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Comparative study of analgesic effects of ropivacaine and dexmedetomidine with that of ropivacaine and fentanyl for lower abdominal and lower limb orthopaedic surgeries

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***Abstract*---**Introduction: The anesthetic choices for lengthy lower limbs orthopedic procedures may comprise general anesthesia and limited types of regional techniques such as epidural, continuous spinal, or combined nerve blocks. Ropivacaine is a long-acting amide local anesthetic with a potentially improved safety profile when compared to bupivacaine. Dexmedetomidine and fentanyl are two such adjuvant drugs that have been used in combination with bupivacaine or ropivacaine to enhance the analgesic efficacy of the drugs and that facilitate early achievement and prolongation of block. Material and Methods: This is a Comparative, prospective and single study of postoperative epidural analgesia was done in 140 patients, posted for elective surgeries selected randomly, after approval from Ethical committee, conducted over a period of 6 months. Patients of either sex with age between 18 to 60 years. ASA grades I and II. Elective lower limb Orthopaedic and lower Abdominal surgery were included. Patients` refusal, Spinal deformities. Bleeding disorders, Neurological deficit. Local skin infection around the site of needle insertion and Allergic to local anaesthetic drugs were excluded.

Results: A total of 140 patients of either sex selected in this study. It is observed that onset of analgesia in Group-A (RD) (0.2% Ropivacaine + 1mcg/kg Dexmedetomidine) was 9.20 min. When compared to Group-B (0.2% Ropivacaine + 1mcg/kg Fentanyl) was 11.23 min, which is statistically significant (P<0.05). It shows Ropivacaine with Dexmedetomidine has faster onset of pain relief when compared to Ropivacaine with Fentanyl, given epidurally. Duration of analgesia in Group-A (Dexmedetomidine + Ropivacaine) was 338min compared to Group-B (Fentanyl + Ropivacaine), which was 259 min. This is statistically significant (P<0.05). Mean duration of analgesia in group A was more compared to group B. Conclusion: The duration of action was longer in Ropivacaine with Dexmedetomidine (mean duration of analgesia was 336.mins) when compared to Ropivacaine with Fentanyl group (mean duration of analgesia 260mins). Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset and establishment of sensory anesthesia, prolonged post-op analgesia, and much better sedation levels.

***Keywords*---**ropivacaine, dexmedetomidine, fentanyl, lower abdominal, lower limb orthopaedic surgeries.

Introduction

The anesthetic choices for lengthy lower limbs orthopedic procedures may comprise general anesthesia and limited types of regional techniques such as epidural, continuous spinal, or combined nerve blocks. [1] However, technical difficulties and lack of facilities including microcatheters or ultrasound machines may preclude some techniques. Despite the conflict, the regional anesthesia may be associated with lower morbidity in major orthopedic surgery than general anesthesia. [2]

Bupivacaine is frequently used as the local anesthetic for brachial plexus anesthesia because it offers the advantage of providing a long duration of action and a favorable ratio of sensory to motor neural block. [3] One of the first local anesthetic agents that emerged as a possible replacement for bupivacaine was ropivacaine. Ropivacaine is a long-acting amide local anesthetic with a potentially improved safety profile when compared to bupivacaine. [4]

There has always been a search for adjuvant in regional nerve block with the drugs that prolong the duration of analgesia but with lesser adverse effects. The search for the ideal additive continues and leads us to try the novel α_2 adrenergic agent dexmedetomidine and an opioid fentanyl. [4]

Dexmedetomidine and fentanyl are two such adjuvant drugs that have been used in combination with bupivacaine or ropivacaine to enhance the analgesic efficacy of the drugs and that facilitate early achievement and prolongation of block. [5] A number of studies have evaluated the efficacy of both the drugs, either independently or in combination with other adjuvants. [6] There are limited or

almost no studies comparing the use of ropivacaine with fentanyl to ropivacaine with dexmedetomidine. Considering the low side effect and excellent postoperative analgesic efficacy of two drugs, it is essential to carry out a comparative evaluation of two drugs for their adjuvant use with ropivacaine in among patients undergoing lower limb orthopedic surgeries.

