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COMPARISON OF EPIDURAL DEXMEDETOMIDINE AND CLONIDINE AS ADJUVANT TO BUPIVACAINE FOR ABDOMINAL HYSTERECTOMY -A RANDOMISED DOUBLE BLIND CONTROLLED STUDY

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ABSTRACT

Background

Epidural anesthesia is useful for providing both intraoperative anesthesia and postoperative analgesia. It provides intra operative hemodynamic stability, reduce perioperative stress response, helps in early mobilisation and thereby reducing complications and improving patient outcome. The quality and duration of analgesia is improved, when a local anesthetic is combined with alpha 2 adrenergic agonist. Aim of our study was to compare epidural dexmedetomidine and clonidine as an adjuvant to bupivacaine with respect to perioperative block characteristics, postoperative analgesia, sedation and hemodynamic profile.

Methodology

In our study, 90 patients of American Society of Anaesthesiologists grading I/ II of ages between 35-55 years posted for elective abdominal hysterectomy, were selected. The patients were randomly divided into three groups. Group B received 10 ml of 0.5% Bupivacaine+1ml of saline, Group BD received 10 ml 0.5% Bupivacaine plus 1.5 µg/kg Dexmedetomidine & Group BC received 10ml 0.5% Bupivacaine plus 2 µg/kg Clonidine epidurally. Hemodynamic parameters, sedation scores & block characteristics were studied.

Results

The 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 BD group. Postoperative analgesia was prolonged significantly in BD group than BC & B group and consequently less epidural top-ups in the first 24 hours.

Conclusion

Dexmedetomidine & clonidine have synergistic action with bupivacaine, when administered epidurally. Dexmedetomidine has a slightly better adjuvant profile compared to clonidine providing early onset of sensory & motor block, adequate sedation and prolonged post-operative analgesia.

KEYWORDS : Epidural, Bupivacaine, Clonidine, Dexmeditomidine, Abdominal Hysterectomy.

Introduction

Epidural anesthesia is a versatile technique which provides peri-operative surgical anesthesia and postoperative analgesia in lower abdominal surgeries. To calm the patients and to eliminate the anxiety component during regional anesthesia, many a time large volumes of local anesthetics are used. A good adjuvant to local anaesthetic can overcome these problems and improve the quality and duration of analgesia. The quality and duration of analgesia and perioperative safety profile is improved when a local anesthetic is combined with alpha 2 adrenergic agonist. 1-4 There are limited studies demonstrating the effects of epidural dexmedetomidine on local anesthetics. Dexmedetomidine is a highly selective 2 adrenergic agonist with an affinity eight times greater than clonidine. Various studies have shown that dose of clonidine is 1.5–2 times higher than dexmedetomidine when used in epidural route. Enhanced sympathoadrenal stability and thereby better haemodynamic profile and decreased oxygen demand make them very useful pharmacologic agents.5-8

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 method. Group B received 10 ml of 0.5% bupivacaine+1ml of saline, Group BD received 10 ml 0.5% bupivacaine plus 1.5 g/kg dexmedetomidine & Group BC received 10ml 0.5% bupivacaine plus 2 g/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, infections, 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 blinded 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 were 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 interspace. 4-5cms of catheter was placed in epidural space. 3ml of 2% lignocaine with 1in 2 lakh adrenaline was given as test dose.

Motor and sensory block checked every 5 minutes for 45 minutes of epidural drug administration. Following block characteristics were observed. Onset and highest dermatomal level of sensory analgesia, complete motor blockade, time to two segment regression and regression to bromage1. Sedation of grading is evaluated 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

Bupivacaine is given in 2 ml increments.

Hemodynamic and respiratory parameters were noted every 5 minutes for 30 minutes and then at 10 minutes interval, thereafter up to 60 minutes and then at 15 minutes interval till the end of surgery. Hypotension (defined as systolic arterial pressure fall more than 20% 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% bupivacaine 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 BD group (BD < BC < B group) and was 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 BD & BC groups compared to B group and shorter in BD group compared to BC group (p value <0.01) (Table I).

Table I: Demographic Data and Comparison of block characteristics

Parameters	Group B	Group BD	Group BC	p value
Age (Yrs)	42 ± 2.055	41.64± 2.915	41.48 ± 2.754	0.731
Weight (Kg)	53.44 ± 4.583	53.68± 4.647	53.60± 4.944	0.980
ASA	1.16 ± 0.341	1.26 ± 0.331	1.20 ± 0.416	0.567
Duration of Surgery(mts)	91.32 ± 7.307	88.32 ± 7.809	89.08 ± 10.665	0.382
tT10* (minutes)	9.50 ± 1.640	4.82 ± 1.14	5.980 ± 2.49	<0.05
TCB** (minutes)	24.40 ± 3.70	12.40 ±2.36	16.40 ± 2.46	<0.05

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

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

Table II: Comparison of maximum sensory level achieved

	T2	T3	T4	T5	T6	*Row Totals*
Group B	0 (0.97) [0.97]	1 (3.54) [1.83]	5 (10.96) [3.24]	17 (10.96) [3.33]	6 (2.58) [4.54]	29
Group BD	3 (1.10) [3.28]	8 (4.03) [3.90]	17 (12.47) [1.65]	5 (12.47) [4.47]	0 (2.93) [2.93]	33
Group BC	0 (0.93) [0.93]	2 (3.42) [0.59]	12 (10.58) [0.19]	12 (10.58) [0.19]	2 (2.49) [0.10]	28
Column Totals	3	11	34	34	8	**90 (Grand Total)**

The chi-square statistic is 32.1485. The p-value is .000088.

