

Original Research Article

To Compare the Effect of Dexmedetomidine, Clonidine and Fentanyl on Intraoperative Hemodynamics When Used as Adjuvant in Epidural Anaesthesia in Lower Limb Orthopedic Surgeries

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Abstract

Background & Methods: The aim of the study is to compare the effect of Dexmedetomidine, Clonidine and Fentanyl on intraoperative hemodynamics when used as adjuvant in epidural anaesthesia in lower limb orthopaedic surgeries. All the patients were underwent pre anaesthetic evaluation and were shifted to procedure room on the day of surgery. Drug and equipment necessary for resuscitation and general anesthesia were kept ready and 2 IV access using 18G cannula were secured and 500ml of RL infusion started which was given to all patients half an hour before anesthetic procedure as pre-loading.

Results: The present study observed a statistically highly significant drop (using ANOVA) in diastolic blood pressure among patients of Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$). Study observed a statistically highly significant drop in systolic blood pressure among Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$).

Conclusion: All patients in three groups were comparable according to sex & type of surgery and duration of surgery with no significant statistical difference. ($p > 0.05$). Study concluded a statistically highly significant drop in systolic blood pressure among Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$). Study observed a statistically highly significant drop (using ANOVA) in diastolic blood pressure among patients of Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$).

Keywords: hemodynamic, Dexmedetomidine, Clonidine, Fentanyl, epidural & anaesthesia.

Study Design: Prospective randomized Comparative study

1. Introduction

Epidural anaesthesia is the one of the most commonly used procedure for lower abdominal and limb surgeries[1]. It provides not only peri-operative surgical anaesthesia but also post-operative analgesia. Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgeries. Epidural blockade is one of the most useful and versatile procedures in modern anaesthesiology. It is unique as it can be placed at virtually any level of the spine, allowing more flexibility in its application to clinical practice[2].

The safe, effective administration of an epidural block begins with a thorough knowledge of the anatomy of the vertebral column, ligaments and blood supply, the epidural space, spinal canal and nearby associated structures[3].

The human vertebral column comprises of 7 cervical, 12 thoracic and 5 lumbar vertebrae. At the caudal end, the 5 sacral vertebrae gets fused to form the sacrum, and the 4 coccygeal vertebrae are anatomically fused to form the coccyx[4].

The normal spinal column is straight when viewed dorsally or ventrally. When viewed from the side, there are two ventrally convex curvatures in the cervical and lumbar regions, giving the spinal column the appearance of double C[5].

Adding adjuvant accelerates onset and prolongs sensory and motor blockade. Dexmedetomidine, a specific alpha 2 adrenoreceptor agonist acts via post synaptic alpha 2 receptors, having main action of sedation, anxiolysis and analgesia without causing significant respiratory depression, thus giving this drug its uniqueness. Clonidine which is also an alpha 2 adrenoreceptor agonist acting via stimulating pre synaptic adrenoreceptor having main action of antihypertension, sedation, anxiolysis and analgesia. It is useful adjuvant to local anaesthetics for postoperative analgesia after major abdominal surgeries and orthopaedic surgeries. It enhances both sensory and motor blockade duration of epidural injection of local anaesthetics[6]. Fentanyl which is a highly selective mu-agonist opioid, acting via interacting with Gi protein receptor having main actions of analgesia and respiratory depression. The most significant effect of it is bradycardia of vagal origin and respiratory depression. The present study is being undertaken to evaluate the variation in intraoperative hemodynamic of Dexmedetomidine 1.0µg/kg in comparison to Clonidine 2µg/kg and 1mcg/kg Fentanyl when used as adjuvants to 0.75% Ropivacaine for epidural block in lower limb orthopedic surgeries[7].

2. Material and Methods

Present study was conducted in the Tertiary Care Centre after IEC approval. All patients undergone pre anaesthetic evaluation were shifted to procedure room on the day of surgery. Drug and equipment necessary for resuscitation and general anesthesia was kept ready and 2 IV access using 18G cannula were secured and 500ml of RL infusion started which was given to all patients half an hour before anesthetic procedure as pre-loading. Base line vitals were recorded. All the equipment's and emergency drugs necessary to administer epidural anaesthesia was checked and kept ready. The patient was placed in sitting position and after identification and marking of anatomical landmarks sterile painting and draping was done. With all aseptic measures the skin over L3-L4 interspace was anesthetized with 2ml of 2% Lignocaine.

45 patients enrolled in this study were randomized using computer generated table into 3 groups; Group A received Ropivacaine with Dexmedetomidine, Group B received Ropivacaine with Clonidine, Group C received Ropivacaine with Fentanyl.