The present study evaluated dexmedetomidine as an add on to epidural ropivacaine in patient undergoing major orthopaedic lower extremity surgery, and found it to be safe without any serious side effects and to have a significantly greater analgesic and local anesthetic-sparing effect in the early postoperative period, compared to fentanyl. Our results are consistent with previous studies regarding the synergic analgesic effect of dexmedetomidine when added to local anesthetics via caudal, epidural, or intrathecal route. [7]

Material and Methods

This is a Comparative, prospective and single study of postoperative epidural analgesia was done in 140 patients, posted for elective surgeries selected randomly, after approval from Ethical committee, conducted over a period of 6 months.

Inclusion criteria

Patients of either sex with age between 18 to 60 years. ASA grades I and II. Elective lower limb Orthopaedic and lower Abdominal surgery.

Exclusion criteria

Patients` refusal, Spinal deformities. Bleeding disorders, Neurological deficit. Local skin infection around the site of needle insertion and Allergic to local anaesthetic drugs. All patients were thoroughly examined and assessed pre-operatively for any cardiovascular, respiratory or any other systemic illness and spinal deformities. The nature of the procedure was explained and the patients were taught to assess the intensity of pain using the visual analogue scale (VAS). In the visual analogue scale the patients were shown a scale of 10 cm length. Zero end of the scale was taken as 'No pain' and 10 cm mark as 'Maximum pain'. Intensity of pain increases gradually from '0' to '10'. Patients were instructed to point the intensity of pain on the scale.

Procedure

With all aseptic precautions, epidural space was found with 18G Tuohy needle at L2 - L3 space by loss of resistance using air injection technique in sitting position and 18 G epidural catheter was threaded through this needle for 5-cms in the cephalad direction in epidural space and properly fixed. Afterwards using a 25G spinal needle lumbar puncture was done in L3-L4 intervertebral space. After appearance of CSF at the hub of spinal needle, 3.5cc 0.5% hyperbaric Bupivacaine was injected into subarachnoid space, the spinal needle removed. The anaesthesia was started with spinal anaesthesia & then when patient started complain of pain after surgery epidural analgesia was started.

Group A: Patients received 15ml of 0.2% Ropivacaine + 1mcg/ kg of Dexmedetomidine Group B: Patients received 15ml of 0.2% of Ropivacaine + 1mcg/kg of Fentanyl.

Results

A total of 140 patients of either sex selected in this study.

Table 1: Age Distribution

Age (in years)	Group -A (N=70) RD		Group-B(N=70) RF	
	No. of patients	Percentage	No. of patients	Percentage
18 to 30	16	22.85	17	24.28
30 to 40	26	37.14	25	35.72
40 to 50	18	25.71	20	28.58
50 to 60	10	14.3	8	11.42
Total	70	100	70	100
Mean±SD	38.30 (±8.86)		40.83 (±9.33)	

In table 1 shows age distribution of the patients in both the groups. The minimum age in both groups was 18 years. The maximum age in both groups was 60years respectively. In group RD the Mean age was 38.30(±8.86) and in RF group the mean was 40.83 (±9.33) There was no significant difference in the age of patients between the Group RD and Group RF. Both groups were similar with respect to age distribution

Table: 2 Sex Distribution between Group A and Group B

Sex	Group -A (N=70) RD		Group-B (N=70) RF	
	No of patients	Percent %	No of Patients	Percent%
Male	54	77.1	50	71.4
Female	16	22.9	20	28.6

There were 54 males and 16 females in Ropivacaine + Dexmedetomidine group and there were 50 males and 20 females in the Ropivacaine + Fentanyl group. No significant difference was observed in sex wise distribution of the cases between two groups

Table: 3: Onset of analgesia

	Mean duration for onset of analgesia (in min)	*SD*	Significance *(p)*
Group A(N=70)	*9.20*	*±3.59*	*P= 0.00113 (S)*
Group B(N=70)	*11.23*	*±4.23*	

It is observed that onset of analgesia in Group-A (RD) (0.2% Ropivacaine + 1mcg/kg Dexmedetomidine) was 9.20 min. When compared to Group-B (0.2% Ropivacaine + 1mcg/kg Fentanyl) was 11.23 min, which is statistically significant

(P<0.05). It shows Ropivacaine with Dexmedetomidine has faster onset of pain relief when compared to Ropivacaine with Fentanyl, given epidurally in Table 3.

