

Original Research Article

A randomised controlled trial to compare two different doses of dexmedetomidine as an adjunct to ropivacaine in epidural analgesia for hip surgeries

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Abstract: Epidural analgesia remains the gold standard for postoperative pain relief for the patients undergoing hip surgeries. This study was conducted to find the optimum dose of dexmedetomidine in combination with ropivacaine for prolonging the duration of postoperative analgesia using different doses of dexmedetomidine as an adjunct to ropivacaine in patients undergoing hip surgeries. Ninety patients of ASA I-II class, aged between 20–80 years, were recruited in the study. The patients were randomly allocated into three groups; ropivacaine + normal saline(R), ropivacaine+dexmedetomidine 0.5µg/kg (RD_{0.5}) and ropivacaine + dexmedetomidine 1µg/kg (RD₁). Group R patients received epidural 0.2% Ropivacaine 2mg (10 ml) with 1ml normal saline, group RD_{0.5} patients received 0.2% Ropivacaine 20mg (10ml)with 0.5µg/kg dexmedetomidine and group RD₁ patients received 0.2% Ropivacaine 20 mg (10 ml) with 1µg/kg dexmedetomidine. Cardio-respiratory parameters, sedation scores, various block characteristics like time for two segment regression and to T₁₀ segment regression, duration of analgesia, frequency of rescue analgesia, adverse effects if any were noted in each case. The statistical analysis was done using SPSS Version 15.0 statistical Analysis Software. Dose dependent increase in duration of analgesia was observed in group RD_{0.5} and RD₁ as compared to group R but heart rate and blood pressure were significantly lower and sedation scores were higher in study groups as compared to control group R. Hypotension and bradycardia were observed maximum with group RD₁ followed by group RD_{0.5} and group R. Although the duration of postoperative analgesia was prolonged in 1µg/kg dexmedetomidine group as compared to 0.5µg/kg but increase in incidence of side effects with increase in dose overshadows this benefit.

Keywords: Hip Arthroplasties, dexmedetomidine, epidural analgesia, ropivacaine.

INTRODUCTION

Regional anesthesia techniques are currently most popular and are being used extensively in orthopaedic hip surgeries. Hip surgery is very painful procedure for patients and inadequate control of pain may result in higher incidence of chronic postsurgical pain[1]. This may lead to decreased ambulation and increased postoperative morbidities like increased incidences of postoperative pulmonary, thromboembolic and cardiac complications, prolonged hospital stay and worsened patient oriented outcomes such as quality of life[2,3]. Various methods which are commonly used for pain relief in postoperative period are epidural, local anaesthetic alone or along with

adjuncts, patient controlled analgesia (PCA) with or without opioids, and non-steroidal anti-inflammatory drugs (NSAIDS). Among these methods epidural LA with adjuncts are the most effective tool in providing dynamic pain relief after major surgical procedures[4]. Postsynaptic activation of central α_2 receptors results in sympatholytic effect leading to hypotension and bradycardia, an effect judiciously used to attenuate the stress response of surgery[5]. Previously clonidine, was used as an analgesic adjunct in perioperative conditions and pain therapy. However dexmedetomidine is currently the most effective α_2 agonist available with a relatively high ratio of $\alpha_2:\alpha_1$ activity (1620:1 as compared to 220:1 for clonidine) It has recently been

investigated for its analgesic effects when given epidurally and has the potential to become an alternative to clonidine.

In this study, we compared two different doses of dexmedetomidine as an adjunct to ropivacaine in epidural for postoperative analgesia in patients of hip surgeries. Aim of this study was to compare the duration of postoperative analgesia and to find the optimum safe dose of dexmedetomidine with epidural ropivacaine which provides analgesia with minimal effects on haemodynamic stability and other side-effects.