An 16G Touhy needle was passed through this space and advanced slowly until it enters the epidural space which was confirmed by loss of resistance technique. Then an 16G epidural catheter was passed through the needle into epidural space and secured with minimum of 3-4cm within the space. 3ml of 2% Lignocaine with adrenaline 1:200000 was given as test dose to confirm the proper placement of catheter.

Inclusion Criteria-

After approval from Institutional Ethics Committee and informed written consent 45 patients of either sex of ASA Grade I and II, age ranging from 20 to 60 years scheduled for lower limb orthopaedic surgeries under epidural block was enrolled in this study.

Exclusion Criteria-

1. Patient refusal.
2. Patients on anti-coagulation treatment (INR >1.5).
3. Patients with congenital abnormalities of lower spine and meninges.
4. Patients with active disease of CNS.
5. Patients with history of allergy to local anesthetics or Alpha-2 adrenergic agonists.
6. Patients with uncontrolled systemic illness like diabetes mellitus, hypertension, etc.
7. Patients with uncorrected hypovolemia.
8. Patient Local site infection.

3. RESULT**TABLE 1- DISTRIBUTION OF PATIENTS ACCORDING TO GENDER IN THREE GROUPS**

Gender	Group A (RD)		Group B (RC)		Group C (RF)		P value
	n	%	N	%	n	%	
Male	08	53.3	10	66.7	09	64	0.83
Female	07	46.7	05	33.3	06	40	
Total	15	100	15	100	15	100	

Majority of patients in present study was males in all the groups. Males constituted 53.3% & 66.7% of population in group A and B respectively whereas 60% patients in group C was males. The gender distribution in present study in the three groups using chi square test was observed to be comparable (p=0.83).

Table 2- DURATION OF SURGERY IN THREE DIFFERENT GROUPS

Duration of surgery (min)	Group A (RD)		Group B (RC)		Group C (RF)		P value
	Mean	SD	Mean	SD	Mean	SD	
	93.90	6.61	96.50	09.43	97.97	12.10	0.15

Above table represents mean duration of surgery amongst the patients of three groups. Mean duration of surgery in group A was 93.90±6.61 minutes whereas the mean duration of surgery in Group B and C was 96.50±09.43 and 97.97±12.10 respectively. Test of significance (ANOVA test) observed no statistically significant difference in duration of surgery among the three groups, (p=0.15).

Table 3- COMPARISON OF SYSTOLIC BLOOD PRESSURE AT VARIOUS TIME INTERVALS BETWEEN THE GROUPS

Systolic Blood pressure (mmHg)	Group A (RD)		Group B (RC)		Group C (RF)		P value
	Mean	SD	Mean	SD	Mean	SD	
Basal	123.80	3.699	122.87	4.167	123.13	4.066	0.65
5 minute	124.27	3.956	124.27	3.352	124.67	3.032	0.88
10 minute	119.00	4.835	118.73	3.982	118.27	4.258	0.81
15 minute	117.53	3.589	112.27	7.478	112.33	7.068	0.002
20 minute	116.53	5.303	110.93	10.748	109.20	9.419	0.005
25 minute	115.47	5.117	109.67	9.728	108.67	9.178	0.004
30 minute	115.00	5.324	108.13	9.909	107.53	9.258	0.001

40 minute	115.00	5.139	108.80	10.823	107.13	9.108	0.002
50 minute	115.20	5.549	109.43	11.398	107.87	9.641	0.007
60 minute	113.80	5.616	109.60	11.993	108.00	9.896	0.05
70 minute	114.73	4.283	108.60	10.702	108.20	8.903	0.005
80 minute	114.73	4.472	109.07	11.064	109.13	9.947	0.02
90 minute	115.33	4.373	109.20	11.075	109.73	10.086	0.02
105 minute	115.73	4.226	108.93	10.031	109.73	9.976	0.005
120 minute	116.00	4.267	109.60	9.733	109.73	9.450	0.004
135 minute	116.27	4.093	114.07	5.860	114.73	6.136	0.28
150 minute	116.87	4.321	115.53	5.770	116.00	5.872	0.62
180 minute	117.27	4.185	114.20	7.902	115.07	8.267	0.23
210 minute	117.80	4.405	115.73	4.571	116.47	4.862	0.22

Mean systolic blood pressure at baseline was 123.80 ± 3.69 , 122.87 ± 4.16 and 123.13 ± 4.066 mmHg in group A, B and C respectively. ANOVA test was used to compare three groups. The present study observed a statistically highly significant drop in systolic blood pressure among Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$).