Table: 4 Duration of Analgesia in minutes

	Mean duration of analgesia (in min)	SD	Significance
Group A (N=70)	338.45	±27.21	(P<0.05)
Group B (N=70)	259.63	± 21.34	

Duration of analgesia in Group-A (Dexmedetomidine + Ropivacaine) was 338min compared to Group-B (Fentanyl + Ropivacaine), which was 259 min. This is statistically significant (P<0.05). Mean duration of analgesia in group A was more compared to group B in Table 4.

Table-5: Level of analgesia: (Chi-square test)

LEVELS	Group-A (n)	%	Group-B (n)	%	p VALUE
T8	0	0	0	0	CHI SQ =3.434 D.F.=2 P= 0.13
T9	6	8.6	6	8.6	
T10	18	25.7	16	22.8	
T11	30	42.9	20	28.6	
T12	16	22.8	28	40	

Table-6: Comparison of Oxygen Saturation in between Group A and Group B

Time interval	Oxygen Saturation% Group A		Oxygen Saturation% Group B		Group A Vs Group B
	Mean	SD	Mean	SD	
Base value	98.10	3.16	97.85	2.53	
15 min	96.38	3.22	92.64	4.81	<0.00
30 min	96.50	3.13	92.68	4.39	<0.00
45 min	95.11	2.96	96.10	3.41	0.48
1 hr.	95.89	2.93	97.38	2.81	0.18
2 hr.	98.22	2.95	97.62	2.84	0.12
3 hr.	95.88	2.90	97.60	2.82	0.45
4 hr.	98.34	2.86	97.95	2.93	0.31
5 hr.	98.58	2.68	97.71	2.89	0.06
6 hr.	98.84	2.69	98.25	2.79	0.09

- In Group RD, the mean baseline oxygen saturation was 98.10 with a standard deviation of 3.16.
- In Group RF, the mean baseline oxygen saturation was 97.85 with a standard deviation of 2.53
- On comparing the two groups there was statistically significant difference from 15 to 30 minutes (p value>0.05) between the groups.
- It was observed that oxygen saturation decreased in RD group from 15 mins upto 30 mins compared to RF group in Table 6.

Table 7. Comparison of VAS between group A and group B

Time interval	VAS group A		VAS group B		P
	Mean	SD	Mean	SD	
Base value	6.80	0.70	6.60	0.65	
15 min	0.97	1.8	2.78	0.90	<0.00
30 min	0.79	0.99	3.00	0.80	<0.00
45 min	2.04	0.90	3.20	0.70	<0.00
1 hr.	2.76	0.99	3.58	0.70	<0.00
2 hr.	2.80	0.91	3.78	0.90	<0.00
3 hr.	2.37	0.80	4.08	0.87	<0.00
4 hr.	3.65	2.6	4.54	0.85	<0.00
5 hr.	2.80	2.37	4.80	0.77	<0.00
6 hr.	4.78	2.59	5.30	0.60	<0.00

The mean baseline VAS score in Group RD was 6.80 with a standard deviation of 0.70, whereas in Group RF it was 6.60 with a standard deviation of 0.65 in Table 7.

