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To Evaluate Efficacies of Dexmedetomidine and Clonidine as an Adjuvants in Epidural Anaesthesia with Ropivacaine

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Abstract

Aim: To evaluate efficacies of dexmedetomidine and clonidine as adjuvants to ropivacaine in Epidural Anaesthesia in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods: A randomized prospective study to compare the efficacies of dexmedetomidine and clonidine as adjuvants to ropivacaine in epidural anaesthesia (60 patients in each group.) Patients who were ASA physical status class I and II, Age 18-60 years , either sex, Height 150-170 cms and Elective lower limb orthopaedic surgeries are included in study.

Results: Present study was undertaken to compare the efficacy of epidural Clonidine or Dexmedetomidine with ropivacaine in patients undergoing elective lower limb orthopaedic surgeries. 120 ASA I and II patients of either sex,posted for elective lower limb orthopaedic surgeries were chosen for the study and the patients were divided into two groups of 60 each. Group RC received 17ml of 0.75% of ropivacaine with clonidine 30mcg. Group RD received 17ml of 0.75% of ropivacaine with dexmedetomidine 50mcg. The time of onset of sensory block was tested with bilateral pin prick method and motor block was assessed by onset of Bromage scale 3, and it was found that the onset of sensory block with Dexmedetomidine was earlier compared to Clonidine. During the procedure we observed bradycardia was more in Dexmedtomedine and hypotension was more in Clonidine Group. Bradycardia was treated successfully with vagolytic agents. Hypotension was successfully treated with vasopressors. Also few patients developed nausea and dry mouth, which were negligible. Intraoperatively sedation score was assessed using Ramsay Sedation Scale and there was higher incidence of sedation with Dexmedetomidine group. Regression of motor block to Bromage 1 was observed and the time to regression was significantly prolonged to 450.6±29.37 in the Dexmedetomidine group while it was 343.2±30.99 in the Clonidine group. Post operative analgesic requirement was low in Dexmedetomidine group compared to Clonidine group.

Conclusion: In conclusion, Dexmedetomidine (50mcg) is a better adjuvant when administered epidurally with ropivacaine 0.75% than clonidine (30mcg), as there is significantly longer duration of sensory and motor block, additional benefits of intraoperative sedation and prolonged post-operative analgesia.

Keywords: Dexmedetomidine; Clonidine; Epidural Anaesthesia; Ropivacaine.

Introduction

The task of medicine is to preserve,restore health and to relieve pain [1]. Relief of pain is the main challenge faced by anaesthesiologist and this is the reason why various techniques of pain relief have been developed over ages [2]. Epidural anaesthesia is the most commonly used technique for providing not only peri-operative anaesthesia but post-operative analgesia in lower abdominal and limb surgeries as it has the benefit of providing anaesthesia

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for prolonged duration with repeated doses. New amide local anaesthetic Ropivacaine has minimal cardio-vascular and central nervous system toxicity as well as lesser propensity of motor block during post-operative epidural analgesia [3,4,5]. Opioids like fentanyl have been used traditionally as an adjuvant for epidural administration in combination with lower dose of local anaesthetics to achieve the desired anaesthetic effect as it provides dose-sparing effect of local anaesthetic and superior analgesia [6]. Efforts to find a better adjuvant in regional anesthesia are underway long. Many techniques and drug regimens with partial or greater success have been tried from time to time to calm the patients and to eliminate the anxiety component during regional anaesthesia. The intense motor block,continuous supine position for a prolonged duration and the inability to move the body during regional anaesthesia brings a feeling of discomfort and phobia in many patients [7]. Alpha 2 adrenergic agonists have both analgesic and sedative property when used as adjunct in regional anaesthesia. Dexmedetomidine is a highly selective alpha2 adrenergic agonist with an affinity of eight times greater than clonidine. The stable haemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacologic agents [8]. Prolongation of lumbar epidural analgesia using a single-shot technique has been achieved by various adjuvants like epinephrine, opioids, ketamine and alpha 2 agonists. The rationale to combine these drugs is that the component drugs may produce analgesia by additive or even synergistic mechanisms and that the combination may allow reduced doses of each drug and correspondingly fewer dose-related side effects. With this background information after receiving instituitional ethics committee approval we planned a double-blind prospective randomized clinical study at our institute with an aim to compare the analgesic and sedative effects of both these drugs when used epidurally as adjuvants to ropivacaine in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods

A randomized prospective study to compare the efficacies of dexmedetomidine and clonidine as adjuvants to ropivacaine in epidural anaesthesia (60 patients in each group).

