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Comparison of epidural ropivacaine vs bupivacaine with addition of fentanyl or dexmedetomidine in major lower limb orthopaedic surgery

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Abstract

Background: Adequate analgesia following major lower limb orthopaedic surgeries is necessary for both intra and post-operative pain relief, to promote early ambulation and improved patient outcome.

Aim: To study and compare the analgesia and patient satisfaction when using the local anesthetic drugs ropivacaine and bupivacaine with the adjuvants, fentanyl or dexmedetomidine in major lower limb orthopaedic surgeries.

Materials and Methods: 80 patients undergoing major lower limborthopaedic surgeries under combined spinal epidural anaesthesia were randomly divided into 4 groups. **Group RF** received Ropivacaine 0.2% with Fentanyl 2µg/ml, **Group RD** received Ropivacaine 0.2% with Dexmedetomidine 2µg/ml, **Group BF** received Bupivacaine 0.125% with Fentanyl 2µg/ml and **Group BD** received Bupivacaine 0.125% with Dexmedetomidine 2µg/ml as epidural infusion. Effective analgesia, sensory level, motor block, patient satisfaction were measured. The statistical analysis was done using ANOVA, student 't' test, Mann- whitney test and chi square test. P value < 0.05 was taken as statistically significant.

Results: Group Bupivacaine with dexmedetomidine had a very high patient satisfaction and analgesia when compared to the other groups.

Conclusion: Addition of epidural Bupivacaine with dexmedetomidine as an adjuvant provides slightly better analgesia and patient satisfaction when compared to ropivacaine with dexmedetomidine or fentanyl in patients undergoing major lower limb orthopaedic surgeries.

Keywords: Bupivacaine, Ropivacaine, Dexmedetomidine, Fentanyl

Introduction

Adjuvants are commonly used with local anaesthetics in both spinal and epidural anaesthesia since long. They are usually added to increase duration of anaesthesia or improve the quality of analgesia at lesser local anaesthetic dose requirements.[1-3]

Large volumes of local anaesthetics if used, increases the possibilities of local anaesthetic toxicity and hemodynamic instability. Many adjuvants to epidural injection have been used to decrease such complications.[4] They provide sedation, hemodynamic stability, and provides prolonged postoperative analgesia.[5]

Opioids have been commonly used as adjuvants in neuraxial anesthesia. Now alpha-2 agonists are also being used for this purpose. Other group of drugs like N-methyl D-aspartate (NMDA) antagonists have also been tried, but each of them have their own adverse effect profile and may influence the hemodynamic parameters.[6]

Major lower limb orthopaedic surgeries are particularly important as adequate pain relief is necessary in these patients both intraoperatively as well as postoperatively to promote early ambulation and discharge from hospital.[7]

Lumbar epidural analgesia provides superior pain relief and early mobilization especially when local anaesthetic is combined with an adjuvant. Various adjuncts can be added to these infusions with the local anaesthetic drugs.[9,10] Bupivacaine was the first long acting amino-amide local anaesthetic agent being used. Ropivacaine is identical to bupivacaine in terms of onset, quality and duration of sensory block but seems to produce less motor block. In fact, the reduced cardiovascular toxicity compared to bupivacaine is a distinct feature of ropivacaine.[12]

Epidural fentanyl has been used effectively as an alternative to morphine and has been shown to induce fewer complications when compared with epidural morphine.[1] Dexmedetomidine is a newer alpha-2 agonist which has got sedative, anxiolytic, analgesic, and hemodynamic effects when used via epidural route.[2,3] It causes hypotension and bradycardia but they are manageable and further it has the advantage of lack of opioid related side effects like respiratory depression, pruritus, nausea, and vomiting.[15]

Here we compare 0.125% bupivacaine and 0.2% ropivacaine with the addition of fentanyl and dexmedetomidine in epidural space for major lower limb orthopaedic surgeries.

Aims and Objectives

The aim of the study was to compare the analgesia and quality of patient satisfaction when using an epidural infusion of our different drug regimens namely, Ropivacaine with Fentanyl, Ropivacaine with Dexmedetomidine, Bupivacaine with Fentanyl, Bupivacaine with Dexmedetomidine, in patients undergoing major lower limb orthopaedic surgeries.