Time to; a) 2 segment regression, b) regression to Bromage 1 and c) to first rescue epidural top up is significantly more in the BD group followed by BC and B group (Table III).

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

Table III: Comparison of Postoperative Block characteristics

Variable	Group B	Group BD	Group BC	P value (between groups)
T2S* (minutes)	107.60 ± 5.95	182.60 ±16.4	148 ± 5.27	<0.01
Tb1** (minutes)	135.8 ± 8.12	224 ± 17.96	185 ± 8.16	<0.01
Tfr*** (minutes)	196 ± 8.77	386 ± 35.68	294 ± 13.76	<0.01
TD**** (milligrams)	71.22 ± 8.82	53.36 ± 8.13	62.96 ±9.40	<0.01

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

Maximum deviation of hemodynamic parameters from baseline was slightly lower in BD & BC groups compared to B group (Table:IV).

Table IV: Vital Parameters

Parameter	Group B	Group BD	Group BC	P-Value(betweegroups) n
Max. deviation of HR(beats/mt) from baseline. (0-120mts of surgery)	18.8 ± 3.4	12 ± 6.21	14 ±7.01	B & BD p Value <0.01 B & BC p Value <0.01 BD & BC p Value 0.04
Max. deviation of Systolic BP (mm Hg)from baseline. (0-120mts of surgery)	28±6.21	22±8.31	24±7.13	B & BD p Value <0.01 B & BC p Value <0.01 BD & BC p Value 0.085
Max. deviation of Diastolic BP (mm Hg)from baseline. (0-120mts of surgery)	14±3.14	4±3.14	6±3.02	<0.01
Change in Resp. Rate/mt from baseline	3.3±1.02	3.01±1.1	3.11±1.01	B & BD p Value 0.068 B & BC p Value 0.211 BD & BC p Value 0.526

Sedation score is higher in BD group compared to other groups. It is higher in BC group compared to B group, but statistically not significant (Table:V).

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:V).

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

RSS	GroupB	Group BD	Group BC	P-Value
2	8	18	13	0.31844
3	0	4	1	
MPS	5.28 ± 0.737	4.76 ± 0.723	5.12 ± 0.666	B&BD: <0.01 B&BC: 0.381 BD&BC: 0.05

RSS- Ramsay Sedation Score; MPS- Maximum pain score over 24hrs

There is statistically significant difference in maximum pain score

attained over 24 hrs between B & BD groups. There was no statistically significant difference between B & BC groups or BD & BC groups. There were no statistically significant difference in side effects between the groups (Table:VI).

Table VI: Comparison of side effects

Side effects	Group B	Group BD	Group BC	*Row Totals*
Nausea & Vomiting	2 (1.26) [0.44]	1 (1.41) [0.12]	1 (1.33) [0.08]	4
Dry Mouth	3 (5.35) [1.03]	7 (5.98) [0.17]	7 (5.67) [0.31]	17
Shivering	6 (3.46) [1.86]	2 (3.87) [0.90]	3 (3.67) [0.12]	11
Mephentermine requirement	4 (4.09) [0.00]	5 (4.57) [0.04]	4 (4.33) [0.03]	13
Atropine Requirement	2 (2.83) [0.25]	4 (3.17) [0.22]	3 (3.00) [0.00]	9
Column Totals	17	19	18	**54 (Grand Total)**

The chi-square statistic is 5.5732. The *p*-value is .694915. The result is not significant at $p < .05$.

Discussion

α-2 agonists provide sedation, analgesia, anxiolysis, hypnosis, sympatholysis and cause less respiratory depression when used as adjuvant in epidural anesthesia. Dexmedetomidine is eight times more specific and highly selective α-2 adrenoreceptor agonist compared to clonidine.[9-12] 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 bupivacaine improves the quality of anesthesia and efficacy of local anaesthetic agent, which was supported by the previous studies[13,14,15] 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.[13] Unlike our study Salgado et al.[15] and Shaikh SI et al.[16] 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 (BD) compared to the other groups which was similar to findings of the Schnaider TB et al.6, Bajwa SJ et al [13], Saravana Babu M et al.[14] and Shaikh SI et al.[16]

Maximum deviation of heart rate and blood pressures from baseline were least in the BD group followed by BC group and then B 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.[14-19]

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 bupivacaine & bupivacaine-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 & clonidine have synergistic action with bupivacaine, when administered epidurally. Dexmedetomidine has a better adjuvant profile compared to clonidine providing early onset of sensory & motor block, adequate sedation, prolonged post-operative analgesia and stable hemodynamics.

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