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A COMPARATIVE STUDY OF ROPIVACAINE 0.50% WITH CLONIDINE VERSUS ROPIVACAINE 0.50% WITH FENTANYL FOR EPIDURAL ANESTHESIA IN LOWER LIMB ORTHOPEDIC SURGERIES

Anaesthesiology

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ABSTRACT

Aim- To evaluate and compare the efficacy, analgesic effects, post operative analgesia of epidurally administered Clonidine or Fentanyl along with Ropivacaine for patients undergoing lower limb orthopedic surgeries.

Method- Prospective, randomized, double blinded study on 60 patients (ASA I&II) undergoing lower limb orthopedic surgery. Patients were divided into two groups with 30 patients in each group. Patients in one group were given Ropivacaine+ Clonidine and patients in other group were given Ropivacaine +Fentanyl as epidural anesthesia. Various sensory and motor block characteristics along with hemodynamic parameters were measured following standard procedures. Level of sedation was assessed using Ramsay's sedation scale. Appropriate statistical tests were performed using SPSS (Version 23).

Result- Time taken for sensory onset (T10 level), complete motor block was significantly earlier in Clonidine group as compared to Fentanyl group. Clonidine was better in achieving sensory level up to T6 and T4 level. Total duration of analgesia in Clonidine group was significantly prolonged. Time of first rescue analgesia and two segment regression time was significantly delayed in Clonidine group. Hemodynamic parameters (SBP, DBP, MAP, pulse rate, O2 saturation level) were comparable in both the drug groups, with more hypotensive effect in Clonidine group. In addition to this, incidence of sedation and side effects were comparable in both the drug groups.

Conclusion- Clonidine in combination with Ropivacaine is better drug than Fentanyl with Ropivacaine for epidural anesthesia in case of lower limb surgery as far as sensory &motor block characteristics and side effect profile are concerned.

KEYWORDS

Clonidine, epidural anesthesia, Fentanyl, lower limb orthopedic surgery, Ropivacaine.

INTRODUCTION-

Epidural anesthesia is nowadays the most commonly used technique for providing not only perioperative surgical anesthesia but postoperative analgesia in all surgical procedures carried on lower abdomen, pelvis and lower limb. Epidural procedure is definitely better than general one by blocking nociceptive impulses derived from operative site, less blood loss and reduced incidence of deep vein thrombosis with possibility of local anesthetic toxicity (Liu et.al. 1995). It is able to maintain continuous anesthesia after placement of an epidural catheter, thus allowing long surgical procedure possible (Tuohy 1944). In recent years, anesthetic drug Ropivacaine has increasingly replaced Bupivacaine as local anesthetic agent. Addition of epidural adjuvant can improve the effectiveness of local anesthetic by escalating the block and duration of analgesia (Agarwal et.al.2016). It also facilitates some side effects associated with required higher dose of Ropivacaine alone (Landau et.al. 2002). Clonidine, an α2-adrenoreceptor agonist, is used as an adjuvant to epidural anesthetics to enhance the analgesic effect. Adjuvant Clonidine reduces the dose requirement of the anesthetic agent that come up with stable cardiovascular course during anesthesia (Acalovschi et.al.1997). However, Clonidine is associated with sedation, hypotension and bradycardia (Reid 1981). Another potential adjuvant Fentanyl, a μ-opioid receptor agonist, enhances the neuraxial analgesia, although side effects such as pruritus, nausea, vomiting is common (Cherng et.al. 2005). Fentanyl has relatively rapid onset of action following administration (Sindhu et.al. 2015). It is important to note that both Clonidine and Fentanyl alone are unable to produce required adequate analgesic effect. These adjuvants are potent only with local anesthetics such as Ropivacaine.

Present study was conducted to compare clinical efficacy of Clonidine with Fentanyl as adjuvant to epidural Ropivacaine (0.50%) with emphasis on sensory and motor block profile, monitoring of hemodynamic parameters and side effects in patients admitted for lower limb surgery.

