Original Research Article

Effects of epidural dexmedetomidine on ropivacaine induced epidural anesthesia and post-operative analgesia in women undergoing vaginal hysterectomy: A randomized double-blind control trial

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Abstract

Objective: To find out the effects of addition of epidural dexmedetomidine to ropivacaine on post-operative analgesia, and sensory and motor block characteristics. **Methods:** Total 78 adult females belonging to ASA status I and II were divided in to two groups; group RS: received 20 ml of 0.75% injection ropivacaine and 1 ml of normal saline, and group RD: received 20 ml of 0.75% injection ropivacaine and 1ml dexmedetomidine through epidural route. Duration of post-operative analgesia, sensory and motor block characteristics were compared between these two groups. **Results:** Duration of analgesia was longer in group RD in comparison to group RS (520.82±93.13 vs. 424.61±48.06 minutes, p< 0.0001). Total number of rescue analgesics required per patient was higher in group RS in comparison to group RD (2.76±0.48 vs. 1.61±0.49, p< 0.0001). For both sensory and motor block, onset was faster (for sensory 9.48±1.80 vs.16.48±2.76 minutes; for motor13.51±1.50 vs. 20.05±2.75 minutes respectively) and duration was longer (for sensory 478.46±92.86 vs. 396.66±49.54; for motor 393.33±85.69 vs. 341.79±44.35 minutes respectively) in group RD in comparison to group RS. **Conclusion:** Addition of dexmedetomidine to ropivacaine via epidural route improves post-operative analgesia.
Key Words: epidural, dexmedetomidine, post-operative pain, sensory block, motor block

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INTRODUCTION

Lumbar epidural anesthesia since its introduction in 1921 by Fidel Pages has gained a wide popularity.[1] In prolonged lower abdominal and lower limb surgeries under subarachnoid block, it improves both surgical anesthesia and post-operative analgesia [2, 3]. For epidural anesthesia ropivacaine is the most preferred local anesthetic agent, because of its minimal cardiovascular and central nervous system toxicity and lesser degree of motor block in comparison to bupivacaine [4]. Fentanyl is a commonly used as intrathecal adjuvant to prolong intraoperative as well as postoperative analgesia, but it also produces many unwanted effects like pruritus, nausea, vomiting, urinary retention, delayed respiratory depression and increased incidence of motor block [5]. In this context α2 agonists (like clonidine and dexmedetomidine) are better, as their epidural administration produce sedation, analgesia, hypnosis and sympatholysis with lesser side effects [6]. Dexmedetomidine is preferred over clonidine, as former has eight times greater affinity for α2 agonist in comparison to latter drug. Hypotension and bradycardia

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are the main side effects associated with α2 agonists [7]. Few studies have suggested that epdiduraldexmedetomidine produces prolonged postoperative analgesia with minimal side-effects when added to ropivacaine in epidural and caudal anaesthesia [8-11]. We planned this study to find out the effects of addition of epidural dexemedetomidineto epidural ropivacaine on analgesia, and sensory and motor block characteristics in women posted for vaginal hysterectomy. Side effect profile like excessive sedation, respiratory depression, hypotension, bradycardia, nausea, and vomiting were also compared. Analgesic properties were measured by duration of post-operative analgesia and frequency of need of rescue analgesics, former being the primary outcome measure.