MATERIALS AND METHOD

After obtaining the Institutional Research and Ethics Committee approval, written informed consent for this randomized controlled trial was obtained from ninety patients of ASA I, II aged between 20-80yr scheduled for hip arthroplasty of 1.5 to 3hrs duration, over the period of one and half year. Patients with uncontrolled and labile hypertension, using α 2-antagonists, noted to have dysrhythmias on ecg, or allergic to study drugs were excluded from study. Sample size calculation was done on the basis of the previous study. The primary outcome was taken as duration of postoperative analgesia and assuming 85% of study power and 5% α error; the minimum sample size was calculated to be 27 patients per group were required. Therefore, thirty patients in each group were planned.

The patients were allocated one of the 3 groups by random number chart. Random number was enclosed in sealed envelope and opened by one of the investigators to know the type of study drug. The study drug solution was prepared by a nonparticipant staff blinded to study and given to the investigator. The anaesthesiologist who collected the postoperative data was blind to the type of study drug administered to the patient.

Group R patients received epidural 0.2% Ropivacaine 20mg (10 ml) with 1ml normal saline. Group RD(0.5) patients received epidural 0.2% Ropivacaine 20mg (10 ml) with 0.5 μ g/kg dexmedetomidine (preservative free) diluted in 1ml normal saline and Group RD1-patients received epidural 0.2% Ropivacaine 20mg (10 ml) with 1 μ g/kg dexmedetomidine (preservative free) diluted in 1ml normal saline. After antiseptic skin preparation and sterile draping, lumbar epidural puncture was done in sitting position by midline approach at the level of L₃-L₄ vertebra with 18-G Touhy epidural needle in sitting position and location of epidural space was confirmed

by loss of resistance to saline technique. A test dose of 3ml of 2% lignocaine with (1:2lac) adrenaline was administered into epidural space and thereafter epidural catheter secured at 3-5cm into the epidural space. Then one space below subarachnoid block given using 26G spinal needle and 3ml of 0.75% isobaric Ropivacaine was given after confirming the free flow of CSF.

In post-operative period when sensory level(of subarachnoid block)regressed up to T₁₀ dermatome, study drug solution was given in epidural catheter in supine position and sensory level was assessed by pinprick sensation using a blunt 26-G needle along the mid-clavicular line bilaterally at 5, 10, 15, 20, 25 and 30 min, and then every 15 min for 24 hours. All patients were monitored for systolic, diastolic, mean blood pressure, heart rate, oxygen saturation, respiratory rate, level of sedation and side effects like dry mouth, nausea, vomiting etc. every 5 min for half an hour and then every 10 minute till one hour, 15 min for next one hour in recovery room . The level of sedation recorded from 1 to 6 on Ramsay sedation score[6] at 5, 10, 15, 20, 25 and 30 min, and then every 15 min for 24 hrs in postoperative period. The time for two segment regression and to T₁₀ segment regression was recorded. Any hypotension (MAP < 70 mmHg) episode was treated with injection mephentermine 3 mg bolus and episodes of bradycardia (HR< 50 beats/min) were treated with intravenous atropine 0.02 mg/kg. Severity of pain was measured using a 10 cm visual analogue scale (VAS) at hourly interval for next 6 hours after epidural block and then at 8th, 10th, 12th, 15th, 18th and 24th hour. The postoperative rescue analgesia was provided by 0.2% ropivacaine 10ml bolus in epidural when patient gave first complaint of pain (VAS \geq 3) and patients were additionally monitored for every five minutes for half an hour, and in case of any failure in epidural technique partial block or inadequate analgesia, diclofenac sodium 75 mg slow i.v. infusion in 100ml normal saline was given. The time to request for first rescue analgesia (pain free interval), frequency of rescue analgesia required and total dose of ropivacaine was noted in each case. The statistical analysis was done using SPSS Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean \pm SD. Student 't' test, The ANOVA test, Paired "t" test were applied wherever required. Level of significance was decided by "p" value and p <0.05 was taken as significant and 0.001 highly significant.

RESULTS.