Table 4- COMPARISON OF DIASTOLIC BLOOD PRESSURE AT VARIOUS TIME INTERVALS BETWEEN THE GROUPS

Diastolic Blood pressure (mmHg)	Group A (RD)		Group B (RC)		Group C (RF)		P value
	Mean	SD	Mean	SD	Mean	SD	
Basal	83.27	3.352	83.07	3.657	83.53	3.104	0.87
5 minute	85.27	3.084	84.93	2.766	84.87	3.181	0.86
10 minute	78.27	3.513	79.13	3.627	79.13	3.589	0.56
15 minute	76.47	3.471	71.47	5.329	71.53	5.399	0.001
20 minute	75.47	3.998	69.47	6.078	69.87	5.704	0.001
25 minute	75.13	4.158	69.67	6.456	69.20	6.206	0.001
30 minute	74.20	4.342	67.53	6.163	68.00	6.560	0.001
40 minute	73.60	4.438	67.87	6.847	67.80	6.692	0.001
50 minute	74.07	4.346	67.93	6.443	68.13	6.927	0.001
60 minute	73.60	4.107	70.40	7.815	68.87	6.426	0.05
70 minute	73.47	4.455	69.27	7.268	68.33	6.370	0.004
80 minute	73.67	4.037	69.47	7.592	68.33	6.082	0.003
90 minute	74.13	4.297	69.47	7.592	69.47	7.682	0.01
105 minute	74.40	4.407	70.40	6.420	70.13	6.323	0.008
120 minute	75.07	4.448	70.60	7.318	70.53	7.276	0.01
135 minute	76.13	4.783	75.00	5.502	75.73	5.502	0.70
150 minute	76.60	4.553	76.33	5.707	76.60	5.876	0.98
180 minute	76.53	4.066	75.00	5.913	76.47	6.230	0.48
210 minute	76.53	4.066	75.87	4.265	77.07	4.510	0.56

The diastolic blood pressure at baseline was comparable among three groups. The mean diastolic blood pressure at baseline in group A, B and C was 83.27 ± 3.352 mmHg, 83.07 ± 3.65 mmHg and 83.53 ± 3.104 mmHg. The present study observed a statistically highly significant drop (using ANOVA) in diastolic blood pressure among patients of Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$).

Table 5: COMPARISON OF HEART RATE AT VARIOUS TIME INTERVALS BETWEEN THE GROUPS

Pulse rate (per minute)	Group A (RD)		Group B (RC)		Group C (RF)		P value
	Mean	SD	Mean	SD	Mean	SD	
Basal	78.70	4.75	78.90	6.20	78.70	6.19	0.97
5 minute	79.80	5.7	80.10	6.2	80.07	5.75	0.98
10 minute	74.23	5.18	73.43	4.56	73.10	4.17	0.63
15 minute	71.43	5.74	70.03	4.92	70.87	4.88	0.58
20 minute	70.33	6.86	65.43	6.54	65.97	6.18	0.008
25 minute	68.37	6.99	63.83	6.0	64.30	5.82	0.01
30 minute	67.50	7.05	63.63	5.94	64.27	5.47	0.04
40 minute	67.17	6.60	62.73	5.81	63.90	5.60	0.02
50 minute	66.53	6.30	66.40	6.04	66.60	6.39	0.99
60 minute	66.13	6.05	66.20	5.62	66.67	5.64	0.93
70 minute	67.03	5.38	66.57	4.85	68.33	6.06	0.43
80 minute	67.27	5.13	66.77	4.95	67.90	5.64	0.71
90 minute	67.53	4.73	65.77	4.61	67.30	4.55	0.28
105 minute	67.13	5.85	67.30	6.48	69.03	6.22	0.23
120 minute	66.90	5.19	66.47	4.95	67.77	4.38	0.49
135 minute	67.73	4.77	66.97	4.38	68.10	4.59	0.76
150 minute	68.43	4.76	66.87	5.14	68.67	5.94	0.85
180 minute	69.17	3.92	68.17	3.58	69.93	4.06	0.45
210 minute	69.53	4.09	68.23	3.64	69.37	5.03	0.89

Mean baseline heart rate in patients of group A was 78.70 ± 4.75 per minute, 78.90 ± 6.20 per minute in group B and 78.70 ± 6.19 per minute in group C. From 20 minutes following anesthesia, statistically significant difference (using ANOVA) amongst 3 groups was observed with mean heart rate of 70.33 ± 6.86 , 65.43 ± 6.54 and 65.97 ± 6.18 per minute in group A, B and C respectively. The present study observed statistically highly significant drop (using ANOVA) in heart rate among Group B and C during 20 to 40 mins ($p < 0.05$). There was no significant difference in mean heart rate thereafter, throughout the observation period.

4. DISCUSSION

In present study, 17ml of 0.75% Ropivacaine with $1.0 \mu\text{g/kg}$ Dexmedetomidine was given to the patients of Group A (RD); 17ml of 0.75% Ropivacaine along with $2 \mu\text{g/kg}$ Clonidine was given to patients of Group B (RC) whereas Group C (RF) patients was given 17ml of 0.75% Ropivacaine with 1mcg/kg Fentanyl.