METHODS

This prospective, randomized, double blind trial with 1:1 allocation ratio was carried out in a teaching hospital of Western Rajasthan, India. The study was approved by ethical committee of the institute. Eighty patients, aged 35-65 years, weighed 50-75kg, and belonged to American Society of Anesthesiologists I or II status, who were scheduled to undergo elective vaginal hysterectomy were enrolled in to the study group. Informed written consent was obtained from all the enrolled patients, and only those who consented to participate in the study were included. Patients with coagulation disorders, pre-existing neurological disease, anatomical abnormalities of spine, infection at the local site, known allergy to local anesthetics, anticipated difficult intubation, and patients on medications like hypnotics, narcotic analgesics or sedatives were excluded from the study.After eight hours of fasting, on arrival in operation theatre multichannel vital sign monitor was attached to the patient to record heart rate, blood pressure, ECG and SPO_2. A wide bore (18G) cannula was inserted to infuse ringer lactate solution as a maintenance fluid. After painting and draping, 3 ml of 1% lidocaine was infiltrated in L 3-4 interspace via 26 G needle in sitting position followed by insertion of eighteen-gauge Tuohy needle in epidural space using loss of resistance technique. A test dose of 3 ml 2% lidocaine with adrenaline 1:200,000 was infused via Tuohy needle to exclude subarachnoid and intravascular placement of needle. After confirming the position of needle in epidural space, a 20G multi-hole epidural catheter was threaded and it was fixed at 5cm in epidural space. Following randomization; group RS: received 20 ml of 0.75% injection ropivacaine and 1 ml of normal saline through epidural route, and group RD: received 20 ml of 0.75% injection ropivacaine and 1ml dexmedetomidine (1.5 µg kg-1 dissolved in normal saline up to 1ml) through epidural route. The operation was started after achieving adequate sensory block at T_8 dermatome. In case of failed epidural block (block grade <1 for both sensory and motor block after 30 minutes of local anesthetic administration), patients were given general anesthesia, and these were excluded from the study. Various anesthetic properties like duration of analgesia, requirement of rescue analgesic, onset and duration of sensory and motor block, and side effects between the two groups were compared. Quality of analgesia was assessed using visual analogue (VAS) scale on a 0-10 centimeter scale, where a score of 0 represents no pain and 10 is the worst pain imaginable [12]. Patient was asked to slide the cursor along the ruler to represent the intensity of the pain. Pain on VAS was measured every half an hour, till 3 hours, and then every 1hour till 6 hours followed by every 2 hours till next 24 hour postoperatively by a trained nurse. Rescue analgesia (10ml of 0.20% ropivacaine) was administered via epidural catheter whenever VAS score was ≥ 4 or as requested by the patient. Duration of analgesia was calculated from activation of epidural block to need of first rescue analgesic. Sensory block was assessed by loss of sensation to pin prick test method in the midline using a 22 gauge blunt hypodermic needle at every 5 minutes interval until T_8 dermatome was reached and then at every 15 minutes interval until no change in level occurred [13]. Onset of sensory block to T_8 dermatome level, maximum level of sensory block achieved, time taken to achieve maximum sensory level and duration of sensory block (interval from epidural administration of drug until the regression of sensory block to L_5 dermatome) was noted. Response to pin prick test was graded as; 0-no loss of sensation, 1-analgesia (touch sensation), and 2-anesthesia (no sensation). The degree of motor block was assessed by modified Bromage score at every 5 minutes for first 30 minutes and then every 15 minutes till a score of 3 was achieved [14]. Sedation was assessed by Ramsay sedation score at every 5 minutes interval for first 30 minutes and then every 15 minutes interval till completion of surgery [15].For hemodynamic stability, mean arterial pressure, heart rate (HR), oxygen saturation (SPO_2) and respiratory rate (RR) were recorded every 5 minutes till 30 minutes and thereafter every 15 minutes till the end of surgery and then 2 hourly postoperatively for the next 24 hours.Incidence of side effects like nausea, vomiting, bradycardia (fall in HR >30% from baseline or HR <50 beats per minute, hypotension (fall in SBP > 30% from baseline or MAP < 60mmHg), excessive sedation(Ramsay sedation score ≥4), shivering, respiratory depression (respiratory rate <10 per minute or SPO_2<90%) were recorded till 24 hours post-operative period. For allocation concealment and randomization, identical envelops were numbered

from one to eighty, and these were sealed after inserting group code as per random number generated online (from graphpad.com) for two groups. This process was done by a person not actively involved in the study. In the theater, envelope bearing the patient's sequence number was opened, and drugs were administered as per the code by a separate anesthetist (A1), not involved in anesthetic management. Hemodynamic parameters, anesthetic characteristics, and side effects were assessed and recorded by second anesthetist (A2), who was actively involved in patient care. After completion of trial data were segregated in to two groups by A1 and were handed over to statistician.

Statistical analysis

Duration of analgesia was the primary outcome, and based on the results of previous study required sample size was less than 10 in each group keeping 95% CI and 90% power [16], sample size calculated for duration of sensory and motor block was also less than 10 in each group. We conveniently enrolled 80 patients to include 40 in each group. All collected data were first transferred to Microsoft excel sheet and were analyzed by statistical package for social science (SPSS) software version 24. Qualitative data were analysed by Fisher's exact test. Quantitative data between the two groups were compared by using Student's t test. For all statistical analysis, p value less than 0.05 was considered significant.