Materials and Methods

The study was a randomized double blinded study. It was conducted after approval by the hospital ethical committee and after receiving patient's informed consent for participation in the study.

Eighty patients of ASA physical status 1 or 2, of either sex, aged between 18 to 55 years, who underwent any major lower limb orthopaedic surgery were taken up in the study.

Exclusion Criteria:

- Allergic to amide anesthetics
- Any chronic major medical illness
- Heart block or dysrrhythmias
- Taking anti-adrenergic drugs/calcium channel blockers/ACE inhibitors
- Taking any anticoagulant therapy
- Hepatic failure/ Renal failure

All patients were thoroughly assessed prior to the surgery with routine investigations. The patients were pre-medicated with T. Ranitidine 150mg HS and T. Alprazolam 0.25mg HS on the previous night and at 6AM in morning on the day of surgery.

Randomization and Blinding: The patients were randomized using computer generated random numbers table into 4 groups. They received the drugs as follows:

GROUP RF: Ropivacaine 0.2% with Fentanyl 2µg/ml

GROUP RD: Ropivacaine 0.2% with Dexmedetomidine 2µg/ml

GROUP BF: Bupivacaine 0.125% with Fentanyl 2µg/ml

GROUP BD: Bupivacaine 0.125% with Dexmedetomidine 2µg/ml

The serial number generated by the table was kept in a sealed envelope and each envelope was opened just prior to the starting of the case by an anesthesiologist who did not take any further part in the study.

All drugs were freshly prepared in the theatre by an assistant blinded to patient management and data collection. Instructions for drug preparation were provided in sealed envelopes prepared beforehand based on the group assignment of patients. The drugs were prepared and loaded in the epidural infusion pumps and they were labeled according to the serial number in the envelope.

Each patient was started on epidural infusion based on their serial number. Personnel involved in patient management and drug preparation were not aware of the group assignment.

Heart rate (HR), ECG leads II and chest lead V 5, non-invasive blood pressure (NIBP), pulse oximetry (SpO_2) were monitored attached.

Once the patient was shifted into the operating room, the Datex-OhmedaS/5 Avance work-station monitor was. An intravenous cannula was placed and the patient was preloaded with 500 ml of crystalloids.

An epidural catheter was placed at L3-L4 interspace using 18G Tuohy needle by loss of resistance technique and a test dose of 3ml of 2% lignocaine with 1in 200,000 epinephrine was given after noting vitals.

Then at the same level, using a 26G Quincke needle, by free flow of CSF technique, 3.2 ml of hyperbaric bupivacaine was given and the patient was made to lie in supine position. Surgery was allowed to start once the level of T10 was attained.

Analgesia (VAS scores), sensory level, motor blockade and patient satisfaction was recorded every 30 minutes till 120 minutes and then again at the end of surgery.

The patient was started on epidural infusion of any of the drug regimen according to his/her serial number 90 minutes after the onset of effect of initial anesthesia at 5ml/hr using a infusion pump[Baxter 2C1009 INFUSOR LV5 Flow rate: 5 mL/hr, manufactured by Baxter (India) Private Limited]. The infusion was continued into the postoperative period. The patient vitals were monitored in the postoperative period:

The following were measured,

1. Effectiveness of analgesia provided, i.e. wound pain by VAS scale[25]
   a. At rest
   b. At movement (from supine to sitting position)
2. Sensory level
3. Motor block (by Bromage scale)[26]
4. Patient Satisfaction Score[27]

All of the above said parameters were measured immediately on shifting to recovery room and then at 30minutes, 2hours, 4hours, 8hours, 16 hours and 24 hours.

Pain was measured by using a Visual Analogue Scale score ranging from 0 to 10 (0=no pain; 10=worst pain imaginable).[25] It was measured when the patient was at rest as well as when he/she moved from supine to sitting position. Sensory level was elicited using painful stimulus of pin prick. Motor block was measured by using the Bromage Scale ranging from grade I to grade IV.[26] Finally the patient satisfaction (quality of analgesia) was measured by a 4-point scale (as judged by the patients themselves) ranging from 1 to 4. (1=poor; 4=excellent)[27]

Other secondary parameters like NIBP, HR, RR, SpO_2 and adverse effects if any, like sedation, nausea, vomiting, pruritus was recorded.

