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Comparative Study of Epidural Dexmedetomidine with Clonidine as Adjuvant to Isobaric Ropivacaine in Abdominal Hysterectomy

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ABSTRACT
Background: *Aim of the study was to compare epidural α2 adrenergic agonists, Dexmedetomidine and Clonidine as adjuvant to Isobaric Ropivacaine with respect to block characteristics, postoperative analgesia, sedation and hemodynamics.*
Methodology: *Ninety female patients of ASA physical status I and II, between 35-50 years of age scheduled for elective abdominal hysterectomy, were selected. The patients were randomly divided into three groups. Group R received 12 ml of 0.75% ropivacaine+1ml of saline, Group RD received 12 ml0.75% ropivacaine plus 1.5 µg/kg dexmedetomidine & Group RC received 12ml0.75% ropivacaine plus 2 µg/kg clonidine epidurally. Effects on hemo dynamics & respiratory parameters, sedation& block characteristics were noted.*
Results: *Demographic profile, duration of surgery and side effects were comparable and statistically non-significant in all the three groups. Onset of sensory analgesia at T10 and establishment of complete motor blockade was significantly earlier in the RD group. Postoperative analgesia was prolonged significantly in the RD group and consequently less epiduraltop-ups postoperatively in the first 24 hours. Sedation scores were much better in the RD group and highly significant on statistical comparison (P<0.0001).*
Conclusion: *Dexmedetomidine & Clonidine are effective epidural adjuvants to Ropivacaine, dexmedeto-midine being a better neuraxial adjuvant compared to clonidine for providing early onset of sensory & motor block, sedation and prolonged post-operative analgesia.*
Keywords: *Epidural, Ropivacaine, Clonidine, Dexmeditomidine, Abdominal Hysterectomy.*

Introduction

α-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia.[1] The stable haemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability, less thromboembolic events and other complications make them very useful pharmacologic agents.[2,3,4] Dexmedetomidine has anα-2 affinity eight times greater than clonidine.

Materials and Methods

After hospital ethics committee approval and written informed consent, 90 female patients of ASA grades I and II, between 35-55 years of age, and posted for elective abdominal hysterectomy,

were selected. Patients were allocated into three groups (n=30) randomly using sealed envelope. Group R received 12 ml of 0.75% Ropivacaine+1ml of saline, Group RD received 12 ml 0.75% Ropivacaine plus 1.5 µg/kg dexmedetomidine & Group RC received 12ml 0.75% Ropivacaine plus 2µg/kg clonidine epidurally. Hemodynamic parameters, sedation scores & block characteristics were studied.

This randomised double blind controlled study was conducted in Department of Anesthesiology, KMCT Medical college, Calicut between August 2014-2016. Exclusion criteria included bleeding disorders, infection, morbid obesity, patient refusal, allergies to amide local anesthetics, history of uncontrolled hypertension and diabetes. Tab.Lorazepam 1mg, Tab. Ranitidine 150mg and Tab. Domperidone 10mg were given as premedicants 1-2 hrs before surgery. The study medication was administered by an anaesthesiologist not involved in the care of patient or collection of data. The principal investigator blind to the identity of study medication, monitored and managed the patients and collected data.

All patients were educated about the methods of sensory or motor assessments before the procedure. Preloading with 10 ml/kg of crystalloid was done before the initiation of the procedure. Preoperatively patients were taught to analyse pain according to VNRS (0-no pain to 10- worst imaginable pain). Monitors connected and baseline heart rate, Non invasive blood pressure and oxygen saturation were noted before procedure. Lumbar epidural block with 18G Tuohy needle is performed in right or left lateral position in 1st or 2nd lumbar inter space. 4-5cms of 20G epidural catheter placed in epidural space. 3ml of 2% lignocaine with 1in2 lakh adrenaline given as test dose.

Motor and sensory block checked every 5 minutes for 45 minutes of epidural drug administration. Following block characteristics are observed. Onset and highest dermatomal level of sensory analgesia, complete motor blockade, time to two segment regression and regression to bromage1. Sedation assessed using Ramsay Sedation Score. Sensory level assessed by bilateral pin prick method and spirit swab and motor level by Modified Bromage scale. If desired level is not obtained within 30 minutes, additional dose of Ropivacaine is given in 2 ml increments.

Hemodynamic and respiratory parameters were noted every 5 min for 30 min and then at 10 min interval, thereafter up to 60 min and then at 15 min interval till the end of surgery. Hypotension (defined as systolic arterial pressure fall more than 20% mmHg from baseline value) is treated with inj. Mephenteramine or Ephedrine and heart rate <50 beats/min is treated with 0.6 mg of inj. atropine. Intravenous fluids were given as per body weight and operative loss requirement. Complications like anxiety, nausea, vomiting, pruritus, shivering and dry mouth were recorded. Onset of pain (4 in VNRS scale) is managed by top-up doses of 8 ml of 0.125% Ropivacaine postoperatively.

