, but with significant side effects, eg: hallucination with Ketamine, excessive nausea and vomiting with Neostigmine, as well as sedation and bradycardia with Clonidine which limit their usefulness.

Midazolam[1] is a widely available water soluble benzodiazepine that has been shown to have an analgesic effect by its action on the benzodiazepine GABA receptor complex, when administered via subarachnoid or epidural route. Midazolam also provides amnesia and sedation without major side effects like neurotoxicity.

Ropivacaine belongs to pipecoloxylidides and is homologous to bupivacaine and mepivacaine. It provides more differential block when given epidurally, allowing for a better separation between sensory and motor block. Great advantages of Ropivacaine are its better cardiac profile and low systemic toxicity than both Bupivacaine and Levobupivacaine. This makes it excellent for use in obstetrics and in post operative epidural pain relief.

MATERIALS AND METHODS

After local ethics committee approval and obtaining informed consent, this prospective randomized double blind study was conducted in the department of Anaesthesiology in association with department of Gynaecology at Government General hospital, Nellore. Sixty female patients, of ASA I and II grade, aged 30-60 years, scheduled for elective vaginal hysterectomy were randomized into two groups according to random numbers table. Patients with history of coagulation abnormalities, CNS disorders, peripheral neuropathies, spine anomalies, cardiovascular disorders, infections on the back are excluded from the study.

GROUP A – Receiving epidural anaesthesia with 18ml 0.75% Ropivacaine + 2ml Normal Saline.

GROUP B – Receiving epidural anaesthesia with 18ml 0.75% Ropivacaine and preservative free Midazolam 2mg in 2ml.

Drugs are prepared by an anesthesiologist who was not involved in the performance of epidural block or patient care to control the bias. The patients were advised to remain nil oral after midnight, the day prior to surgery and to take Tab. Ranitidine 150 mg P.O and Tab. Alprazolam 0.25 mg P.O the night before surgery. No premedication is given on the day of surgery.On arrival to the operation theatre, standard monitoring is established (pulse oximetry, non invasive blood pressure, electro cardiography). Intravenous access secured with an 18G cannula. Under strict aseptic precautions, Epidural block performed with standard technique with a Tuohy needle 18G needle, by the loss of resistance to saline technique. 20G Epidural catheter inserted an secured. The inter space chosen was L3-4, if the attempt at this level failed, the L2-3 level was the next choice. Test dose with 3 ml of 1.5% lignocaine with adrenaline (5 µg/ml) injected and patient monitored for signs of intravascular or subarachnoid injection for 5 min. Study drug injected epidurally slowly after ensuring that an aspiration was negative for blood or CSF. Once the level of analgesia was assessed, oxygen was administered through a polymask at 5liters/min flow rate, throughout the surgery.

Parameters Studied:

1. Assessment of Sensory blockade using pin prick.
2. Assessment of Motor Blockade by Modified Bromage Scale

3. Haemodynamic Parameters
4. Assessment of Sedation by using scoring system of Chernic et al.
5. Respiratory rate
6. Visual Analogue pain score (VAS) was used to asses pain,
7. Intra operative and post operative complications like nausea, vomiting, pruritus, shivering.

Statistical analysis was done by students t test, Pvalue>0.05-not significant, < 0.05-significant, P value <0.01-highly significant.

RESULTS

The demographic data and duration of surgery were comparable in both the groups.

There is no statistically significant change in pulse rate, systolic and diastolic blood pressure throughout the intraoperative period as depicted in figure Ⅰ and Ⅱ .difference between respiratory rate and oxygen saturation between the two groups is not statistically significant.

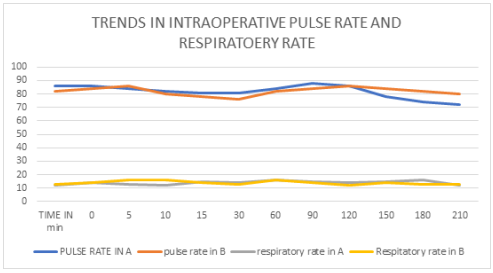

FIGURE I showing no significant change in pulse rate and respiratory rate in both the groups

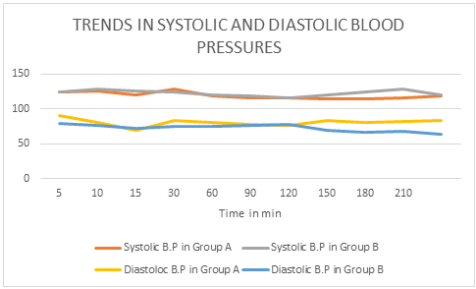

Figure Ⅱ showing mean intraoperative systolic and diastolic blood pressures in both the groups