Both intraoperatively and postoperatively, hypotension was treated by 3mg boluses of intravenous mephentremine and bradycardia was treated by 0.3mg boluses of intravenous atropine. Rescue analgesia was given with 75mg diclofenac intravenously if VAS score was more than 5 at any time in between or if the epidural infusion was stopped.

Statistical Analysis: Sample size was estimated based on the study of Senard M et al with effect size of 1 for four groups.[27] Our sample size came out to be 12 subjects per group at a power of 90% and confidence

interval of 95%. For possible dropouts, it was decided to include 20 patients per group.

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 18.0 for Windows). Mean and medians were calculated for all quantitative variables (HR, NIBP, SpO_2) and for measuring their dispersion, standard deviation or standard error was calculated. Normality of data was checked by measures of Kolmogorov Smirnov tests of normality.

For normally distributed data (Age, weight, duration of surgery) means of four groups was compared using one way ANOVA followed by student t test, in case significant difference was observed.

For ordered categorical data (VAS score, bromage grade, patient satisfaction score) Kruskall Wallis test followed by Mann –Whitney test for two groups was applied.

Qualitative or categorical variables (nausea, vomiting, sedation, pruritus, respiratory depression) were described as frequencies and proportions. Proportions were compared by using Chi square or Fisher's exact test whichever was applicable. All statistical analysis tests were two tailed and P value < 0.05 was taken as significant.

Results

Eighty patients who underwent major lower limb orthopaedic surgeries were enrolled in the study and divided into four random groups RF, RD, BF and BD. The demographic characteristics like Age, Sex, Weight, ASA physical status and total duration of surgery were similar in all the four groups and did not show any significant statistical difference. (P >0.05) [Table 1]

Table 1: Patients Demographics

		Group RF	Group RD	Group BF	Group BD	P value	
Age*		39±11.2	42.45±12.29	41.9±11.96	41.95±11.82	0.545	
Weight*		62.4±7.68	66.65±10.8	64.75±10.64	63.75±10.33	0.587	
Duration of surgery*		173.75±48.8	180.75±49.07	157±41.6	158.75±36.01	0.259	
SEX	M	14(70%)	15(75%)	15(75%)	14(70%)		
	F	6(30%)	5(25%)	5(25%)	6(30%)		
ASA Status	I	12(60%)	15(75%)	11(55%)	11(55%)		0.519
	II	8(40%)	5(25%)	9(45%)	9(45%)		

*Values are expressed as Mean±SD; n=20 in each group

All patients in RD group and BD group had no pain intraoperatively (VAS=0), one patient in RF group complained pain (VAS=2) at 90 minutes and one patient from BF group complained of pain (VAS=1) at 60 minutes, 90minutes and 120minutes. Other patients from these groups had no pain (VAS=0) in the intraoperative period. However there was no statistical significance.[Table 2]

Table 2: VAS SCORE (INTRA OP)

Time (mins)	Group RF	Group RD	Group BF	Group BD	P value
30	0	0	0.05±0.224	0	1.000
60	0	0	0.05±0.224	0	1.000
90	0.15±0.671	0	0.05±0.224	0	1.000
120	0	0	0.05±0.224	0	1.000

The mean VAS scores when the patient is at rest, in the post-operative period among the four groups are depicted in Table 3. It shows that there is no statistically significant difference in VAS score at rest among the four groups at all the points of time except at 16 hours and 24 hours (P=0.033 and P=0.030 respectively) where the mean VAS score of group BD was lesser than the other three groups. So further intergroup comparisons were done using mann-whitney U test.

At 16 hours, and 24 hours the mean ranks of VAS score of group BD was lesser than group RF (17.15 vs 23.85, P=0.051), group RD (17.45 vs 23.55, P=0.074) and group BF (15.6 vs 25.4, P=0.005). The difference was statistically significant between groups BF and BD.