In our study ninety four patients were recruited out of which four patients were excluded from the study because of partial or failed epidural block. On

comparing the data statistically, no significant difference among the groups was observed with respect to mean age, BMI, and ASA grade ($P>0.05$) -(Table 1)

There was statistically significant intergroup difference in mean SBP ($P<0.05$) with fall in SBP was more in group RD0.5 and RD1 as compared to group R whereas no statistically significant intergroup difference in mean SBP ($P>0.05$) in between group RD0.5 and RD1 during any time interval.

Baseline mean HR in Groups R, RD0.5 and RD1 was 82.06 ± 10.21 , 82.93 ± 8.59 and 88.50 ± 9.44 bpm respectively. A gradual decrease in mean HR in all the three groups was observed following administration of drug. A maximum decline in HR value was observed at 30 min post drug administration in Group R (77.06 ± 8.68), 60 min in Group RD0.5 (69.06 ± 5.96) and 50 min post drug administration in Group RD1 (68.03 ± 7.85). (FIG:1). There was no significant difference seen in between RD0.5 and RD1 except at 60 min when heart rate was lower in group RD1.

At all intraoperative intervals, there was no significant change in respiratory rate and mean oxygen saturation remained above 97% in all the three groups showing no significant intergroup difference. Time taken for two segment regression was significantly higher in group RD0.5 and RD1 as compared to group R ($P<0.001$) similarly regression time was higher in group RD1 as compared to group RD0.5.(FIG:2) Duration of analgesia was significantly higher in group RD0.5 and RD1 as compared to group R ($P<0.001$)

similarly analgesia time was high in group RD1 as compared to group RD0.5.(FIG:3)

Frequency of rescue analgesia was significantly higher in group R as compared to RD0.5 and RD1 ($P<0.001$) similarly frequency was high in group RD0.5 as compared to group RD1.(FIG:4)

In Group R total dose of ropivacaine as rescue analgesia in 24 hrs was maximum with a mean value of 103.00 ± 17.04 mg, 79.00 ± 18.44 in group RD0.5, 67.00 ± 12.90 mg in Group RD1. Total dose of rescue analgesia was significantly lower in group RD0.5 and RD1 as compared to group R ($P<0.001$) similarly value was significantly low in group RD1 as compared to group RD0.5.

Mean value for Ramsay sedation score was 2.33, 3.01 and 3.26 in Groups R, RD0.5 and RD1 respectively It reveals no significant intergroup difference between group RD0.5 and RD1 ($p>0.05$) whereas sedation score was significantly higher in both groups as compared to group R ($p<0.001$).

Hypotension and bradycardia were observed maximum with group RD1(11 and 6 patients respectively) followed by group RD0.5(5 patients each) and group R (4 patients of hypotension only). 1 patient had dry mouth in group R, 2 patients in group RD0.5, and 5 in group RD1, while nausea was observed in 3, 2, and 6 patients respectively in group R, RD0.5, and RD1.

Table 1: Demographic and Group wise distribution of patients

SN	Characteristic	Group RD1 (n=30)	Group RD0.5 (n=30)	Group RD1 (n=30)	Statistical significance (ANOVA)
1.	Mean Age \pm SD (Years)	57.20 \pm 6.90	57.50 \pm 8.11	57.83 \pm 9.11	CD=4.15; p=0.521
2.	Mean BMI \pm SD (kg/m ²)	20.44 \pm 2.62	20.71 \pm 2.61	20.64 \pm 2.41	CD=1.31; p=0.621
3.	ASA Grade (No., %)				$\chi^2=0.609$; p=0.738
	I	26 (86.66%)	25 (83.33%)	24 (80%)	
	II	4 (13.33%)	5 (16.66%)	6 (20%)	

Table 2: Comparison of block parameters between three groups:

