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**ORIGINAL ARTICLE**

**COMPARATIVE STUDY OF EPIDURAL CLONIDINE VERSUS DEXMEDETOMIDINE AS AN ADJUVANT TO BUPIVACAINE FOR POST OPERATIVE ANALGESIA IN INFRA UMBILICAL SURGERIES UNDER COMBINED SPINAL EPIDURAL ANAESTHESIA**

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**ABSTRACT**

**INTRODUCTION:** Postoperative pain is an acute pain which starts with surgical trauma and ends with tissue healing. Clonidine is an alpha-2 receptor agonist. Dexmedetomidine is a super selective alpha-2 agonist made up of medetomidine's dextrogyrous enantiomer. They produce analgesia with haemodynamic changes and minimum side effects. **METHODS:** A clinical study of 70 cases of ASA grade 1 & 2 between the age group 25-65yrs undergoing abdominal, obstetrical, gynaecological and orthopaedic surgeries under epidural anaesthesia. At the end of surgery patients were allocated to receive either of (Group - C) Clonidine 2 µg/kg with 5 ml of Normal saline. (No = 35) or (Group - D) Dexmedetomidine 1 µg/kg with 5 ml of Normal saline. (No = 35). Cardio-respiratory effects like Pulse rate, blood pressure, respiratory rate and side effects like nausea, vomiting, pruritus, hypotension, sedation, respiratory depression were studied. Continuous data was analyzed by student's "t"-test and categorical data by Chi-square test and possible significance has been determined considering it statistically significant if the P value < 0.05. **RESULTS:** The duration of analgesia in group-D (440.57 + 45.89 (SD) min) was significantly more when compared to group-C (325.71+ 48.89 (SD) min). In comparison of Group C and Group D, by using the unpaired student t test, highly significant difference in VAS was seen from 2.5 hours till 6hrs in between the groups. In addition Group D patients did not experience pain till 7<sup>th</sup> and 8<sup>th</sup> hour but Group C patients experienced pain at the end of 6 hours itself. Highly significant difference in sedation score was seen from 0 min till 6hrs in between the groups. In addition sedation was prolonged in Group D patients till 7<sup>th</sup> to 8<sup>th</sup> hours, but in Group C the sedation was persisting up to 4 hours. **CONCLUSION:** It was concluded that epidural dexmedetomidine provides an excellent and prolonged duration of analgesia when compared to epidural clonidine. Longer duration of analgesia along with good sedation was also seen when compared with clonidine group.

**Keywords:** Comparative study, Epidural Clonidine, Dexmedetomidine.

**1. INTRODUCTION**

Postoperative pain is an acute pain which starts with surgical trauma and ends with tissue healing. The use of conventional local anaesthesia like bupivacaine and lignocaine has been unable to provide anaesthesia for longer surgery or analgesia for longer duration. Continuous epidural analgesia with a catheter has been implemented for these purposes (Roger, 1995). Various modalities have been tried for the management of postoperative pain (Bridenbaugh et al., 1998).

Clonidine being an alpha-2 receptor agonist, produces analgesia without any respiratory depression. Furthermore, in low to moderate doses it causes no haemodynamic instability. Dexmedetomidine, made up of medetomidine's dextrogyrous enantiomer, is currently considered a super selective alpha-2 adrenergic agonist which when administered by epidural route, had analgesic properties and potentiates the effects of local anaesthetics (Boico et al., 1988). It acts on both pre and post synaptic sympathetic nerve terminals and central nervous system. Most of the controlled, double blind perioperative period studies demonstrate efficacy and specific advantages of dexmedetomidine over clonidine.

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## 2.METHODS

A clinical study of 70 cases of ASA grade 1 & 2 between the age group 25-65 yrs undergoing abdominal, obstetrical, gynaecological and orthopaedic surgeries under Combined Spinal Epidural anaesthesia. Patients with a history of known sensitivity to the drugs used, patients with gross spinal deformity, peripheral neuropathy or with contraindications to neuraxial block – local systemic infections, coagulation disorders, hypovolemia, signs of raised intracranial tension, uncontrolled hypertension and patients on tricyclic anti-depressants, alpha-2 adrenergic agonists or opioids were excluded from the study.