MATERIALS AND METHODS-

Present randomized double blinded study was conducted on randomly selected 60 patients who were divided in two groups -Ropivacaine+ Clonidine (R+C) and Ropivacaine + Fentanyl (R+F), with 30 patients in each group with ASA grade I and II status. Patients in the age group of 18-50 years, scheduled for undergoing elective lower limb orthopedic surgery and who gave written consent, were included in the study. Preoperative evaluation including detailed medical and surgical history, drug intake history, clinical evaluation, airway assessment were done for each patient under study. Visual Analogue Scale (VAS) was explained in detail to the patients in the preoperative period. Under strict aseptic precautions, Lumbar epidural anesthesia was performed using 17G Tuohy needle with patients in the sitting position in L3-L4 inter space and location of epidural space was confirmed by loss of resistance technique. Epidural catheter (19G) advanced cephalad 3–5cm into the epidural space. A test dose of 3 ml of 2% lignocaine with adrenaline was administered into epidural space and thereafter epidural catheter was secured and patients were placed supine. The anesthetist who prepared the drug combination did not participate in the monitoring or assessment of the patient. The person who performed the epidural block as well as monitoring was blinded from which group the patient belongs.

Patients of group R+C received epidural solution of 15 ml of 0.50% Ropivacaine with 1μg/Kg of Clonidine, and patients of group R+F received solution of 15 ml of 0.50% Ropivacaine with 1μg/Kg of Fentanyl.

All statistical practices were performed using SPSS version 23.

OBSERVATION AND RESULT-

Total 60 patients (30 in each group) participated in the present study. No significant difference in sex, age, weight was found between two drug groups. Thus, the two drug groups had comparable demographic profile (Table 1).

Table 1- Demographic parameters of two drug groups

Characteristics	R+C	R+F	p-value	Statistical output
Sex				
Male	24 (80.00%)	26(86.70%)	0.480	Non-significant
Female	06(20.00%)	04(13.30%)		

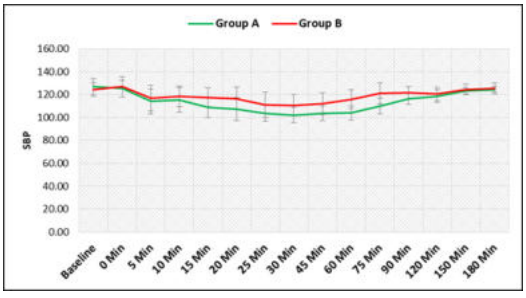
Age (Y)	40.16±01.82	41.60±03.82	1.864	Non-significant
Weight (Kg)	60.13±03.53	60.23±04.11	0.101	Non-significant

Baseline of hemodynamic characteristics such as SBP, DBP, MAP, PR and O2-saturation were also comparable in both the drug groups (Table 2).

Table 2- Baseline hemodynamic parameters in two drug groups

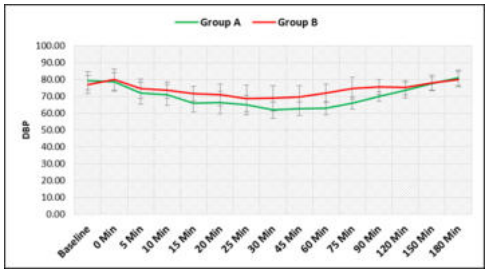
Characteristics	R+C	R+F	p-value	Statistical output
SBP	127.13±07.00	124.40±05.90	0.108	Non-significant
DBP	79.27±05.39	77.00±05.30	0.106	Non-significant
MAP	98.43±05.05	92.63±04.92	0.093	Non-significant
PR	83.47±06.01	83.80±05.39	0.822	Non-significant
O2-saturation	99.63±0.61	99.80±0.41	0.317	Non-significant

SBP was significantly lower in R+C group than in R+F group at 15 min to 90 min time intervals. Thereafter differences were comparable in both the drug groups up to 180 min (Graph 1).