Discussion

Dexmedetomidine is a potent α-2 adrenergic agonist with an affinity eight times greater than that of clonidine and is associated with rapid onset of sensory block, prolonged local anesthetic action, and decreased postoperative pain intensity in both adults and children when used. [8] Although the precise mechanisms are not well understood, the wide distribution of α-2 adrenergic receptors in the central and peripheral nervous systems play a key role in mediating the effects of neuraxial dexmedetomidine. [9] Dexmedetomidine causes local vasoconstriction and hyperpolarization, delaying the absorption of local anesthetics and prolonging their effects. [10] Another possible mechanism is its central analgesic effect through spinal and supraspinal actions, inhibiting the activation of spinal astrocytes and microglia, decreasing the release of nociceptive substances, and regulating nociceptive transmission. [11] After epidural administration, dexmedetomidine rapidly diffuses into the cerebrospinal fluid and reaches binding sites in the spinal cord because of its lipophilicity, and its analgesic effect is up to five times greater with epidural administration compared with systemic administration. [12]

When adding an adjuvant to epidural local anesthetics in patients, the most important issues should be the safety and side-effect profile of the drug, as well as using the lowest effective dose. Aside from the special considerations that should be kept in mind with the population, there are additional aspects to consider in patients undergoing extensive lower extremity orthopedic surgery. As seen in the results of the present study, the majority of patients requiring extensive orthopedic procedures are often diagnosed with cognitive impairment. The daunting task of assessing pain in young patient is greater in this special patient population, as well as the potential of deleterious effects of opioids or local anesthetic toxicity. The r-FLACC pain scale is useful in these patients, as certain characteristic descriptors, such as verbal outbursts, tremors, increased

spasticity, jerking movements, and respiratory pattern changes, such as breath holding and grunting, are included. [13]

The most important finding of the present study is that the VAS score at postoperative 6 h was significantly lower for patients who received dexmedetomidine than for those receiving fentanyl. Moreover, the required bolus doses of ropivacaine were decreased by roughly 50% during the first 6 h after surgery when dexmedetomidine was used, compared to fentanyl. Postoperative pain is usually most intense in the early postoperative period, and the fact that bolus attempts with patient-controlled analgesia (PCA) was decreased by nearly 50% during this period seems to reflect the effectiveness of dexmedetomidine as an adjuvant to epidural ropivacaine. Bolus doses of epidural ropivacaine during the first postoperative 6 hours were lower in the dexmedetomidine group than in the fentanyl group, whereas the total doses of epidural ropivacaine were not significantly different during the first 6 hours after surgery in both groups. This can be interpreted as a result of the small amount of bolus doses compared to the total dose.

Although epidural analgesia is the preferred modality for postoperative pain management after major lower extremity surgery in children, the dose and role of epidural dexmedetomidine is not well known in this patient population. Based on the results of previous dose-finding studies of caudal dexmedetomidine, 1 μg/kg epidural dexmedetomidine was used in the present trial. [14] Dose-dependent adverse effects of dexmedetomidine include hypotension, bradycardia, and sedation. [15] In our study, we observed a clinically acceptable decrease in heart rate and mean arterial pressure during the 30 minutes during which patients received 1 μg/kg epidural dexmedetomidine. Reportedly, 1–2 μg/kg caudal dexmedetomidine given as an adjuvant is associated with prolonged sedation, but without delayed discharge from the post-anesthesia care unit (PACU) due to oversedation. [16]

Although there was a trend of prolonged emergence time with dexmedetomidine, compared to fentanyl, in our present study, the difference was not statistically significant and also did not seem to be clinically relevant. Despite the clinically safe results observed in our study with regards to possible adverse effects of dexmedetomidine, we were not able to find any difference in respiratory depression, nausea and vomiting, urinary retention, or pruritis between the two groups. Although adding 0.4 μg/kg/h epidural fentanyl to local anesthetic provided better analgesia in children who underwent femoral osteotomy, this adjuvant increased pruritus, nausea and vomiting, and antiemetic use. [17] This discrepancy might be explained by differences in postoperative epidural analgesia regimens. Unlike the previous studies in which adjuvants were given continuously after surgery, epidural adjuvants were given only with the initial loading dose of ropivacaine in the present study.

Conclusion

The duration of action was longer in Ropivacaine with Dexmedetomidine (mean duration of analgesia was 336.mins) when compared to Ropivacaine with Fentanyl group (mean duration of analgesia 260mins). Dexmedetomidine seems

to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset and establishment of sensory anesthesia, prolonged post-op analgesia, and much better sedation levels. However further studies are required to evaluate both the drugs.

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