Patients were visited on the previous day of the surgery, a detailed medical history was taken and systemic examinations were carried out. Basic laboratory investigations like complete haemogram, bleeding time, clotting time, blood sugar, blood urea, serum creatinine, and urine analysis were carried out routinely on all patients. ECG was done in patients more than 40 years of age and chest X-ray when indicated. The entire procedure was explained to the patient and asked to notify after surgery when the patient experiences pain. Patients were also explained about Visual Analogue Scale (VAS) and were taught how to express the degree of pain on the scale. A written consent was taken from the patient. Tab. Diazepam 5-10mg orally was given on the previous night. Patients were kept nil orally for 8 hrs before surgery.

All patients were operated under Combined Spinal Epidural (CSE) using 4ml of 0.5 % heavy Bupivacaine in spinal anaesthesia and 0.5% isobaric Bupivacaine in epidural as required till the end of surgery. The patient was made to lie supine on the operation table. Routine monitors like NIBP, pulse oximetry, ECG were connected. Baseline blood pressure, heart rate and respiratory rate were noted. An I.V. line was secured with 18 G cannula and infusion was started. The patient was placed in sitting position or right lateral or left lateral. With all aseptic precautions, a skin wheal was raised at L2-L3 interspace with 2ml of 2% lignocaine. The epidural space was identified using a 18G Tuohy needle with loss of resistance to air technique. Then 18G Portex epidural catheter was passed through the epidural needle till about 2-3 cm of the catheter is in epidural space. The needle was withdrawn and 3cc of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter as a test dose and observed for any intravascular or intrathecal injection. Lumbar puncture was performed then by mid line approach by using disposable Quincke spinal needle (23G) at L3 – L4 intervertebral space and injected 4 ml of heavy 0.5% Bupivacaine. Then the catheter was fixed to the back. Isobaric Bupivacaine 0.5% was injected as required till the end of surgery. At the end of surgery patients were allocated to receive either of **Group – C** Clonidine 2 µg /kg with 5 ml of Normal saline. (No = 35). **Group – D** Dexmedetomidine 1µg /kg with 5 ml of Normal saline. (No = 35). No narcotics were administered throughout the intra-operative period. Pain was assessed by visual analogue score (VAS) every 15 min in 1/hr and at 1.5,2,2.5,3,3.5,4,5,6,8,12,24 hrs post operatively. **Visual Analogue Scale (VAS)** was used to assess the intensity of pain and pain relief. This scale consisted of a 10 cm line, marked at 1cm each, on which patient expresses the

degree of pain by placing a point. Mark "0" represents no pain and mark "10" represents worst possible pain. The time at which rescue analgesic (reappearance of pain with VAS >4/10) was given is noted and the patient was asked to give a global assessment of the overall effectiveness of the analgesic treatment (quality of analgesia). In post operative period, they were asked to express the intensity of pain.

**Sedation** scores were assessed every 15 minutes both intra and post operatively using a four point score Grade 0 - Patient wide awake. Grade 1 - Patient is sleeping comfortably, but responding to verbal commands. Grade 2 - Deep sleep but arousable. Grade 3 - Deep sleep, unarousable.

Post operatively, monitoring of VAS scores and sedation scores were continued until the time of regression of sensory block to L1 dermatome. At the time at which rescue analgesia was given, the patient was asked to give a global assessment of the over all effectiveness of the analgesic treatment. **Quality of analgesia** was assessed depending on this as noted below and compared in both the groups.

TABLE 1 : QUALITY OF ANALGESIA

Pain Score	Pain Relief
0	No Pain Relief
1	Poor Pain Relief
2	Fair Pain Relief
3	Good Pain Relief
4	Excellent Pain Relief

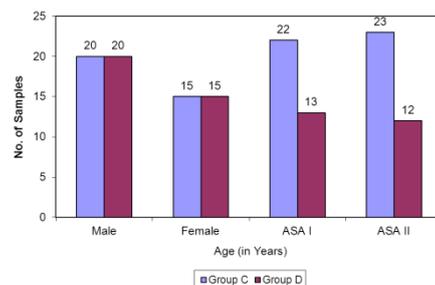
Continuous data was analyzed by student's "t"-test and categorical data by Chi-square test and possible significance has been determined considering it statistically significant if the P value < 0.05.