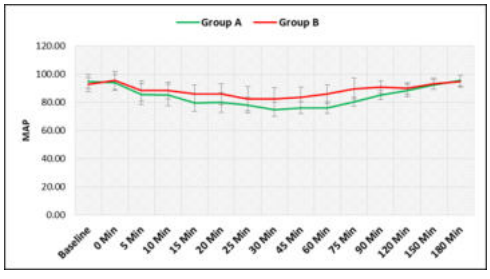


Graph 01- Intraoperative systolic blood pressure (SBP) at different time interval in two drug groups.

Similar patterns were observed in case of DBP and MAP (Graph 2 &3).

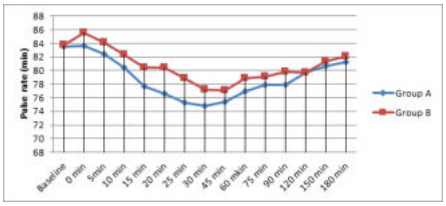


Graph 02- Intraoperative diastolic blood pressure (DBP) at different time intervals in two drug groups.

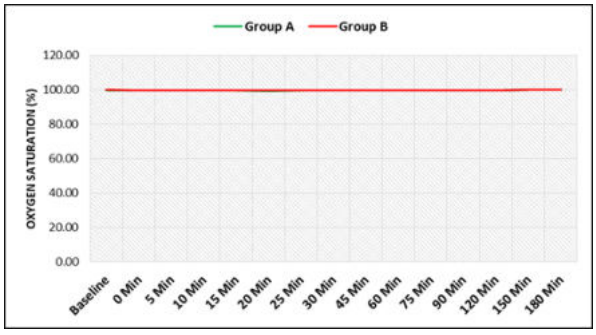


Graph 03- Comparison of mean arterial pressure (MAP) at different time intervals in two drug groups.

Pulse rate differences between the two drug groups were non-significant at all time intervals except at 20 min (graph 4) whereas O2 saturation level was no-significant at all time intervals (Graph 5).



Graph 04- Pulse rate (PR) in two drug groups at different time intervals.



Graph 05-Intraoperative oxygen saturation (%) in two drug groups.

Mean time of sensory onset at T10 level was significantly earlier in case of R+C group, in comparison to R+F group. In addition to this, time taken for complete motor block was significantly earlier in R+C group, than in R+F group. Mean duration of analgesia was significantly prolonged in case of R+C group in comparison to R+F group. This resulted in significantly delayed time of first rescue analgesia and two segment regression time in R+C group than in R+F group. Therefore, it can be concluded that Clonidine in combination with Ropivacaine is better than Fentanyl with Ropivacaine in terms of motor and sensory block characteristics (Table 3).

Table 3- Motor and sensory block characteristics of two drug groups-

Characteristics (min)	R+C group	R+F group	p-value	Statistical output
Sensory onset at T10 level	13.86±0.68	14.40±0.96	0.014	Significant
Complete motor block	19.00±03.05	23.33±03.03	<0.0001	Significant
Duration of analgesia	335.83±41.32	285.17±25.91	<0.0001	Significant
First rescue analgesia	373.67±45.64	314.10±28.40	<0.0001	Significant
Two segment regression time	115.60±05.51	106.86±05.17	0.067	Significant

Maximum sensory level achieved have also been worked out at different dermatome levels (Table 4).

Table 4- Intergroup comparison of distribution of maximum sensory level achieved-

Max. sensory level achieved	Group R+C		Group R+F		p-value	Statistical output
	No.	%	No.	%	0.033	Significant
T4	05	16.66%	01	03.34%		
T6	20	66.66%	14	46.66%		
T8	04	13.34%	12	40.00%		
T10	01	03.34%	03	10.00%		
Total	30	100.00%	30	100.00%		

Differences in sedation score at different time intervals in two drug groups are as follows (Table 5).

Table 5- Sedation score in two drug group.