Table 3: VAS at Rest (POST OP)

Time (hours)	Group RF	Group RD	Group BF	Group BD	P value
0	0.10±0.44	0	0	0	0.392
0.5	0.30±0.65	0.25±0.55	0.10±0.30	0.25±0.78	0.698
2	1.00±1.58	0.90±1.03	0.85±0.87	0.40±0.78	0.267
4	1.55±1.19	1.90±1.11	1.85±0.93	1.15±0.93	0.141
8	2.30±0.74	2.30±0.97	2.30±0.97	1.55±1.19	0.062
16	2.45±1.05	2.30±0.86	2.60±0.88	1.80±0.89	0.033
24	2.50±0.75	2.35±0.58	2.50±0.76	2.10±0.91	0.030

All values are Mean±SD; n=20 for each group

The mean VAS scores while the patient is moving from supine to sitting position are depicted in Table 4. The differences in the mean VAS scores were not statistically significant except at 8 hours. Inter group comparison using Mann-Whitney test, showed lower mean ranks of VAS score for group BD against all the three groups: RF (15.58 vs 25.43, P=0.006), RD (15.33 vs 25.68, P=0.004) and BF (16.75 vs 24.25, P=0.035). It shows that the VAS scores was lower in group BD than other three groups at 8 hours in the postoperative period and the difference was statistically significant.

Table 4: VAS on Moving (Post OP)

Time (hours)	Group RF	Group RD	Group BF	Group BD	P value
0	0.10±0.44	0.05±0.224	0	0	0.567
0.5	0.35±0.81	0.30±0.73	0.25±0.55	0.25±0.78	0.856
2	1.05±1.27	1.25±1.76	1.10±1.02	0.45±0.75	0.114
4	1.9±1.25	2.40±1.14	2.05±0.99	1.40±1.09	0.083
8	2.75±1.02	2.85±1.13	2.45±1.09	1.60±1.22	0.010
16	2.90±0.71	2.80±1.05	2.80±1.00	2.10±1.07	0.057
24	2.95±0.60	2.70±0.92	2.75±0.78	2.65±0.93	0.401

All values are Mean±SD; n=20 for each group.

Rescue analgesia was required in the post-operative period for 30 patients distributed over the four groups. But it had no statistically significant difference.(p = 0.214)[Table 5] It is represented graphically in Fig. 1.

Table 5: Rescue Analgesia Used (Post OP)

		Group RF	Group RD	Group BF	Group BD	P value
Rescue Analgesia Used	Y	9(45%)	7(35%)	10(50%)	4(20%)	0.214
	N	11(55%)	13(65%)	10(50%)	16(80%)	

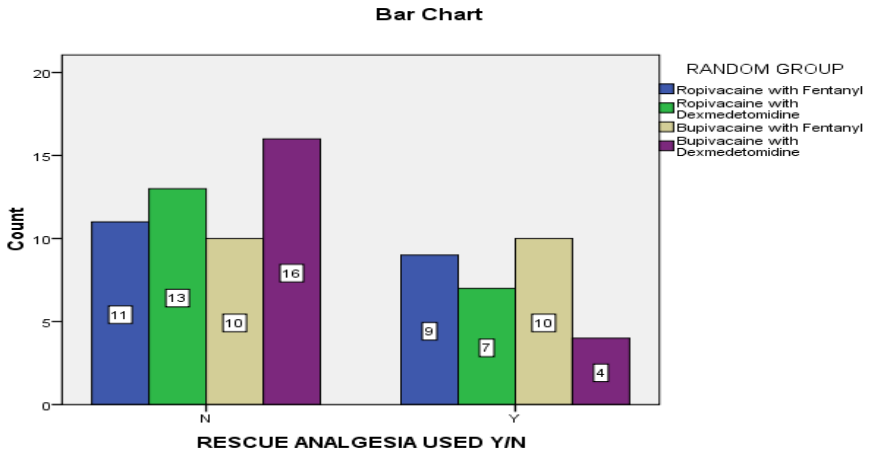

Fig. 1: Use of rescue analgesia (Postop)

The highest sensory level achieved at various points of time intra operatively were comparable among the four groups at any point of time. The difference was not statistically significant at any point of time. The sensory levels among the four groups at these points of time are given in Table 6.