Inclusion Criteria

Patients who were ASA physical status class I and II, Age 18-60 years, either sex, Height 150-170 cms and Elective lower limb orthopaedic surgeries.

Exclusion Criteria

Patients who were ASA grade 3 and above, Height <150cm and >170cm, Opioid dependant, History of drug allergy to clonidine, dexmedeto-midine, amide-local anaesthetic, Patients with skeletal abnormalities, Neurological involvement/disease, Psychiatric diseases and Contraindications of central neuraxial blockade. 60 patients were allocated in each group, posted for elective lower limb (orthopaedic) surgery.

Thorough pre Anaesthetic check up was done one day prior to the surgery and laboratory investigations were noted. The procedure of Epidural anaesthesia was explained to the patients in local language and patients were put NPO 6hours for solids and 3hours for liquids. Patients were premedicated with tab.ranitidine 150mg and tab.alprazolam 0.5mg the night prior surgery. Keeping the operating room ready with necessary drugs and equipment and securing intravenous access in the pre-anaesthesia holding area baseline vitals were noted.A balanced salt solution (ringer lactate) 500ml was given over a period of 20-30minutes after shifting the patients into the operating room. Patients were administered epidural block in either sitting position or lateral position in L3-4 or L4-5 space with 18G touhy needle and epidural catheter was secured 5cms into epidural space and test dose of 3ml of 2% lignocaine hydrochloride solution containing adrenaline 1:2,00,000 was injected. Group RC: Receives 17ml of 0.75% of ropivicaine with 30mcg clonidine. Total volume = 17.2ml+0.8ml NS = 18cc. Group RD: Receives 17ml of 0.75% of ropivicaine with 50mcg dexmedetomidine. Total volume = 18cc.The bilateral pin-prick method to evaluate and check the sensory level & modified bromage scale for motor block. Modified bromage scale, 0 – No block, 1 – Inability to raise extended legs, 2 – Inability to flex knee and 3– Inability to flex ankle & foot. Time of onset of sensory block level at T10, peak sensory block level, motor block level, intensity of motor block and duration of analgesia was recorded. Ramsey sedation scale for sedation score was used. Patient is anxious and agitated or restless or both. Patient is cooperative, oriented and tranquil. Patient responds to commands only. Patient has a brisk response to a light glabellar tap or loud auditory stimulus. Patient asleep, sluggish response to light glabellar tap or loud auditory stimulus. Patient doesn't respond to painful stimulus. Heart rate(HR), blood pressure (NIBP), O_2 saturation (SpO_2) were monitored continuously and recordings were made every for every 5 minutes during the first 30 minutes, every 10 minutes till the end of surgery and every 30 minutes post operatively. Comparision of post operative block characteristics, Mean time to 2 segment regression, Mean time for regression to

bromage 0, Time to first epidural top-up and Any side effects like hypotension (defined as systolic arterial pressure falling more than 20% mmHg) was noted and treated with inj. Mephentermine 6mg in bolus doses and bradycardia (heart rate <50 bpm) was noted and treated with inj. Atropine 0.6mg. A Comparative two group randomized clinical study with 120 patients with 60 patients in Group RC (Clonidine) and 60 patients in Group RD (Dexmedetomidine) is undertaken to study the changes in haemodynamics and side effect. Statistical analysis was done by applying Chi-square test, Anova test and students t test to analyse the data, p value was determined. P > 0.05 is not significant. P < 0.05 is significant. P < 0.001 is highly significant.

Results

One Hundred Twenty patients were allocated in two groups; 60 patients were administered dexmedetomidine and remaining 60 patients were administered clonidine as adjuvant.

Table 1 shows There is a slight difference in the age in between both the groups. In group dexmedetomidine the mean age was 42.00±7.46 and in clonidine group it was 37.80±6.19 and it is statistically significant (P value < 0.05). There is no statistically significant difference in the male and female population in both the groups (P value >0.05). The average height is also similar in both the study groups and does not hold any statistical significance (P value>0.05). In dexmedetomidine group 28 patients out of 60 attained the highest dermatomal level of sensory analgesia (T4). In clonidine group 15 out of 60 patients attained the same level. In dexmedetomidine group 29 individuals attained highest dematomal level of T6 whereas, 30 patients in clonidine group attained the same level. In clonidine group 2 individuals out of 60 attained a maximum sensory level of T10. There is a statistically significant difference between dexmedetomidine and clonidine regarding highest dermatomal level of sensory analgesia. The P value being 0.001. The average time taken to attain sensory anaesthesia in dexmedetomidine group is 10minutes whereas, in clonidine it is 18minutes. The average time taken to attain a motor blockade to modified bromage scale 3 in dexmedetomidine group is 12minutes but in clonidine group it is 17minutes. There is a statistically significant difference between dexmedetomidine and clonidine with regards to the time taken for establishment of highest sensory and motor blockade to bromage 3 respectively. The P value being <0.001. The mean level of sedation in dexmedetomidine group is 3 and that in clonidine group is 2 which is statistically significant. The P value being <0.001.