Parameter	Group	Mean	StdDev	SE of Mean	95% CI for Mean		P-Value	Sig Diff Between
					Lower Bound	Upper Bound		
Peak Sensory Level [†]	G- R	6.83	1.21	0.22	5.38	6.28	0.840	
	G-RD0.5	6.63	1.03	0.19	5.25	6.02		
	G- RD1	6.80	1.10	0.20	5.39	6.21		
RSS	G-R	2.33	1.12	0.15	1.12	3.09	<0.001*	G-R vs G-RD0.5 ($P<0.001$)
	G-RD0.5	3.01	1.43	0.25	2.34	4.66		G-R vs G-RD1 ($P<0.001$)
	G-RD1	3.26	1.11	0.22	2.40	3.85		

Parameter	Group	Mean	StdDev	SE of Mean	95% CI for Mean		P-Value	Sig Diff Between
					Lower Bound	Upper Bound		
T 2 SegReg (min)	G-R	109.50	13.41	2.41	58.58	68.42	<0.001 *	G-Rvs G-RD0.5 (P<0.001)
	G-RD0.5	119.50	15.72	2.67	80.37	91.30		G-Rvs G-RD1 (P<0.001)
	G-RD1	129.00	15.66	2.62	65.92	76.62		G-RD0.5 vs G-RD1(P<0.001)
Duration of Analgesia(mi n)	G-R	281.16	33.77	5.81	156.61	180.39	<0.001 *	G-R vs G-RD1 (P<0.001)
	G-RD0.5	312.00	32.53	7.02	241.94	270.66		G-RD0.5vs G-RD1(P<0.001)
	G-RD1	373.50	71.47	7.31	202.09	231.98		G-Rvs G-RD0.5 (P<0.001)
Frequency of Rescue analgesia	G-R	3.43	0.56	0.144	0.48	1.17	<0.000 *	G-R vs G-RD0.5 (P<0.001)
	G-RD0.5	2.63	0.61	0.144	0.04	0.720.		G-Rvs G-RD1(P<0.001)
	G-RD1	2.23	0.430	0.144	0.86	1.55		G-RD0.5vs G-RD1(P<0.001)
Total Dose of Rescue Analgesics in 24 hrs [†]	G-R	103.00	17.04	0.15	3.00	3.60	<0.001 *	G-R vs G-RD0.5 (P<0.001)
	G-RD0.5	79.00	18.44	0.11	2.20	2.67		G-R vsG-RD1(P<0.01)
	G-RD1	67.00	12.90	0.10	2.43	2.84		G-RD0.5vs G-RD1(P<0.001)

† Kruskal-Wallis test

* denotes significant difference

Table3 : Showing distribution of cases according to side effects in all the three groups

SIDE EFFECTS	GROUP R		GROUP RD 0.5		GROUP RD1	
	NO.	%	NO.	%	NO.	%
NIL	23	76.66	20	66.66	2	6.66
BRADYCARDIA	0	-	5	16.66	6	20
DRY MOUTH	1	3.33	2	6.66	5	16.66
HYPOTENSION	4	13.33	5	16.66	11	36.66
NAUSEA & VOMITING	3	10	2	6.66	6	20