Mean onset time of sensory block was 9.117 ± 0.597 min and 8.933 ± 0.521min in Group A & B respectively with a P value of 0.2101 which is statistically not significant. Time taken for the onset of motor blockade is less in Group B but it is statistically not significant (Group A , 20.13±3.75 , Group B, 18.83 ± 3.64, P value 0.1782). Mean sensory level achieved was T6.37±±0.11andT6.33±0.48 in Group A and B respectively with a P value of 0.815which is statistically not significant. The time for two segment regression was 150.3±7.16min and 153.33 ± 6.48min in Group A and B respectively with a P Value of 0.1259 which is statistically not significant as shown in table Ⅰ. Duration of Motor blockade is 204.83 ± 16.53min and 211.67 ± 14.67min in Group A and B, P Value is 0.909 which is statistically not significant

Table Ⅰ Sensory block

Parameters	GROUP A Mean ±SD	GROUP B Mean ±SD	P value	Significance
Sensory level	T6.37±0.61	T6.33±0.48	0.8157	NS
Onset of sensory block(min)	9.11±0.597	8.933±0.21	0.2101	NS
Two segment regression (min)	150.31±7.16	153.33±6.48	0.1259	NS

as shown in table Ⅱ.

Table Ⅱ Motor blockade (min)

Onset	20.13±3.75	18.83±3.64	0.1782	NS
Duration	204.83+16.53	211.67+14.67	0.909	NS

Table Ⅳ Duration of analgesia (min)

	Group A	Group B
Mean	304.33	318.00
S.D	25.15	25.78
P value	0.0421 (p < 0.05) Significant	

Table Ⅳ shows the mean + SD of duration of analgesia of two groups. Difference between them is statistically significant (P<0.05)

Table Ⅴ Sedation

Grade	Group A	Group B
0	0	1(3%)
1	0	13(43%)
2	0	16(53%)
3	0	0

Sedation scores in Group A were 0, whereas in Group B Grade 0 (3%) , Grade I (43%), Grade II (53%) and Grade III 0% as shown in Table Ⅴ , when analyzed statistically P value is <0.01 which is highly significant.

Shivering is noticed in 4 patients in Group A and 3 in Group B which is statistically not significant. Although 4 patients, 2 in each group complained of nausea, none of the patients had vomited. No pruritis noticed in both the groups.

DISCUSSION

The advantages of epidural anaesthesia is its versatility of being administered either as a single bolus injection or as multiple injections of the drug through a catheter for prolonged periods for post operative analgesia. Epidural analgesia after surgery in addition to providing patient comfort can also facilitate accelerated recovery as patients receive not only effective pain relief but also early post operative intake of oral nutrition, reduction in peri operative stress responses and organ dysfunction, avoidance of fatigue with lowered incidence of deep vein thrombosis, early mobilization and minimal hospital stay.

Spinal and epidural administration of local anaesthetics, with or without adjuvants like opioids, benzodiazepines not only improve quality of intraoperative anaesthesia but also provides good post operative analgesia without major side effects.

Epidural ropivacaine provides more differential block which is advantageous, and with a better cardiac profile with lower systemic toxicity makes it a good choice over bupivacaine.

Midazolam[1], a short acting benzodiazepine has been widely used as a premedicant and as an agent to produce conscious sedation, particularly in ICU. Epidural midazolam exerts its analgesic effect through GABA- Benzodiazepine receptor binding sites in the dorsal horn of spinal cord. Epidural midazolam provides distinct advantage over systemic administration as the quality of anaesthesia is better and haemodynamics are well maintained. Sedation is less and side effects are no more frequent or severe as compared to intravenous midazolam.

For epidural anaesthesia in our study, we have used a combination of local anaesthetic and preservative free midazolam adding Central analgesic, sedative and amnesic effects to the epidural anaesthesia. Another rationale for these combinations is to reduce the dosage of the individual agents with concomitant reduction in the severity of side effects.

In the present study sixty female patients with ASA grade I and grade II posted for vaginal hysterectomy were divided into two

groups of thirty each. Group A received 18 ml 0.75% Ropivacaine + 2 ml normal saline and Group B received 18 ml 0.75% Ropivacaine + 2 ml (2mg) preservative free Midazolam by epidural route.

The parameters measured in both the groups included haemodynamic measurements of pulse, blood pressure, respiratory rate, oxygen saturation, onset and duration of sensory and motor blockade, duration of analgesia, peri operative complications.