Time interval	R+C group	R+F group	p-value	Statistical output
0 min	01.00±00.00	01.00±00.00	01.00	Non-significant
15 min	01.03±0.18	01.07±0.25	0.557	Non-significant
30 min	01.60±0.56	01.27±0.45	0.017	Significant
45 min	01.77±0.63	01.23±0.43	0.001	Significant
60 min	01.63±0.67	01.10±0.31	<0.0001	Significant
120 min	01.13±0.35	01.00±00.00	0.040	Significant
180 min	01.00±00.00	01.00±00.00	01.00	Non-significant

Although most patients in both groups showed no side effects, various side effects have been observed in patients of two drug groups with different proportion. Moreover, differences in proportion were non-significant, i.e. the two drug groups have comparable safety profile (Table 6)

Table 6- Various Side effects observed in two drug groups.

Side Effects	Group A		Group B		p-value	Statistical output
	No.	%	No.	%		
None	17	56.7%	17	56.7%	0.110	Non-significant
Bradycardia	2	6.7%	0	0.0%		
Bradycardia+ Hypotension	1	3.3%	0	0.0%		
Dry mouth	3	10.0%	0	0.0%		
Hypotension	6	20.0%	4	13.3%		
Nausea	1	3.3%	5	16.7%		
Pruritus	0	0.0%	1	3.3%		
Shivering	0	0.0%	1	3.3%		
Vomiting	0	0.0%	2	6.7%		

DISCUSSION-

Baseline mean SBP was similar in both the drug groups. It started decreasing up to 30 min after epidural block, returned to baseline level gradually in both the drug groups. The difference in SBP was significantly less in R+C group between 15 min to 90 min interval. Hence SBP was similar during respective time interval between two drug groups. We observed similar initial declining trend and later on increasing trend in case of DBP and MAP also in present study. Sindhu et al (2015) reported hypotensive action of Clonidine. Here we also found the similar hypotensive situation in R+C group but it was manageable. In addition to this Nigam et al (2017) reported similar non- significant difference in SBP between R+C and R+F group.

Difference in mean oxygen saturation was non- significant between the two drug groups during the procedure. Non-significant difference between oxygen saturation level of R group, R+C group and R+F group from baseline to 180 min have been observed by Sindhu et al (2015) and Bajwa et al(2010). Present finding in our study is similar to observations in these previous studies.

Statistically pulse rate was similar except at 20 min in both drug groups in the present study. Fall in heart rate was significant in R+C group when compared to R+F group at 15 min and 30 min in studies conducted by Sindhu et al (2015) and Agarwal et al (2016)**.** Mean HR was comparable during the entire procedure and were non-significant between R+C and R+F group in studies conducted by Bajwa et al (2010) and Nigam et al. (2017). Therefore, present observation is similar to these previous results.

In the present study the mean time of sensory onset at T10 level in R+C group was significantly earlier in comparison to R+F. Agarwal et al (2016) and Bajwa et al(2010) noted early onset in R+F group than in R+C group. All these workers used 0.75% Ropivacaine, against 0.50% in the present study. Nigam et al(2017) reported onset time of adequate sensory analgesia at T10 at 6.58±0.66 min in R+C group and 6.87±0.35 min in R+F group. Our result is in agreement with that of Nigam et.al (2017).

We observed significant differential effects of drugs on sensory level achieved at various dermatome levels and R+C was better than R+F in this regard. In the present study R+C was better than R+F in achieving maximum sensory level of T6 and T4. Agarwal et al (2016), Bajwa et al (2010) and Kohli et al. (2016) mentioned comparable median maximum sensory level achieved in R+C and R+F groups at T6, T6-7 and T5-6, respectively.

The mean time of complete motor block in R+C group was 19.00±3.05 min, while it was 23.33±3.03 min in case of R+F group. In other words ,time taken for complete motor block was significantly earlier in group R+C than in group R+F. Sindhu et al (2015), Agarwal et al (2016), Bajwa et al (2010) and Nigam et al (2017) reported earlier complete motor block in R+F group than in R+C group. Although difference in time of complete motor block was reported in both the drug groups. Complete motor block at 19.00±3.05 min in R+C group in present study is close to that reported by Nigam et al (2017), and Bajwa et al (2010). In the same manner, time of complete motor block in R+F group of 23.33±3.03 min in present study is comparable to that reported by Agarwal et al (2016).