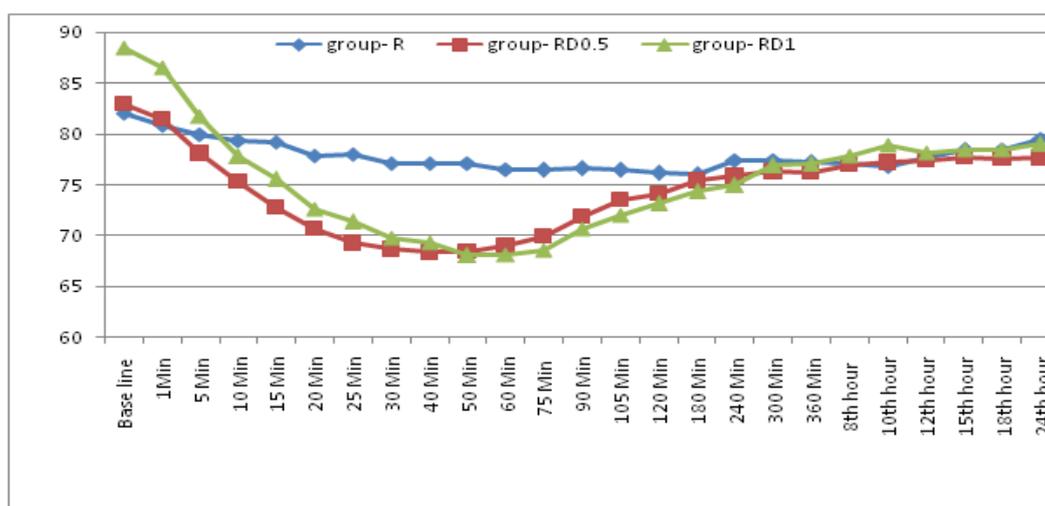


Fig 1: Comparison of mean heart rate at different time intervals

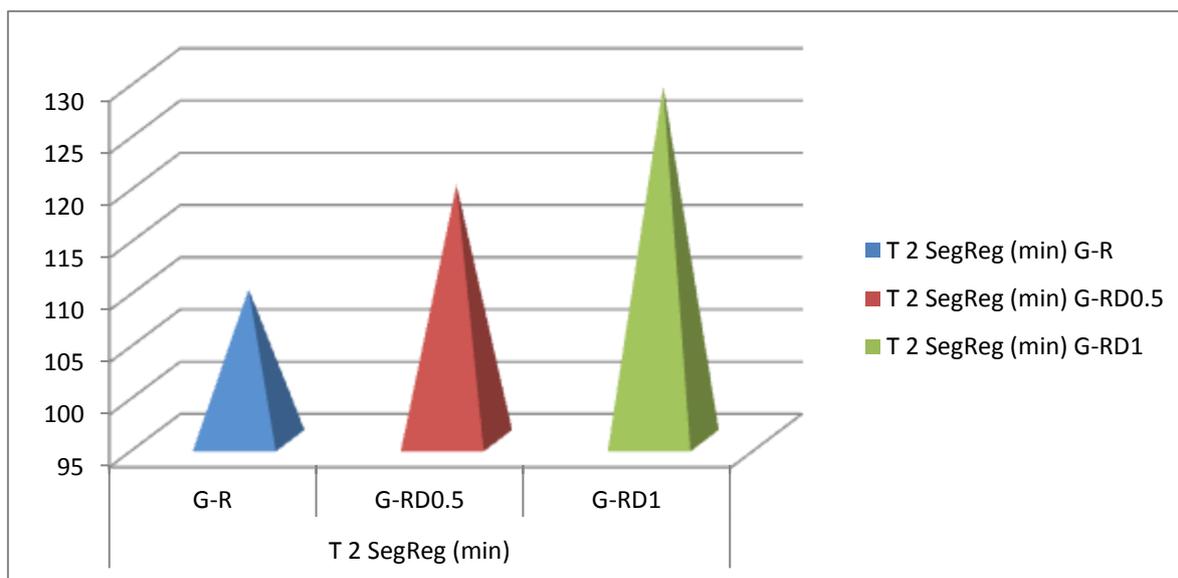


Fig 2: Comparison of different time durations for block to regress: by 2 segments