Table 6: Regression of sensory level (Intra op)

Time (min)	Group RF				Group RD				Group BF				Group BD			
	Upto T12	L1-L5	S1-S5	NIL	Upto T12	L1-L5	S1-S5	NIL	Upto T12	L1-L5	S1-S5	NIL	Upto T12	L1-L5	S1-S5	NIL
30	20	0	0	0	20	0	0	0	20	0	0	0	20	0	0	0
60	20	0	0	0	20	0	0	0	20	0	0	0	20	0	0	0
90	20	0	0	0	20	0	0	0	20	0	0	0	20	0	0	0
120	20	0	0	0	20	0	0	0	19	1	0	0	20	0	0	0

The sensory levels were similar at various points of time among the four groups and the differences among the groups were not statistically significant (P>0.05) except at 8 hours (P=0.016) postoperatively. At this point of time, the sensory level regression was most in group RD and least in group BF. [Fig. 2].

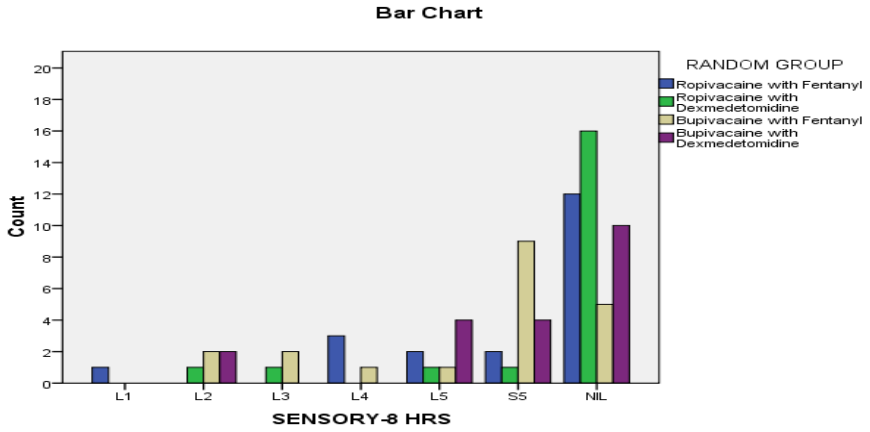

Fig. 2

In the intraoperative period, all the eighty patients had complete motor blockade (Bromage grade IV). In the post-operative period, the mean ranks of the bromage score was significantly higher among the groups BD and BF at 30 minutes, 2 hours, 4 hours, 8 hours and 16 hours than the other two groups.[Table 8] So Mann-whitney U test was applied for further comparison between the groups.

Table 8: Bromage score (Post op)

Time (hours)	Group RF	Group RD	Group BF	Group BD	P value
0	40.05	38.08	44.00	39.88	0.409
0.5	37.65	31.10	44.20	49.05	0.030
2	33.38	29.20	48.93	50.50	0.001
4	32.95	28.68	49.10	51.28	0.001
8	31.53	31.53	47.48	51.48	0.002
16	31.93	35.78	42.63	51.68	0.003
24	38.00	39.98	39.98	44.05	0.252

All values are expressed as Mean Ranks; n=20 for each group

From 30 minutes to, 16 hours, group BD had significantly higher motor blockade than group RF and RD. (P=0.007). Group BF had significantly higher motor blockade than group RF (P=0.041).

But there was no statistically significant difference between group BF and the other three groups.

The patient satisfaction was similar in all the four groups during intraoperative period with no significant statistical difference[Table 9].