## 3.RESULTS

A clinical study of 70 cases of ASA grade 1 & 2 between the age group 25-65 yrs undergoing abdominal, obstetrical, gynaecological and orthopaedic surgeries under Combined Spinal Epidural anaesthesia was undertaken for achieving our objectives. The demographic characteristics in both the groups did not show any statistical significant difference.

TABLE 2: DEMOGRAPHIC PROFILE

Group	Male	Female	ASA I	ASA II	Age (yrs) Mean
Group C	20	15	22	23	46.88
Group D	20	15	13	12	41.91

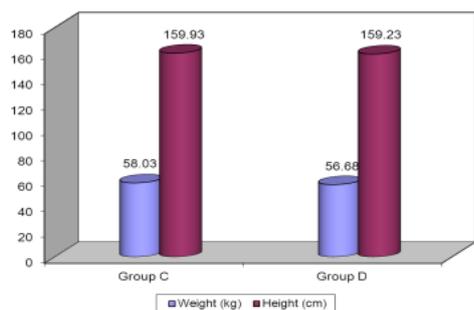


The mean age in both the groups are comparable (46.88 yrs in Group C and 41.91 yrs in Group D). The maximum and minimum age in Group C was 65yrs and 25yrs and in Group

D was 65yrs and 25yrs. The ASA status and the sex incidence in both Group C and Group D are also similar. The mean weight and height in Group C and Group D are comparable (58.0kg and 56.7kg).

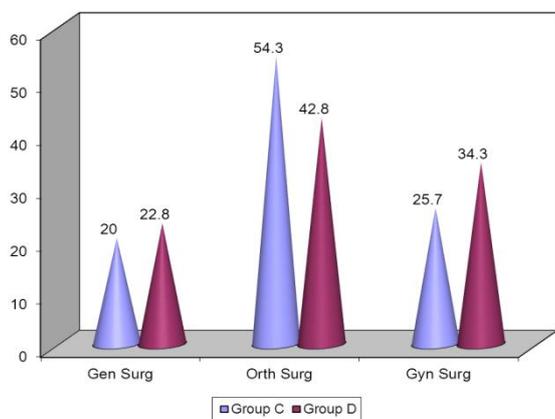
**TABLE 3 : ANTHROPOMETRIC COMPARISON GRAPH SHOWING ANTHROPOMETRIC COMPARISON**

	Group C	Group D
Weight (kg)	58.03	56.68
Height (cm)	159.93	159.23



**TABLE 4 : TYPE OF SURGERY**

Groups	Gen Surg	Orth Surg	Gyn Surg
Group C	7 (20.0%)	19 (54.3%)	9 (25.7%)
Group D	8 (22.8%)	15 (42.8%)	12 (34.3%)



**GRAPH SHOWING TYPES OF SURGERY**

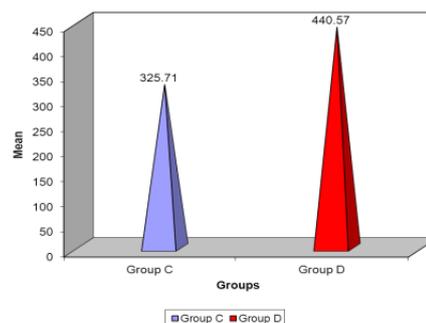
In both the groups, orthopaedical surgeries constituted maximum with 54% (Group C) and 43% (Group D) respectively. All the surgical procedures are comparable in both in groups.

Duration of analgesia in Group C was 325.71 ± 48.89 (SD) and Group D was 440.57 ± 45.89 (SD). The statistical analysis by Students unpaired “t” test showed that time of duration of analgesia in Group D was significantly more when compared to Group C (t=9.659, P<0.00001). In the Group D (Table 7), 2 patients experienced pain at 3hrs, 8

patients (22.86%) at 6 hrs, 19 patients (54.28%) at 7hrs, 35 patients (100%), at 8hrs post operatively. After 8 hrs all patients experienced pain.