Results

Statistical analyses were carried out with ANOVA (Analysis of Variance) and Chi-square tests. P-value <0.05 was considered as significant.

Three groups were comparable with respect to demographic variables, ASA and duration of surgery (Table 1). Onset of sensory block at T10 is taken as interval between administration of drug and sensory block at T10 dermatome. Onset of sensory block at T10 dermatome is faster in the RD group (RD <RC < R group) and is statistically significant (p <0.01) (Table 1).

Time to complete motor block (TCB) is the time interval between drug administration and attainment of complete motor block in modified Bromage scale. It is shorter in both RD &RC groups compared to R group and shorter in RD group comparing to RC group (p value <0.01) (Table 1).

Maximum sensory level achieved is higher in RD group and lowest in R group. These differences are significant with a p value <0.01 when compared using chi-square test (Table 2).

Time to; a) 2 segment regression, b) regression to Bromage 1 and c) to first rescue epidural top up is significantly more in the RD group followed by RC and R group (Table 3).

Epidural top up with 8 ml of 0.125% Ropivacaine is given for postoperative analgesia during first 24 hours. Total dose required to provide adequate analgesia was least in RD group followed by RC and R group. This difference is statistically significant with p value < 0.01(Table 3).

Maximum deviation of hemodynamic parameters from baseline was slightly lower in RD &RC groups compared to R group (Table: 4).

Sedation score is higher in RD group compared to other groups. It is higher in RC group compared to R group, but statistically not significant (Table:5).

Efficacy of analgesia was assessed by checking the maximum pain score attained using VNRS (Verbal Numeric Rating Scale). VNRS was assessed and epidural top ups were given when VNRS was 4 or above (Table: 5). There is statistically significant difference in maximum pain score attained over 24 hrs between R&RD groups. There were no statistically significant difference between R&RC groups or RD &RC groups. There were no statistically significant difference in side effects between the groups (Table: 6).

Table I: Demographic Data and Comparison of block characteristics

Parameters	Group R	Group RD	Group RC	p value
Age (Yrs)	44 ± 3.055	43.64± 3.915	43.48 ± 3.754	0.872
Weight (Kg)	57.44 ± 5.583	57.68±5.647	57.60±5.944	0.989
ASA	1.16 ± 0.374	1.16 ± 0.374	1.20 ± 0.408	0.914
Duration of Surgery(mts)	93.32 ± 7.307	90.32 ± 7.809	91.08 ± 10.665	0.453
T10* (minutes)	15.60 ± 2.30	9.42 ± 1.41	10.80 ± 2.49	<0.05
TCB** (minutes)	37.60 ± 4.70	21.20 ±3.36	28.40 ± 4.06	<0.05

*Onset time of sensory block at T10 dermatome; **Time to complete motor block

Table II: Comparison of maximum sensory level achieved

Results						
	T2	T3	T4	T5	T6	*Row Totals*
Group R	0 (0.67) [0.67]	0 (3.33) [3.33]	6 (11.33) [2.51]	17 (11.67) [2.44]	7 (3.00) [5.33]	30
Group RD	2 (0.67) [2.67]	8 (3.33) [6.53]	15 (11.33) [1.19]	5 (11.67) [3.81]	0 (3.00) [3.00]	30
Group RC	0 (0.67) [0.67]	2 (3.33) [0.53]	13 (11.33) [0.25]	13 (11.67) [0.15]	2 (3.00) [0.33]	30
Column Totals	2	10	34	35	9	90 (Grand Total)

The chi-square statistic is 33.4078. The *p*-value is .000052. The result is significant at $p < .05$

Maximum level achieved is higher in RD group and lowest in R group. These differences are significant with a p value <0.01 when compared using chi-square test.

Table III: Comparison of Postoperative Block characteristics

Variable	Group R	Group RD	Group RC	P value (between groups)
T2S* (minutes)	77.60 ± 3.75	132.60 ±9.25	108 ± 7.21	<0.01
TB1** (minutes)	102.6 ± 5.42	180.4 ± 11.6	143 ± 5.16	<0.01
Tfr*** (minutes)	139 ± 6.57	306 ± 12.3	224 ± 17.2	<0.01
TD**** (milligrams)	150.52 ± 6.82	105.36 ± 7.812	120.96 ±6.410	<0.01

*Time to 2 segment regression;**Time to regression to Bromage 1; ***Time to first rescue top up
****Total 24hour dose of Ropivacaine required for postoperative analgesia.