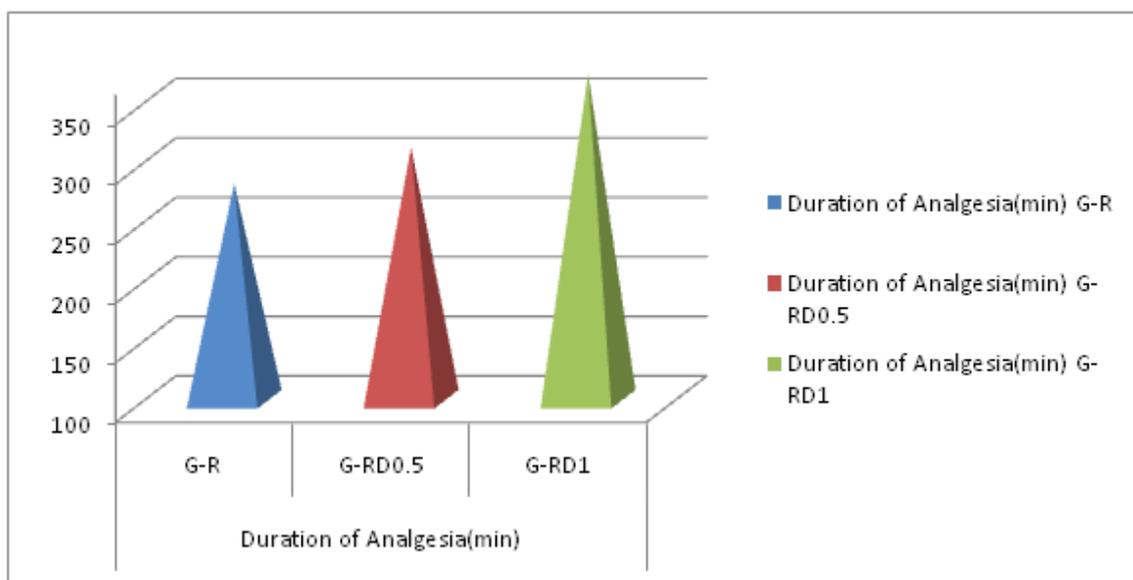


Fig 3: Comparison of different time durations for analgesia

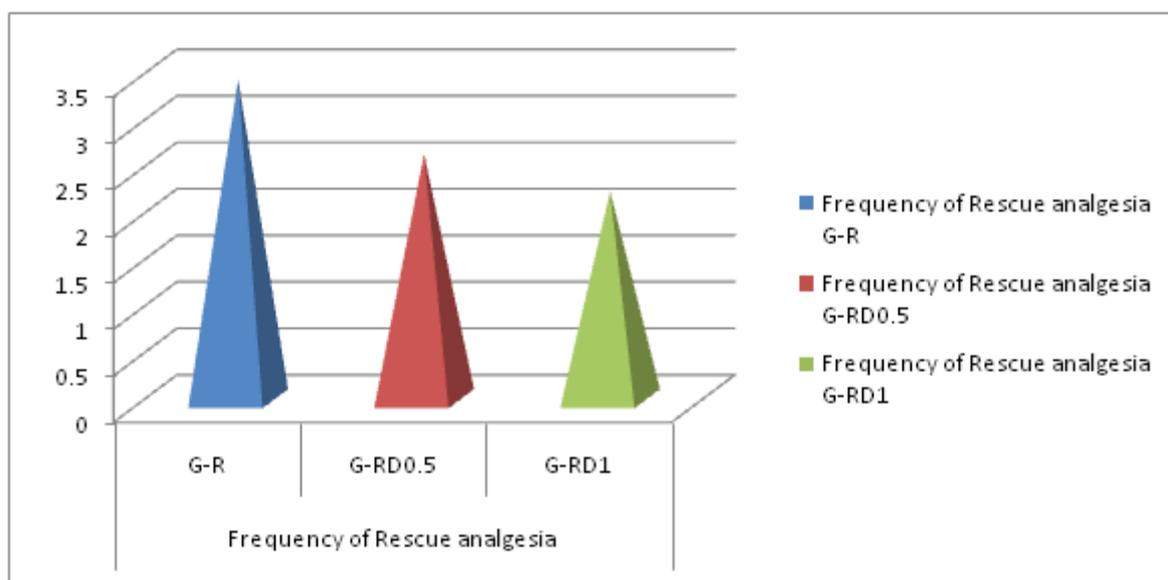


Fig 4: Comparison of frequency of rescue analgesia in between the three groups

DISCUSSION

It has become a common practice to use polypharmacy approach for treatment of postoperative analgesia because no drug has yet been identified that provide adequate analgesia without associated side effects. For this reason various local anaesthetics like Lignocaine, Bupivacaine, Ropivacaine etc. have been used with other analgesics and sedatives as an adjuncts like neostigmine, morphine, fentanyl, clonidine and dexmedetomidine etc.