Table 2 shows that the time taken for 2-segment regression in dexmedetomidine is 229 +minutes as and in clonidine group it is 160 minutes on an

Table 1: Shows demographic parameters in two study groups (n=120), highest dermatomal level of sensory analgesia in two study groups treatment groups (n=120), Onset of anaesthesia in two groups (n=120) and sedation level in both the study groups

Parameter	Dexmed (N=60)	Clonidine (N=60)	P value
Age (Mean ± SD)	42.00±7.46	37.80±6.19	.002
Gender			
Male Frequency (%)	44(73.3)	45(75.0)	1.00
Female Frequency (%)	16(26.7)	15(25.0)	
Height (Mean ± SD)	160.65±5.43	159.87±6.08	.386
Highest dermatomal level of sensory analgesia	**Dexmed (N=60)**	**Clonidine (N=60)**	**P value**
T4	29 (48.3%)	15 (25.0)	0.001
T6	29 (48.3%)	30 (50.0)	
T8	2 (3.3%)	13 (21.7%)	
T10	0 (0.0%)	2 (3.3%)	

Parameter	Groups of treatment	Mean	Mean difference	P value	95% CL Lower	95% CL Upper
Time to achieve highest sensory level	Clonidine	18.10	7.667	<0.001	6.372	8.96
	Dexmed	10.43				
Time for establishment of motor blockade to modified bromage scale 3	Clonidine	17.77	6.050	<0.001	4.681	7.41
	Dexmed	12.80				
Sedation	Dexmed	3.30	0.467	<0.001	0.207	0.726
	Clonidine	2.83				

average and is statistically significant with a P value of 0.001. The average time for rescue top-up is 156 minutes in dexmedetomidine group and in clonidine group it is 123 minutes.The mean difference between the two groups is 33 minutes and does not hold any statistical significance as the P value is 0.162. The average time taken for motor regression to modified bromage scale 0 is 379 minutes in dexmedetomidine group but the in clonidine group it was 283 minutes and it holds high statistical significance as the P value is 0.0001.

Table 3 shows the baseline mean arterial blood pressure in dexmedetomidine group is 96mm Hg and that in clonidine group is 99mmHg with a P value of 0.154 which is statistically insignificant. The mean difference of mean arterial blood pressure in the baseline and pre-op 2 is -2 respectively and does not hold any statistical significance. The pre operative systolic blood pressure in both the study groups was satistically insignificant as the P value is >0.05.

The pre operative diastolic blood pressure in both study groups is insignificant as the P value is >0.05. The pre operative mean arterial blood pressure in both study groups is also insignificant as the P value is >0.05. The intra operative mean arterial pressure in dexmedetomidine group is 97mm Hg and whereas in clonidine is 88mm Hg with a P value of 0.287 which is statistically insignificant. The intra operative systolic blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05. The intra operative diastolic blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05.

The intra operative mean arterial blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05. The intra operative mean arterial blood pressure in both the study groups in the first 30mins after administering the drugs does not hold any statistical significance as the P values at each time interval are >0.05. Initially after the administration of both the study drugs the fall in diastolic blood pressure was more in clonidine group when compared to dexmedetomidine,but the fluctuations in both the groups were minimal. The fall and fluctuations in mean arterial blood pressure was more with clonidine when compared to dexmedetomidine and the MAP was constantly lower in clonidine group.

Table 4 shows the average post operative mean arterial pressure in dexmedetomidine is 87mm Hg and in clonidine is 83mm Hg with a P value of 0.02 which is statistically significant. The P value of post operative systolic blood pressure, diastolic blood pressure and mean arterial blood pressure is statistically significant as it is less than <0.05.