RESULTS

Total 80 patients enrolled initially were randomized in to two groups; group RD and group RS each having 40 participants. Epidural block failed in two patients, one in each group. Thirty nine patients in each group completed the study (Figure 1). Weight, height, blood pressure, heart rate, respiratory rate, and SPO_2 were comparable in both the groups (Table 1).

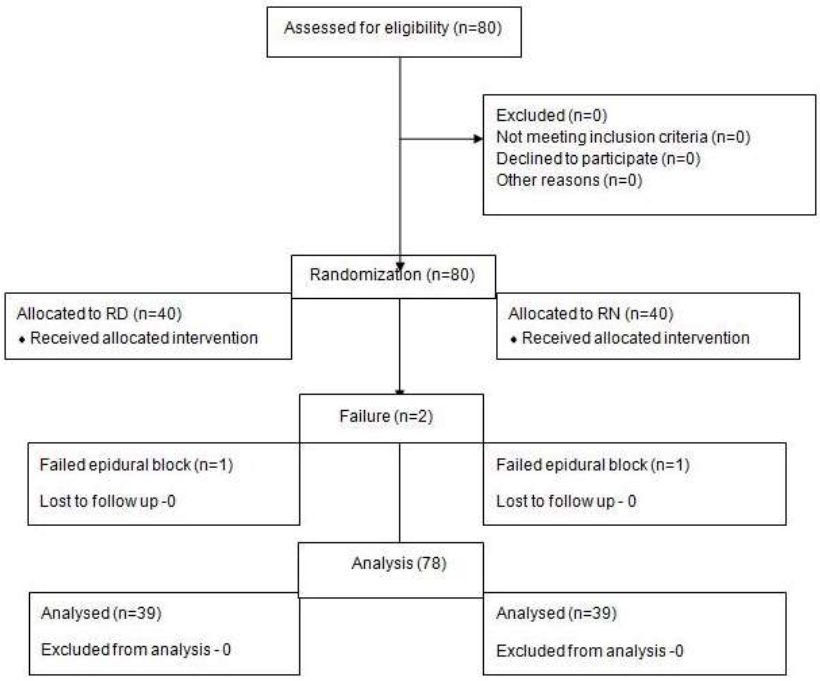

Figure 1: flow of participants in the study

Figure 1:

Table 1: Comparison of baseline clinical and demographic characteristics

Characteristics	Group RS(n=39)	Group RD(n=39)	p
Age (years)	50.61±10.76	50.41±9.97	0.930
Weight (Kg)	57.61±7.29	58.23±5.64	0.678
HR*(per minute)	86.74±6.89	84.25±7.97	0.144
MAP* (mmHg)	89.82±6.09	88.38±6.93	0.334
RR*(per minute)	14.30±1.17	14.0±1.53	0.323
SPO2	98.46±1.14	98.66±1.13	0.428

*HR-heart rate, MAP-mean arterial pressure, RR-respiratory rate

Duration of analgesia was longer in group RD in comparison to group RS (520.82±93.13 vs. 424.61±48.06 minutes, p< 0.0001). Total number of rescue analgesics required per patient was higher in group RS in comparison to group RD (2.76±0.48 vs. 1.61±0.49, p< 0.0001). For both sensory and motor block, onset was faster and duration was longer in group RD in comparison to group RS (table 2 and 3).

Table 2: Comparison of sensory block characteristics in minutes

Sensory block	Group RS (n=39)	Group RD (n=39)	p
Onset	16.48±2.76	9.48±1.80	<0.0001
Time to achieve highest level	25.43±2.54	15.35±1.99	<0.0001
Regression to L5	396.66±49.54	478.46±92.86	<0.0001

Table 3: Comparison of motor block characteristics in minutes

Motor block	Group RS (n=39)	Group RD (n=39)	P
Onset (M1)	20.05±2.75	13.51±1.50	<0.0001
Time to achieve complete block (M3)	29.69±1.79	24.87±2.78	<0.0001
Duration (regression to M1)	341.79±44.35	393.33±85.69	0.001

The highest sensory block level was up to T5, which was achieved by 28.20% (11/39) patients in group RD and by none in group RN. In the latter group the highest level of sensory block was up to T6, achieved by 35.89% (14/39) participants. Hypotension and nausea were seen only in group RS 5.12% (2/39) each and bradycardia was noted only in group RD 5.12% (2/39). Incidence of shivering in both the groups was comparable; group RS 7.69% (3/39), and group RD 2.56% (1/39) with p value 0.615. No patient in both the groups had respiratory depression or excessive sedation.