Table 9: Patient satisfaction score (intra op)

Time (mins)	Group RF	Group RD	Group BF	Group BD	P value
30	3.96±0.20	3.90±0.30	3.88±0.33	3.94±0.23	0.798
60	3.96±0.20	3.95±0.21	3.88±0.33	3.94±0.23	0.774
90	3.92±0.40	3.95±0.21	3.88±0.33	3.94±0.23	0.905
120	3.96±0.20	3.95±0.21	3.82±0.39	3.94±0.23	0.368

All values are expressed as mean ± SD; n=20 for each group

Table 10: Patient Satisfaction Score (Post Op)

Time (hours)	Group RF	Group RD	Group BF	Group BD	P value
0	42.85	41.10	39.15	38.90	0.737
0.5	38.75	38.75	42.65	41.85	0.810
2	34.98	36.35	37.93	52.75	0.029
4	31.55	39.15	35.08	56.23	0.002
8	30.80	39.10	33.70	58.40	0.000
16	29.03	42.23	32.60	58.15	0.000
24	32.73	43.00	34.60	51.68	0.016

All values are expressed as Mean Ranks; n=20 for each group.

The mean ranks of patient satisfaction score was significantly higher in the group BD than the other three groups at 2 hours (P=0.029), 4 hours (0.002), 8 hours (P=0.000), 16 hours (P=0.000) and 24 hours (P=0.016). At 16 hours and 24 hours, it was also higher in group RD than groups RF and BF but lesser than BD. So further intergroup comparisons were done using Mann-whitneyU test [Table 10].

Discussion

In this prospective, randomized, double blinded study we compared the effects of four different drug regimens given as infusion via epidural route for postoperative pain relief. Patients undergoing major lower limb orthopaedic surgeries were included in the study.

In each group 20 patients were included and the outcome measures were analgesia and quality of patient satisfaction in the first 24 hours of the postoperative period. Epidural infusions of 0.125% bupivacaine and 0.2% ropivacaine with either fentanyl (2µg/ml) or dexmedetomidine (2µg/ml) were used for postoperative pain relief after any major lower limb orthopaedic surgeries. The patients were randomly allocated to each of the four groups and were given combined spinal epidural anaesthesia in a manner standardly practiced in our institute. The epidural infusion was started 90 minutes after the start of the surgery and was continued into the postoperative period.

Analgesia was measured using VAS score and the quality of the patient satisfaction was measured using a 4-point scale used in a previous study.[26] Other than these, the motor blockade (bromage scale) and the sensory level was also noted. Hemodynamic parameters like mean BP, heart rate, SpO_2, respiratory rate and adverse effects were also noted.

The patients in all the four groups had similar demographic profile such as age, sex, weight, ASA status, duration of surgery and the groups were comparable with each other with no significant statistical difference.

The effectiveness of analgesia in the post-operative period given by the epidural infusion was measured using the VAS score while the patient was at rest and when he/she moved from supine to sitting position. There was no difference among the four groups till first 8 hours of the post-operative period while the patient was at rest. However at 16 hours and 24 hours, the group BD had lesser mean VAS scores than other groups. There was not a significantly low VAS score compared to group RD. But when the patient was moving, at 8 hours into post-operative period, group BD had a very statistically significant lower mean VAS score than the other three groups. So overall although all the four groups had a similar VAS score at most of the time points, group BD had lower VAS scores at some points of time and provided slightly better analgesia than other three groups.

The sensory level attained initially and at various points of time both intra-operatively and post operatively were similar in all the four groups. There was no significant difference noted except at 8 hours in the post-operative period.

Motor blockade was similar in the intraoperative period but in the post-operative period it was notably higher in the two groups which received bupivacaine than in the groups which received ropivacaine at 30 minutes, 2 hours, 4 hours, 8 hours and 16 hours in the post-operative period. It was significant statistically. Further intergroup comparison using Mann-whitney U test showed that both BD and BF groups had more motor blockade effect than RD and RF groups. It has been found by various studies that ropivacaine has lesser motor blockade effect when compared to bupivacaine.[12,19] In our study too we found the results to be similar to them.

Patient satisfaction score was measured by a 4-point scale as rated by patients themselves. In our study, we found the mean ranks of patient satisfaction score to be significantly higher in group BD than the other three groups from 2 hours post-surgery till 24 hours. There were no adverse effects like nausea, vomiting, pruritus and respiratory depression. Rescue analgesia in the post-operative period was required in 30 out of the 80 patients. Of them patients from group BD were the least (4 patients), and patients from group BF were the most (10 patients). However this did not bear any statistical significance (P=0.214).