The post operative systolic blood pressure, diastolic blood pressure and mean arterial blood pressure is constantly lower in clonidine group when compared to dexmedetomidine group. The baseline heart rate in dexmedetomidine group is 82/min and

Table 2: Shows two segment regression time, time for rescue top up, time for motor regression, in both the groups

Parameter	Groups of treatment	Mean	Mean difference	P value	95% CL Lower	Upper
2 segment regression Time	Dexmed Clonidine	229.58 160.80	68.783	0.001	55.963	1.604
Time for rescue top up	Dexmed Clonidine	156.67 123.67	33.000	0.162	16.922	82.922
Time for motor regression	Dexmed Clonidine	379.55 283.17	96.383	0.0001	79.102	113.665

Table 3: Shows pre-operative BP, intra-operative BP

Parameter	Groups of treatment	SBP	DBP	MAP	Mean Diff	95% CL Lower	Upper
Pre-op 1 (Baseline)	Dexmed Clonidine	132.85 136.38	81.73 81.72	96.72 99.48	-2.767	6.588	1.054
Pre-op 2 (after fluid bolus)	Dexmed Clonidine	136.10 123.67	83.83 83.53	98.98 101.18	-2.200	5.956	1.556
Intra-op	Dexmed Clonidine	119.11 118.35	76.25 73.87	97.71 88.18	9.52870	8.130	27.19

Table 4: Shows post-operative BP in two study groups, pre-operative heart rate

Parameter	Groups of treatment	SBP	DBP	MAP	Mean Diff	95% CL Lower	95% CL Upper
Post-op (Arterial BP)	Dexmed	116.44	75.50	7.94	4.26250	1.66	6.86
	Clonidine	111.39	71.01	3.68			
Pre-op heart rate (Baseline)	Dexmed		Mean-82.78		-0.450	-4.564	3.664
	Clonidine		Mean-83.23				
Pre-op 2(after fluid bolus)	Dexmed		Mean-85.93		-0.833	-4.572	2.905
	Clonidine		Mean-86.77				

Table 5: Shows descriptive analysis of various anaesthesia related parameters in two study groups (n=120)

Parameter	Dexmed (N=60)	Clonidine (N=60)
Time taken to achieve highest sensory level (Mean ± SD)	10.43±2.35	18.10±4.49
Time taken for establishment of motor blockade to modified broma (Mean ± SD	12.80±2.92	18.85±4.49
Level of Sedation (Mean ± SD)	3.30±0.696	2.83±0.74
2 segment regression time (Mean ± SD)	229.58±42.85	160.80±26.06
Time for rescue top up (Mean ± SD)	156.67±20.82	123.67±32.78
Time for motor regression to modified bromage scale (Mean ± SD)	379.55±56.16	283.17±37.62

in clonidine group is 83/min and holds no statistical significance as the P value is >0.05. The heart rate after administration of a crystalloid bolus in dexmedetomidine is 85/min and in clonidine group it was 86/min. There is no statistical significance as the P value >0.05. The intra operative heart rate in dexmedetomidine is 76/min and in clonidine group is 74/min and does not hold any statistical significance as the P value >0.05.

The post operative heart rate in dexmedetomidine is 73/min and in clonidine group is 74/min and does not hold any statistical significance as the P value >0.05. After administering the study drugs, initially there is a fall in the blood pressure in both the groups, but in dexmedetomidine group the fall is realatively less than that in clonidine group at al time intervals. The post operative heart rate is low in both the study groups, but in dexmedetomidine the fluctutaions are relatively low when compared to clonidine.

Discussion

The present study was performed to compare clonidine and dexmedetomidine in their efficacy as adjuvants in epidural anaesthesia. Various studies have stated that the dose of clonidine is 1.5 – 2 times higher than that of dexmedetomidine when used in epidural route.

In our study design Group RC received 17ml of 0.75% of ropivacaine with clonidine 30mcg and Group RD received 17ml of 0.75% of ropivacaine with dexmedetomidine 50mcg, injected epidurally in patients undergoing elective lower limb orthopaedic surgeries.

The following parameters were observed namely highest dermatomal level of sensory analgesia, time to achieve highest sensory level, time taken for establishment of motor blockade to modified bromage scale 3, time to two-segment regression, time of rescue top-up and changes in haemodynamic parameters. In our study the demographic profile of patients in both groups were comparable with regards to age, height and gender.

Bajwa SJ, et. al. [9], compared the efficacy and clinical profile of two $\alpha 2$ agonists, dexmedetomidine and clonidine in a 50 adult female patients who underwent vaginal hysterectomies under epidural anaesthesia. In their studies the demographic profile, was comparable and statistically non significant in both groups.

In the study done by MS Saravana Babu et. al. [10], the demographic profile of patients in both groups was comparable with regards to age, weight and height and was statistically insignificant.

In our study, on comparing the highest level of sensory anaesthesia in between both the groups, patients who received dexmedetomidine as an adjuvant attained a sensory level of T4 whereas those in clonidine attained a level of T6. The time taken to achieve T4 level was 10 mins in dexmedetomidine and 18 mins in clonidine group. Motor blockade to modified bromage scale 3 was achieved earlier in dexmedetomidine group (12 mins) when compared to clonidine group (17 mins).