**TABLE 5: DURATION OF ANALGESIA (DOA)**

Group	DOA (min)	
	Mean	SD
Group C	325.71	48.89
Group D	440.57	45.89
“t” Value	9.659	
Significance	0.001 (Significant)	



**GRAPH SHOWING DURATION OF ANALGESIA (DOA)**

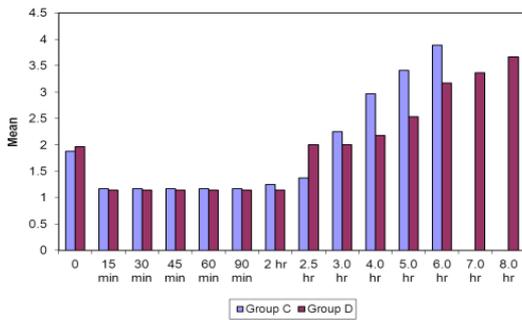
**TABLE 6: COMPARISON OF VISUAL ANALOGUE SCORE**

Time	Group C		Group D		“t” value	Significant
	Mean	SD	Mean	SD		
0 min	1.88	0.53	1.97	0.62	0.594	0.556 (NS)
15 min	1.17	0.38	1.14	0.35	0.373	0.711 (NS)
30 min	1.17	0.38	1.14	0.35	0.373	0.711 (NS)
45 min	1.17	0.38	1.14	0.35	0.373	0.711 (NS)
60 min	1.17	0.38	1.14	0.35	0.373	0.711 (NS)
90 min	1.17	0.38	1.14	0.35	0.373	0.711 (NS)
2.0 hr	1.25	0.50	1.14	0.35	1.160	0.254 (NS)
2.5 hr	1.37	0.60	2.00	0.00	6.215	0.001 (S)
3.0 hr	2.25	0.50	2.00	0.00	3.010	0.001 (S)
4.0 hr	2.97	0.39	2.18	0.39	9.675	0.001 (S)
5.0 hr	3.41	0.56	2.53	0.51	6.588	0.001 (S)
6.0 hr	3.89	0.33	3.17	0.51	4.579	0.001 (S)
7.0 hr	-	-	3.37	0.49	-	-
8.0 hr	-	-	3.67	0.48	-	-

S – Significant NS – Not Significant

In the Group C (table 6), 2 (5.71%) patients experienced pain as early as 60 minutes, 5 patients (14.28%) at 4hrs, 19 patients (54.28%) at 5hrs, 35 patients (100%) at 6hrs post operatively. After 6 hrs all patients experienced pain. In the Group D (Table 7), 2 patients experienced pain at 3hrs, 8 patients (22.86%) at 6 hrs, 19 patients (54.28%) at 7hrs, 35 patients (100%), at 8hrs post operatively. After 8 hrs all patients experienced pain. In comparison of Group C and Group D, by using the unpaired student “t” test, highly significant difference in VAS was seen from 2.5 hours till 6hrs in between the groups. In addition Group D patients didn’t experience pain at 7<sup>th</sup> and 8<sup>th</sup> hour.

COMPARISON OF VISUAL ANALOGUE SCORE



In Group C, after 15 min, 20 patients (57.14%) were asleep (sedation score 3); after 30 min 27 patients (77.14%) were asleep (sedation score 3) ; after 45 min to 240 min 35 patients (100%) of patients were asleep (sedation score 3). By 5 hrs to 6 hrs overall patients were awake. In Group D, after 15 min 27 patients were asleep (sedation score 3) and after 30 min 29 patients were asleep (sedation score 3) from 45 min to 360 mins. 100% of patients were asleep (sedation score 3) upto (91.43%) of patients were asleep at 6 hrs. By 7<sup>th</sup> to 8<sup>th</sup> hour all patients were awake.