Demographic data of both the groups were comparable. Both the groups were comparable in terms of age, height, ASA grading and nature of surgery. The differences in the pulse rate, systolic, and diastolic blood pressures throughout the procedure were statistically not significant. There was significant fall in respiratory rate from baseline in both the groups, still it was never less than 10/min, none of the patient from either group has respiratory depression.

The mean time of onset of sensory block in Group A was 9.117 ± 0.597 min and Group B was 8.933 $\pm$ 0.521 min, P Value is 0.2101 (>0.05), which is statistically not significant, similar to PARVIN SAJEDI et al[2] (2004),who compared epidural lignocaine with 5mg and 3 mg of midazolam. Level of sensory block achieved is T 6.37 ± 0.11 in Group A and T 6.33±0.48 in Group B and P value is 0.8157 (>0.05) which is statistically not significant. According to modified Bromage scale onset of motor block (Bromage III) in Group A was 20.13 $\pm$ 3.75 min and in Group B was 18.83 $\pm$ 3.64 min , P Value is 0.1782 (> 0.05) which is statistically not significant. Onset of motor block was comparable, and statistically not significant. Two segment regression in Group A was 150.3 ±7.16 min and Group B was 153.33 ± 6.48min with a P value of 0.1259 (> 0.05) both were comparable and statistically not significant. Duration of motor blockade (Bromage O) in Group A was 204.83 ± 16.53min and in Group B was 211.67 ± 14.67min, P Value is 0.909 (> 0.05) the values were comparable and statistically not significant.

Sedation

It was found that sedation was induced in all patients in the Group A , when compared to patients in, who Group B had no sedation. Sedation score in the Group A ranged from Grade I to Grade II. When these results are analyzed statistically the P Value was < 0.01, which is statistically highly significant.

In a study by BARIS.S. et al[3], Sedation scores were higher in epidural bupivacaine + midazolam group than epidural bupivacaine only and epidural bupivacaine + fentanyl groups. GULEC S et al [4], Sedation scores were higher in the epidural bupivacaine-midazolam than bupivacaine-morphine groups than bupivacaine only group. According to T.NISHIYAMA,T.MATSUWAKA[5] et al adding midazolam 10-20 mg/hr to continuous epidural infusion of bupivacaine provided better analgesia, amnesia and sedation than bupivacaine only.

Duration of analgesia in Group A was 304.33 $\pm$ 25.15 min and Group B was 318.00 $\pm$ 25.78min. The P Value is 0.0421(<0.05) which is statistically significant. similar findings observed in studies by MOUNIS ABOSEDIRA et al[6], BARIS.S KARAKAYA.D et al[3].

Prolongation of duration of analgesia reported in this study is shorter compared to other studies mentioned earlier. Several reasons exist in explaining the discrepancies between results of this study and other studies. The reasons include a different local anaesthetic solution and concentrations used (ropivacaine , bupivacaine, lignocaine), different kinds of adjuvants added, a more painful type of surgery performed, a different patient population (adult versus paediatric) with the inherent difficulty in reliably assessing pain in the paediatric age group and the volume of drug injected (larger/smaller).

The time of administration of epidural drug is also different like after induction of general anaesthesia, or after completion of surgical procedure. The purpose for which epidural block was given whether it is for surgical procedure or for post operative pain relief may influence the duration of analgesia. In this study, epidural block was given for surgical procedure, where as in some studies (Gulec et al[4] and Kumar et al[7]) mentioned earlier it is for post operative pain relief.

Since the higher doses (75-100µg/kg) were associated with an unacceptable degree of sedation while the lower dose (25µg/ Kg) was less effective. So the dose acceptable may be between 40 to 50µg/kg (50µg/Kg- T.Nishiyama et al[8]).Incidence of side effects like nausea, shivering were comparable in both groups, when analyzed statistically P Value is >0.05 which is not significant. None of the patients had pruritus, respiratory depression, or paradoxical excitement similar to a study by MOUNIS ABOSEDIRA et al[6].

The most commonly used adjuvants to local anesthetics like opioids by intrathecal/epidural route are associated with side effects like respiratory depression, nausea, vomiting, pruritus etc. Whereas Midazolam is effective in prolongation of duration of analgesia with optimal sedation without respiratory depression. Good sedation without respiratory depression is highly desirable[9,10].

Hence, Midazolam may be considered as a good alternative to opioids as an adjuvant to local anaesthetics by epidural route for providing effective intra operative anaesthesia and post operative analgesia without major side effects.

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