Table IV: Vital Parameters

Parameter	Group R	Group RD	Group RC	P-Value (between groups)
Max. deviation of HR(beats/mt) from baseline. (0-120mts of surgery)	9.8 ± 3.4	16 ± 6.21	18 ±7.01	R&RD p Value <0.01 R&RC p Value <0.01 RD &RC p Value 0.247
Max.deviation of Systolic BP (mm Hg)from baseline. (0-120mts of surgery)	12 ±6.21	15 ±8.31	14 ±7.13	R&RD p Value 0.119 R&RC p Value 0.251 RD &RC p Value 0.619
Change in Resp. Rate/mt from baseline	3.3±1.02	3.01±1.1	3.11±1.01	R&RD p Value 0.068 R&RC p Value 0.211 RD &RC p Value 0.526

Heart rate is lower in both RD & RC groups comparing to R group. There is no statistically significant difference between RD&RC groups. There is no statistically significant difference in systolic blood pressure between groups.

Table V: Quality of Sedation and maximum pain score in the groups

RSS	Group R	Group RD	Group RC	P-Value
2	2	24	16	0.589135
3	0	6	2	
MPS	5.12 ± 0.373	4.16 ± 0.323	5.08 ± 0.656	R&RD:<0.01 R&RC:0.773 RD&RC:<0.01

RSS- Ramsay Sedation Score; MPS- Maximum pain score over 24hrs
Sedation score was more in RD>RC>R group, although statistically not significant.

There is statistically significant difference in maximum pain score attained over 24 hrs between R & RD and RD & RC groups.

Table VI: Comparison of side effects

Side effects	GROUP R	Group RD	Group RC	*Row Totals*
Nausea & Vomiting	2 (1.12) [0.69]	1 (1.36) [0.10]	1 (1.52) [0.18]	4
Dry Mouth	3 (3.64) [0.11]	5 (4.42) [0.08]	5 (4.94) [0.00]	13
Shivering	6 (3.08) [2.77]	2 (3.74) [0.81]	3 (4.18) [0.33]	11
Mephentermine requirement	2 (3.36) [0.55]	5 (4.08) [0.21]	5 (4.56) [0.04]	12
Atropine Requirement	1 (2.80) [1.16]	4 (3.40) [0.11]	5 (3.80) [0.38]	10
Column Totals	14	17	19	50 (Grand Total)

The chi-square statistic is 7.5073. The *p*-value is .483015. The result is *not* significant at $p < .05$.

Discussion

α-2 agonists provide sedation, analgesia, anxiolysis, hypnosis, sympatholysis, improve quality and cause less respiratory depression when used as adjuvant in epidural anesthesia.[5-8]Dexmedetomidine is eight times more specific and highly selective α-2 adreno receptor agonist compared to clonidine.[9,10]

There are no studies indicating the equipotent doses of epidural dexmedetomidine and clonidine. Many studies suggested that epidural clonidine at a dose of 1 μg/kg prolongs analgesia without producing unwanted side effects and doses <1 μg/kg dexmedetomidine does not prolong the block of ropivacaine. Hence in our study, we used 1 μg/kg of clonidine and dexmedetomidine as an adjunct to ropivacaine in epidural anesthesia.

The demographic profile, ASA grade and duration of surgery were comparable between the groups. Our study has shown that the addition of either 1.5μg/kg dexmedetomidine or 2μg/kg clonidine as adjuvant to epidural Ropivacaine improves the

quality of anesthesia and efficacy of local anaesthetic agent, which was supported by the previous studies.[11,12,13] Onset and peak levels of analgesia provided by both drugs dexmeditomidine> Clonidine) were statistically significant in our study which was in concordance with the observations of Bajwa et al.[11] Unlike our study Salgado et al.[13] and Shaikh SI et al.[14]found no statistical significance in the onset and peak levels of analgesia provided by both drugs. But it has to be noted that the dose used by them for the study was less than ours. Our study showed statistically significant sedation score in the Dexmeditomidine group (RD) compared to the other groups which was similar to findings of the Bajwa SJ et al [11], Saravana Babu M et al.[12],Shaikh SI et al.[14]andSchnaider TB et al.[15],

Maximum deviation of heart rate and blood pressures from baseline were least in the RD group followed by RC group and then R group. Our findings supports the established fact about α-2 agonists in providing stable perioperative and postoperative hemodynamics compared to previous agents. Vasopressor requirement for the maintenance of stable hemodynamic parameters and changes in respiratory rate from baseline did not reveal statistically significant differences between the groups. Similar hemodynamic & respiratory findings were observed in other studies also.[11-17]

Post operative block characteristics like Time to 2 segment regression, Regression to bromage 1, Time to first rescue top up and comparison of total dose of bupivacaine required for post operative analgesia were all better in the Dexmeditomidine group. These findings were similar to those of Bajwa et al and Salgado et al. There is statistically significant difference in maximum pain score attained over 24hrs between Ropivacaine & Ropivacaine-Dexmeditomidine groups. In our study, no statistically significant difference in sedation score and side effects were noted between the groups, which was similar to those of other studies.

Conclusion

Dexmedetomidine is a better alternative to clonidine in epidural anaesthesia, as far as quality of perioperative anesthesia, post operative analgesia, sedation and stable hemodynamics are concerned.

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