Bajwa SJ [9] et. al. 24 found that addition of dexmedetomidine to ropivacaine as adjuvant resulted in early onset of analgesia as well as prolonged analgesia. Dexmedetomidine not only provided higher

dermatomal spread but also helped in achieving the maximum sensory anaesthetic level in shorter period (10.43±2.35) compared to clonidine (18.10±4.49). Modified bromage scale 3 was achieved earlier (12.80±2.92) in dexmedetomidine group when compared to clonidine group (18.85±4.49). All these initial block characteristics turned out to be statistically significant values on comparison ($p< 0.001$).

MS Saravana Babu et. al. [10] found that addition of dexmedetomidine to ropivacaine as an adjuvant resulted in an earlier onset (7.33±1.76 min) of analgesia as compared to addition of clonidine (8.40±1.61). Dexmedetomidine not only provided early onset but also helped in achieving the peak analgesic level (VAS – 0) in a shorter period (11.66±2.05 min) compared with clonidine (13.20±2.90 min). The sedation score was more and better in dexmedetomidine group than in clonidine group in our study ($P <0.001$).

Anand et al concluded that sedation was more in patients who received dexmedetomidine as adjuvant in caudal block ($P <0.001$).

Bajwa SJ et. al. [9] reported that sedation score was better in dexmedetomidine group when compared with clonidine group which was statistically significant ($P < 0.005$). The average time for 2-segment regression was more in dexmedeto-midine group (229 mins) when compared to clonidine group (160 mins) and the time for motor regression to modified bromage scale 0 was more in dexmedetomidine group (379 mins) whereas in clonidine group, it was less (283mins) in our study.

Vijay et al reported that in dexmedetomidine group the duration of post operative analgesia was upto 15hours, which resulted in a better quality of sleep and a prolonged duration of arousable sedation.

Bajwa SJ, et. al. [9] found that there was decreasing trend in heart rate as well as mean arterial blood pressure in both groups and decrease was statistically significant in clonidine group ($p< 0.005$) when compared with dexmedetomidine group.

Swami SS, Keniya VM, Ladi SD, Rao R [11], compared efficacy of dexmedetomidine and clonidine as adjuvant to local anaesthetics in supraclavicular brachial plexus block in their studies they also found that there was decreasing trend in heart rate as well as MAP in dexmedetomidine group as compared to clonidine group.

Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et. al. [9] observed that dexmedetomidine provided smooth and prolonged post operative analgesia compared to clonidine.

In our study there was prolonged time to two segmental dermatomal regression (229.58±42.85) in dexmedetomidine group as compared to clonidine group (160.80±26.06) as well as return of motor power to bromage 0 (397.55±56.16) in dexmedetomidine group as compared to clonidine group (283.17±37.62), therefore the time to rescue analgesia was comparatively shorter in clonidine group (123.67±32.78) as compared to dexmedeto-midine group (156.67±20.82).

In our study the side effect profile was also comparable with incidence of nausea in clonidine group (10%) compared to dexemedetomedine group (5%) and dry mouth in dexemedetomedine group (20%) compare to clonidine group (10%) which was non statistically significant.

Shobhana Gupta, Virendra Pratap (2014) conducted a study among 60 paediatric patients of ASA status I and II between the age of 1 and 6 years undergoing lower abdominal surgeries. The caudal block was administered with inj. ropivacaine 0.2% with clonidine 2 mcg/kg (group A) and inj. ropivacaine 0.2% with dexmedetomidine 2mcg/kg (group B) after induction with general anesthesia. Hemodynamic parameters were observed before, during, and after the surgical procedure. Postoperative analgesic duration, total dose of rescue analgesia, pain scores, and any side effects were looked for and recorded.

They concluded that addition of dexmedetomidine or clonidine to caudal ropivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side-effects [12].

Nasr DA et. al., (2013) studied the efficacy of caudal dexmedetomidine on stress response and post-operative pain in paediatric cardiac surgeries. They concluded that caudal dexmedetomidine attenuated stress response to surgical trauma and provided better post-operative analgesia [13].

Xiang Q et. al., (2013) studied effect of caudal dexmedetomidine combined with bupivacaine in children undergoing inguinal hernia repair. They found that addition of dexmedetomidine to caudal bupivacaine could reduce the response to hernia sac traction and prolong the duration of post-operative analgesia in children undergoing inguinal hernia [14].

Conclusion

In conclusion, Dexmedetomidine (50mcg) is a better adjuvant when administered epidurally with ropivacaine 0.75% than clonidine (30mcg), as there

is significantly longer duration of sensory and motor block, additional benefits of intraoperative sedation and prolonged post-operative analgesia.

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