Perhaps the most exciting new developments in epidural anaesthesia are the development of non-opioids adjuvant medications, and new epidural anaesthetic formulations. The first of the non-opioids, non-local anaesthetic agent to be extensively studied and approved for use as an epidurally administered analgesic was the alpha-2 adrenergic receptor agonist, clonidine.

For many years, clonidine, has been widely used as an analgesic adjunct in perioperative conditions and pain therapy. Dexmedetomidine is a better neuraxial adjuvant as compared to clonidine for providing early onset of sensory analgesia, adequate sedation and prolonged post-operative analgesia[7]. Optimum safe dose of dexmedetomidine which is to be combined with local anaesthetic is still a dilemma and no evidence is there in literature. This is the first study which has compared two different doses of dexmedetomidine i.e 0.5µ/kg and 1µ/kg when added to LA epidurally for post-operative analgesia, haemodynamic stability and sedation effect in hip

surgeries with a similar surgical and demographic profile (table 2). In our study we observed that a mixture of 0.2% ropivacaine as low as 20 mg when added with different doses of dexmedetomidine (0.5µg/ kg, & 1µg/ kg), injected in the epidural space enhance postoperative analgesia, provides a longer duration of sensory blockade without additional motor blockade, adequate sedation, and stable haemodynamic profile. All these findings coincide with the other studies by Salgado *et al*[10], Anand *et al*[11] and Bajwa *et.al* [8].

Total duration of sensory block was maximum in ropivacaine + dexmedetomidine 1µg/kg than ropivacaine+dexmedetomidine 0.5µg/kg and minimum in ropivacaine group. Duration of analgesia was significantly higher in dexmedetomidine groups as compared to plain ropivacaine. Similarly analgesia time was higher in group RD1 as compared to group RD0.5..

Frequency of rescue analgesia was significantly higher in group RD0.5 and RD1 as compared to group R and value was higher in group RD1 as compared to group RD0.5

Hypotension is a known complication of α2 agonists due to their sympatholytic property. There was a 12% incidence of hypotension in Bajwa *et al*[8]. and 14% in Shahi *et al*[9]. work where as in our study there was a 13.33% incidence of hypotension in group R. 16.66% in group RD0.5 and 36.66% in group RD1.

In our study there was a 16.66% incidence of bradycardia in group RD 0.5 and 20% in group RD1.

These findings correlate well with above mentioned studies and can be explained on the basis of sympatholytic property of α_2 agonists. In our study mean value for Ramsay sedation score was 2.33, 3.01 and 3.26 in Groups R, RD0.5 and RD1 respectively. It reveals no significant intergroup difference between group RD0.5 and RD1 ($P>0.05$) whereas sedation score was significantly higher in both groups as compared to group R ($P<0.001$). Hence we concluded that addition of dexmedetomidine provide adequate sedation without affecting respiration.

Other studies by Salgado *et al*[10]. Anand *et al*[11]. and Bajwa *et.al*[8] also correlate well with the finding of our study that addition of dexmedetomidine produces sedation of patients who were arousable by gentle tactile stimulation.

CONCLUSION

We concluded that the patients receiving addition of dexmedetomidine to epidural ropivacaine 0.2% had longer duration of postoperative analgesia, required less frequent and lesser amount of analgesics, with better haemodynamic stability and acceptable sedation in comparison to ropivacaine. Although the duration of postoperative analgesia was prolonged in 1 μ g/kg dexmedetomidine group as compared to 0.5 μ g/kg but increase in incidence of side effects with increase in dose overshadows this benefit.

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