In comparison of Group C and Group D, by using the unpaired student “t” test, highly significant difference in sedation score was seen from 0 min till 6hrs in between the groups. In addition sedation was prolonged in Group D patients till 7<sup>th</sup> to 8<sup>th</sup> hrs.

TABLE 7: COMPARISON OF SEDATION SCORE GROUP C AND GROUP D

Time	Sedation Score				‘t’ value	Significant
	Group C		Group D			
	Mean	SD	Mean	SD		
0 min	1.00	0.00	1.97	0.62	9.304	0.001 (S)
15 min	1.34	0.34	1.06	0.42	2.612	0.001 (S)
30 min	1.23	0.43	1.00	0.00	3.174	0.001 (S)
45 min	1.28	0.45	1.00	0.00	3.688	0.001 (S)
60 min	1.29	0.26	1.64	0.34	2.119	0.001 (S)
90 min	1.03	0.17	1.52	0.12	2.421	0.001 (S)
2.0 hrs	1.34	0.34	1.06	0.42	2.612	0.001 (S)
2.5 hrs	1.42	0.19	1.11	0.16	2.161	0.001 (S)
3.0 hrs	1.29	0.26	1.64	0.34	2.119	0.001 (S)
4.0 hrs	1.000	0.00	2.17	0.38	18.124	0.001 (S)
5.0 hrs	1.000	0.00	2.57	0.50	18.516	0.001 (S)
6.0 hrs	1.000	0.00	3.08	0.51	24.333	0.001 (S)
7.0 hrs	-	-	3.37	0.49	-	-
8.0 hrs	-	-	3.67	0.48	-	-

S – Significant NS – Not Significant

We observed (table 12) that the patients in Group C had fair (QOA3-45.7%) to good pain relief (QOA4-28.6%) and the patients in Group D had good (QOA3-40.0%) to excellent pain relief (QOA4-51.4%).

COMPARISON OF SEDATION SCORE GROUP I AND GROUP II

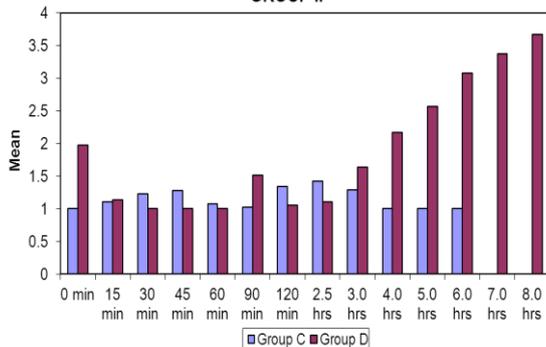
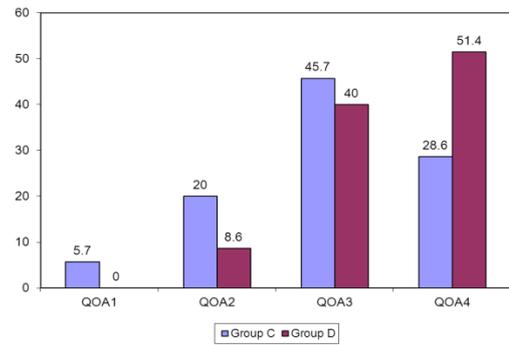


TABLE 8: QUALITY OF ANALGESIA

	QOA1	QOA2	QOA3	QOA4
Group C	2 (5.7%)	7 (20.0%)	16 (45.7%)	10 (28.6%)
Group D	0	3 (8.6%)	14 (40.0%)	18 (51.4%)



GRAPH SHOWING COMPARISON OF QUALITY OF ANALGESIA

4.DISCUSSION

The mean age in both the groups were comparable(table 2). The mean weight and height in group C and D were also comparable (Table 3). All the surgical procedures are comparable in both the groups.