Total duration of analgesia in R+C group was significantly prolonged in comparison to R+F group. Various workers reported different duration of analgesia for both drug combinations. Sindhu et al (2015) reported duration of analgesia of 446.57±12.35 min and 338.07±7.71 min in R+C and R+F respectively. Agarwal et al (2016) mentioned duration of analgesia of 372.07±7.13 min in R+C group, and 357.23±9.36 min in R+F group. The mean total duration of sensory analgesia was 183.33±16.47 min in group R+F, and 242.00±19.72 min in group R+C (Nigam et al. 2017). Comparatively, less duration of analgesia in both the drug groups, 156.78±10.28 min(R+C) and 168.98±7.68 min (R+F) was reported by Bajwa et al (2010). Present result is similar to these previous findings.

Time of first rescue analgesia was significantly delayed in R+C group as compared to R+F group in the present study. Kaur et al (2014) reported low dose of Dexmedetomidine as an adjuvant to epidural Ropivacaine as compared to plain Ropivacaine for rescue analgesia. Clonidine is drug of same chemical family as Dexmedetomidine, therefore it may be argued that result of present study is similar to what reported by Kaur et al (2014).

In the present study two segment regression time was significantly delayed in R+C as compare to R+F. Agarwal et al (2016) showed prolonged regression time in case of R+C (118.70±9.60 min) than in R+F (106.70±12.30 min). Similarly, prolonged two segment regression time in R+C group (138.33±8.74 min) than in R+F (119.67±4.53 min) was reported by Nigam et al (2017). Our result is similar to these previous studies.

The significant differences in sedation score between two groups were observed between 30 min to 140 min. At 180 min, no significant difference in sedation score was observed between two groups. Sindhu et al (2015) and Agarwal et al (2016) observed that incidence of sedation is more associated with R+C group. In present study we also noted significantly high sedation score in R+C group between 30 min to 140 min. However, it is important to note that at 180 min, no significant difference in sedation score was observed between two groups. Thus, both groups are comparable as far as incidence of sedation is concerned.

Statistically, proportions of different types of side effects in two drug groups were non-significant. Kohli et al(2016) argued that a significant number of patients in RF group (33.33%) developed nausea and vomiting. Similarly, dry mouth was another significant side effect (23.3%) in patients of RC group. However, they also reported nausea, vomiting, pruritus and urinary retention to be significantly high in R+F group than in R+C group. Bajwa et al(2010) also reported significantly high incidence of nausea/vomiting and sedation in R+F group, dry mouth in R+C group. In oppose to these, no patients in R+C and R+F, suffered from shivering, nausea, vomiting, urinary retention or dry mouth (Agarwal et al2016). Higher percentage of nausea and vomiting were noticed in R+F group, but the difference was non-significant (Nigam et al2017). Present finding is in agreement with observations in above studies**.**

CONCLUSION-

With due consideration of result and discussion, following conclusions may be drawn in the comparative evaluation of these two adjuvants towards epidural anesthesia in lower limb orthopedic surgeries –

1- Time of sensory onset at T10 level was significantly earlier in case of Clonidine group, as compared to Fentanyl group.
2- Time taken for complete motor block was significantly earlier in Clonidine group, than in Fentanyl group.
3- Clonidine was better than Fentanyl in achieving maximum sensation at different sensory levels specifically up to the level of T6 and T4.
4- Total duration of analgesia in Clonidine group was significantly prolonged in comparison to Fentanyl group.
5- Time of first rescue analgesia was significantly delayed in Clonidine group, than in Fentanyl group.
6- Two segment regression time in Clonidine group was delayed in comparison to Fentanyl group.
7- Hemodynamic parameters (SBP, DBP, MAP, pulse rate, O_2 saturation level) were comparable in both the drug groups, with initial hypotensive trend in Clonidine group.
8- Both Clonidine and Fentanyl groups are comparable as far as incidence of sedation is concerned.
9- Both Clonidine and Fentanyl are comparable as far as side effects are concerned.

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