Bajwa S J et al(2011)[8] observed that the decrease in mean systolic pressure in Group RD and RC but it never recorded 15% below of baseline value and it was statistically insignificant.

At baseline, heart rate in three groups were comparable ($p > 0.05$). However a highly significant drop in heart rate was observed amongst clonidine and fentanyl group in present study as compared to dexmedetomidine group during 20 to 40 mins ($p < 0.05$). No significant difference in heart rate was observed between the three groups after 40 minutes ($p > 0.05$).

We observed a highly statistically significant drop in systolic, diastolic and mean blood pressure among Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$). The fall in B.P was managed by intravenous fluids and doses of mephenteramine 6mg stat.

Rahimzadeh P et al (2018)[9] also observed statistically significant drop in mean arterial pressure during the first 60 minutes block in the patients of fentanyl group as compared to dexmedetomidine group.

Singh B R et al (2015)[10] observed that decrease in mean systolic pressure was seen in both the groups RC and RF at 15 min, 30 min, 60 min and 120 min and difference was statistically significant.

Paul A et al (2017)[11] also observed no statistically significant difference in mean arterial pressure between dexmdetomidine and fentanyl group ($p > 0.05$).

Neha et al (2017)[12] observed no statistical difference in heart rate, blood pressure while comparing clonidine and fentanyl group.

5. CONCLUSION

All patients in three groups were comparable according to sex & type of surgery and duration of surgery with no significant statistical difference. ($p > 0.05$). Study concluded a statistically highly significant drop in systolic blood pressure among Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$). Study observed a statistically highly significant drop (using ANOVA) in diastolic blood pressure among patients of Group B and C from 15 minutes following the block to 120 minutes of the procedure ($p < 0.05$). The present study observed statistically highly significant drop (using ANOVA) in heart rate among Group B and C during 20 to 40 mins ($p < 0.05$). There was no significant difference in mean heart rate thereafter, throughout the observation period.

6. REFERENCES

1. Moraca RJ, Sheldon DG Thirlby RC. The Role of Epidural Anesthesia and Analgesia in surgical Practice. *Ann Surg* 2003; 238(5): 663-73.
2. Wahlander S, Frumento RJ et al. A prospective, double-blind, randomized, placebo controlled study of dexmedetomidine as an adjuvant to epidural analgesia after thoracic surgery. *J Cardiothorac Vasc Anesth* 2005;Oct;19(5):630-5.
3. Korula S, George GM, Ipe S, Abraham SP, Epidural anesthesia and postoperative analgesia for bilateral inguinal mesh hernioplasty; Comparison of equipotent doses of ropivacaine and bupivacaine. *Saudi J Anaest* 2011;5(3):277-81.
4. Eisenach J, Detweiler D, Hood d. Hemodynamic and analgesic actions of epidurally administered clonidine. *Anesthesiology* 1993; 78(2):277-87.
5. Alves TCA, Braz JRC. Clinical evaluation of clonidine associated to ropivacaine for epidural anesthesia. *Rev Bras Anesthesiol* 2002; 52(4):410
6. Salgado PFS, Sabbag AT, Silva PC da, Brienze SLA, Dalto HP, Modolo NSP et al. synergistic effect between dexmedetomidine and 0.75% ropivacaine in epidural anesthesia. *Rev Assoc Medica Bras(1992)* 2008;4(2):110-5.
7. Oriol-lopez SA, Maldonado-Sanchez KA, Hernandez-Bernal CE, Castelazo-Arredondo JA, Moctezuma RL. Epidural dexmedetomidine in regional anaesthesia to reduce anxiety. 2008;31:271-77.

8. Bajwa SJS, 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(2):116-21.
9. Vashishth T, Verma M, Garg S, Sharma G, Vashishth S (2016) Comparative study of dexmedetomidine and fentanyl with ropivacaine 0.75% in epidural analgesia in lower limb orthopaedic surgeries. *National Journal of Medical and Dental Research* 4(3): 201-212.
10. Rastogi B, Singh VP, Mangla D, Gupta K, Jain M (2015) Dexmedetomidine as an adjuvant to epidural 0.75% ropivacaine in patients undergoing infraumbilical surgery: a clinical study. *Glob Anesth Perioper Med* 1(1):
11. Paul A, Nathroy A, Paul T. A comparative study of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in lower limb surgeries. *J Med Sci* 2017;37:221-6
12. Neha Nupoor ,Anand T Talikoti -Epidural Bupivacaine with Dexmedetomidine or Fentanyl for Lower Abdominal and Lower Limb Surgeries *Journal of Clinical and Biomedical Sciences J Clin Biomed Sci* 2016; 6(1):14-19