Kanai A et al compared ropivacaine and bupivacaine epidural infusions in orthopaedic surgeries.[21] They used 0.1%, 0.2% ropivacaine and 0.125% bupivacaine. They concluded both provided equal analgesia, and 0.2% ropivacaine caused slightly more intense motor blockade. But in our study bupivacaine had more intense motor blockade than ropivacaine.

Tuttle AA et al in a previous study also had found that bupivacaine had a quick onset and longer acting motor blockade than ropivacaine while used in same concentrations.[19]

Bajwa SJ et al[4] conducted a study in which they compared dexmedetomidine and fentanyl with ropivacaine in patients undergoing lower limb orthopaedic surgeries. They found that dexmedetomidine plus ropivacaine provided stable hemodynamics, quick onset of action, prolonged analgesia and lower consumption of post-operative epidural analgesia than fentanyl plus ropivacaine. Saravana Babu M et al[22] compared dexmedetomidine and clonidine as adjuvant to ropivacaine in epidural infusion for post-operative analgesia in spine surgeries and found dexmedetomidine to be a better neuraxial adjuvant compared to clonidine. Eskandar AM et al[23] studied the effects of epidural dexmedetomidine and concluded dexmedetomidine as an ideal adjuvant to epidural bupivacaine as it provided stable cardiorespiratory parameters, good postoperative analgesia, reduced local anaesthetic requirement and postoperative analgesic requirements.

Kaur S et al[24] compared ropivacaine and ropivacaine with dexmedetomidine for epidural anesthesia in lower limb surgeries and they found though both groups were effective for anesthesia, dexmedetomidine group was better as it had prolonged sensory block, good postoperative analgesia and better patient satisfaction score.

Gupta K et al[18] also compared efficiency of dexmedetomidine and fentanyl as adjuvants to levobupivacaine in vaginal hysterectomies and found dexmedetomidine to provide better sedation, adequate surgical anesthesia, stable hemodynamics and prolonged postoperative analgesia but no difference as far as sensory block was concerned. This falls in line with the findings of our study.

So on comparison with most of the previous studies, our study seems to reinforce most of the findings of the previous studies. Analgesia was similar among the four groups with group BD providing slightly better analgesia at 8 hours, 16 hours and 24 hours. Sensory level was similar, with group RD having less sensory blockade at just one point of time. Motor blockade was more in group BD followed by group BF. Patient satisfaction was very much higher in group BD almost throughout the entire postoperative period. Hemodynamic parameters were stable and no adverse effects were observed in our study.

Conclusion

We conclude that, of all the four regimen compared above, bupivacaine with dexmedetomidine can be considered better as it provides effective analgesia and a very good patient satisfaction though there is slightly more intense motor blockade than ropivacaine containing groups.

References

1. Benzon HT, Wong HY, Belavic AM, Jr., Goodman I, Mitchell D, Lefheit T, et al. A randomized double-blind comparison of epidural fentanyl infusion versus patient-controlled analgesia with morphine for post-thoracotomy pain. Anesth Analg. 1993;76:316-22.
2. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs. 2000;59:263-8.
3. Jaakola ML, Salonen M, Lehtinen R, Scheinin H. The analgesic action of dexmedetomidine--a novel alpha 2-adrenoceptor agonist--in healthy volunteers. Pain. 1991;46:281-5.
4. Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Saudi J Anaesth. 2011;5:365-70.
5. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J Anaesth. 2011;55:116-21.
6. Vranken JH, Troost D, Wegener JT, Kruis MR, van der Vegt MH. Neuropathological findings after continuous intrathecal administration of S(+)-ketamine for the management of neuropathic cancer pain. Pain. 2005;117:231-5.
7. Mahoney OM, Noble PC, Davidson J, Tullos HS. The effect of continuous epidural analgesia on postoperative pain, rehabilitation, and duration of hospitalization in total knee arthroplasty. Clin Orthop Relat Res. 1990(260):30-7.
8. Kehlet H. Acute pain control and accelerated postoperative surgical recovery. SurgClin North Am. 1999;79:431-43.
9. Richards JT, Read JR, Chambers WA. Epidural anaesthesia as a method of pre-emptive analgesia for abdominal hysterectomy. Anaesthesia. 1998;53:296-8.
10. Rigg JR, Jamrozik K, Myles PS, Silbert BS, Peyton PJ, Parsons RW, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. Lancet. 2002;359:1276-82.
11. Zaric D, Nydahl PA, Philipson L, Samuelsson L, Heierson A, Axelsson K. The effect of continuous lumbar epidural infusion of ropivacaine (0.1%, 0.2%, and 0.3%) and 0.25% bupivacaine on sensory and motor block in volunteers: a double-blind study. Reg Anesth. 1996;21:14-25.
12. McClellan KJ, Faulds D. Ropivacaine: an update of its use in regional anaesthesia. Drugs. 2000;60:1065-93.
13. Salomaki TE, Laitinen JO, Nuutinen LS.A randomized double-blind comparison of epidural versus intravenous fentanyl infusion for analgesia after thoracotomy. Anesthesiology. 1991;75:790-5.
14. Liu SS, Allen HW, Olsson GL. Patient-controlled epidural analgesia with bupivacaine and fentanyl on hospital wards: prospective experience with 1,030 surgical patients. Anesthesiology. 1998;88:688-95.

15. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care. 2000;4:302-8.
16. Gabriel JS, Gordin V. Alpha 2 agonists in regional anesthesia and analgesia. Curr Opin Anaesthesiol. 2001;14:751-3.
17. Goel S, Bhardwaj N, Grover VK. Intrathecal fentanyl added to intrathecal bupivacaine for day case surgery: a randomized study. Eur J Anaesthesiol. 2003;20:294-7.
18. Gupta K, Rastogi B, Guta P, Jain M, Gupta S, Mangla D. Epidural 0.5 % levobupivacaine with dexmedetomidine versus fentanyl for vaginal hysterectomy: A prospective study. Indian J Pain. 2014;28:149-54.
19. Tuttle AA, Katz JA, Bridenbaugh PO, Quinlan R, Knarr D. A double-blind comparison of the abdominal wall relaxation produced by epidural 0.75% ropivacaine and 0.75% bupivacaine in gynecologic surgery. Reg Anesth. 1995;20:515-20.
20. Corning J. Spinal anaesthesia and local medication of the cord. NY Med J. 1885;42:483-5.
21. Kanai A, Nakahara R, Okamoto H, Hoka S. Postoperative analgesia using continuous lumbar epidural infusion of ropivacaine in comparison with bupivacaine. Masui. 2003;52:832-9.
22. Saravana Babu M, Verma AK, Agarwal A, Tyagi CM, Upadhyay M, Tripathi S. A comparative study in the post-operative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for post-operative analgesia. Indian J Anaesth. 2013;57:371-6.
23. Eskandar A, Ebeid A. Effects of epidural dexmedetomidine and low-volume bupivacaine on postoperative analgesia after total knee replacement. Ain-Shams J Anaesthesiol. 2014;7:193-97.
24. Kaur S, Attri JP, Kaur G, Singh TP. Comparative evaluation of ropivacaine versus dexmedetomidine and ropivacaine in epidural anesthesia in lower limb orthopedic surgeries. Saudi J Anaesth. 2014;8:463-9.
25. Ohnhaus EE, Adler R. Methodological problems in the measurement of pain: a comparison between the verbal rating scale and the visual analogue scale. Pain. 1975;1:379-26. Breen TW, Shapiro T, Glass B, Foster-Payne D, Oriol NE. Epidural anesthesia for labor in an ambulatory patient. Anesth Analg. 1993;77:919-24.
26. Chanthong P, Abrishami A, Wong J, Herrera F, Chung F. Systematic review of questionnaires measuring patient satisfaction in ambulatory anesthesia. Anesthesiology. 2009;110:1061-7.
27. Senard M, Joris JL, Ledoux D, Toussaint PJ, Lahaye-Goffart B, Lamy ML. A comparison of 0.1% and 0.2% ropivacaine and bupivacaine combined with morphine for postoperative patient-controlled epidural analgesia after major abdominal surgery. Anesth Analg. 2002;95:444-9.