QOA (QUALITY OF ANALGESIA - TABLE 8):Bajwa et al, (2011) studied Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Postoperative analgesia was prolonged significantly in the RD group (366.62 ± 24.42) and consequently low dose consumption of local anaesthetic (LA) (76.82 ± 14.28 vs 104.35 ± 18.96) during epidural top-ups postoperatively. Sedation scores were much better in the RD group and highly significant on statistical comparison (p<0.001). Incidence of nausea and vomiting was significantly high in the RF group (26% and 12%) while incidence of dry mouth was significantly higher in the RD group (14%) (P<0.05). Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable haemodynamics, early onset, and establishment of sensory anesthesia, prolonged post-op analgesia, lower consumption of post-op local anesthetics for epidural analgesia, and much better sedation levels.

In our study, we observed that the patients in Group C had fair (QOA3-45.7%) to good pain relief (QOA4-28.6%) and the patients in Group D had good (QOA3-40.0%) to excellent pain relief (QOA4-51.4%). The results of our study matches with the study of Bajwa but with good to excellent pain relief in Group D than Group C.

SEDATION (TABLE 7): In our study in Group C, after 15 min, 20 patients (57.14%) were asleep (sedation score 3) ; after 30 min 27 patients (77.14%)were asleep (sedation score 3) ; after 45 min to 240 min 35 patients (100%) of patients were asleep (sedation score 3). By 5 hrs to 6 hrs overall patients were awake.

In Group D, after 15 min 27 patients were asleep (sedation score 3) and in 30 min 29 patients were asleep (sedation score 3). From 45 min to 6 hr, 100% of patients were asleep (sedation score 3). By 7<sup>th</sup> to 8<sup>th</sup> hour all patients were awake.

In comparison of Group C and Group D (table 7), by using the unpaired student t test, highly significant difference in sedation score was seen from 0 min till 6hrs in between the groups. In addition sedation was prolonged in Group D patients till 7<sup>th</sup> to 8<sup>th</sup> hrs.

Our study matches with the study conducted by Bajwa SJ et al, (2011) where he compared dexmedetomidine and fentanyl as an epidural adjuvant analgesia in lower limb orthopedic surgeries. Sedation scores were much better in the dexmedetomidine group and highly significant on statistical comparison ( $p < 0.001$ )

**DURATION OF ANALGESIA (TABLE 5):** In our study, the duration of analgesia (min) in Group C was  $325.71 \pm 48.89$  (SD) and Group D was  $440.57 \pm 45.89$  (SD). The statistical analysis by Student's unpaired t-test showed that time of duration of analgesia in Group D was significantly more when compared to Group I ( $t=9.659$ ,  $P < 0.00001$ ).

In Bajwa SJ et al, (2011) study, the postoperative analgesia was prolonged significantly in the RD group ( $366.62 \pm 24.42$ ) and consequently low dose consumption of local anaesthetic LA ( $76.82 \pm 14.28$  vs  $104.35 \pm 18.96$ ) during epidural top-ups postoperatively. Sedation scores were much better in the RD group and highly significant on statistical comparison ( $p < 0.001$ ). 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, lower consumption of post-op LA for epidural analgesia, and much better sedation levels. So the results of the study, matches with our study.

Thangavelu et al., (2016) study on adding Dexmedetomidine versus clonidine to epidural 0.125% Bupivacaine for postoperative analgesia in patients undergoing upper abdominal surgeries. Statistical analysis showed that the duration of analgesia was prolonged in the patients who received Dexmedetomidine as an adjuvant with local anaesthetic agent ( $417.32 \pm 67.36$  minutes,  $p$  value  $< 0.05$ ). The time to first

rescue analgesia was comparatively delayed in Dexmedetomidine group while comparing with Clonidine group ( $425.6 \pm 64.27$  minutes,  $p$  value  $< 0.05$ ). He concluded that Dexmedetomidine provides both analgesia and sedation with better hemodynamic status while compared to Clonidine used as adjuvants in epidural analgesia. So the results of the study matches with our study.

## 5. CONCLUSION

- ❖ It was concluded that epidural dexmedetomidine.
  - Provides an excellent and prolonged duration of analgesia when compared to epidural clonidine.
  - Longer duration of analgesia along with good sedation was also seen when compared with epidural clonidine.

It can be concluded that epidural dexmedetomidine causes early onset and prolonged duration of post-operative analgesia when compared to clonidine, as an adjuvant.

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