DISCUSSION

The present randomized, double blind trial conducted over 78 adult females undergoing elective vaginal hysterectomy compared analgesic and anesthetic effects of 0.75% ropivacaine (20 ml) with dexmedetomidine (1ml) versus 0.75% ropivacaine (20ml) alone. Duration of post-operative analgesia and need of rescue analgesics were our primary outcome. Among the anesthetic effects; onset, level, and duration of both sensory and motor block were compared. Patients self-report is considered the best indicator of pain. We used visual analog scale to assess analgesia, which has been used earlier, also 12. In our study addition of dexmedetomidine to epidural ropivacaine prolonged the duration of analgesia and also reduced the need of rescue analgesics. Almost similar findings have been observed previously also[17-20.] Pin prick, cold or touch can be used to assess block height, but pair of two of these parameters has been found to be better.[21] We used pin prick method, which has been tested previously also. In the present study addition of dexmedetomidine to ropivacaine resulted in faster onset of sensory block (at T8) than ropivacaine alone. These finding are in concordance with the results of previous studies [16, 19, 22-24]. On the contrary, Kaur *et al*[17] found no effect of addition of dexmedetomidine to ropivacaine on onset of sensory block. Duration of sensory block was longer in group RD (478.46±92.86minutes) as compared to group RS (396.66±49.54minutes) in the present study. These findings support the results of previous studies [17, 23, 25]. In our study duration of sensory block was calculated till regression of sensory block to L5, whereas Kaur *et al* calculated it till regression of sensory block to S1 dermatome. The level of sensory analgesia achieved was higher and faster in dexmedetomidine plus ropivacaine group as compared to ropivacaine alone in our study. The same has been observed previously also.[17,19,25,26] On the contrary, Kaur *et al* found no effect of addition of dexmedetomidine on onset of maximum sensory level. Motor block was assessed by modified Bromage scale, which is the most commonly used method for this purpose [14]. In the present study onset of motor block (modified Bromage scale 1) was earlier and time to achieve maximum motor block (modified Bromage scale 3) was shorter in patients who were administered dexmedetomidine as adjuvant, as has been demonstrated previously also [19, 22, 23, 25]. In contrast in kaur *et al*'s study time to achieve maximum motor block was comparable in both the groups. We also found longer duration of motor block in dexmedetomdine plus ropivacaine group in comparison to ropivacaine alone, which are again in agreement with the previous findings [17, 19, 23]. In the present study side effects were noted in only a small percent of patients in both the groups. Hypotension and nausea were seen only in group RS 5.12% (2/39) each, and bradycardia was noted only in group RD 5.12% (2/39). Incidence of shivering in both the groups was comparable; group RS 7.69% (3/39), and group RD 2.56% (1/39) with p value 0.615. Similar to us Singh *et al* also noted side effects in only a small subset of patients.[20] They found comparable incidence of bradycardia, hypotension and nausea in both the groups (RD and RS). But in their study shivering was more common in RS

group in comparison to group RD (11/30 vs. 1/30). In a striking contrast to these, Kiran *et al* observed a much higher incidence of side effects, like hypotension in 48% and bradycardia in 40% patients in RD group [16]. This fluctuation in side effect profile can be partly explained byheterogeneity of study population, and variability in dosage of drugs used in different studies. The present study proved the additive analgesic effect of epidural dexmedetomidinewhen it is combined withropivacaine. Effects on sensory and motor block characteristics like faster onset and prolonged duration are also almost same in the present as well as previous studies, barring a few exceptions. These latter findings may be confirmed in a large multi-center trial. The major strength of our study was adequate sample size adjusted both for primary and secondary outcomes. Our study population belonged to ASA physical status I and II only that was the major limitation. Inclusion of more sick patients might have altered the effects of dexmedetomidine especially side effect profile.

CONCLUSION:

Addition of dexmedetomidine to ropivacaine via epidural route improves post-operative analgesia. It also shortens the onset and prolongs the duration of both motor and sensory block, but these latter findings require further confirmation.

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