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COMPARISON OF ANALGESIC EFFECTIVENESS OF DEXMEDETOMIDINE VERSUS CLONIDINE AS AN ADJUVANT TO BUPIVACAINE IN EPIDURAL ANAESTHESIA IN PATIENTS UNDERGOING VAGINAL HYSTERECTOMY : A RANDOMIZED DOUBLE BLIND INTERVENTIONAL STUDY AT SMS MEDICAL COLLEGE AND ATTACHED GROUP OF HOSPITALS

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ABSTRACT

BACKGROUND: To compare analgesic effectiveness of Dexmedetomidine (1 mcg/kg) versus Clonidine (2 mcg/kg) as an adjuvant to Bupivacaine in epidural anaesthesia in patients undergoing vaginal hysterectomy.

METHODS: The study was done on 60 patients of (age 30-65 years, weight 40-70 kilograms) ASA grade 1&2. These were randomly allocated in 2 groups of 30 each. They were undergoing vaginal hysterectomy Group A received 20 ml consisting of 15 ml of 0.5% Bupivacaine plus Dexmedetomidine (1µg/kg) diluted in normal saline to make total volume of 20 ml, Group B received 20 ml of consisting of 15 ml of 0.5% Bupivacaine plus Clonidine (2µg/kg) diluted in normal saline to make total volume of 20 ml which was given in the epidural space. Mean Time duration of first rescue analgesia, number of rescue analgesia provided within 24 hours, mean time duration to reach the highest sensory and motor block was seen postoperatively

CONCLUSION: Epidural Dexmedetomidine as an adjuvant to 0.5% bupivacaine provided longer duration of post-operative analgesia and significantly less requirement of total number of rescue analgesia in first 24 hours postoperatively, as compared to epidurally administered clonidine and block characteristics in terms of onset and duration of sensory and motor blockade was better in Dexmedetomidine group

KEYWORDS : Epidural anaesthesia, Vaginal Hystrectomy, Dexmedetomidine, Clonidine, Rescue analgesia.

INTRODUCTION

Pain is defined by International Association for Study of Pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".

Pain in the post-operative period is one of the major factors that prevent early recovery from anaesthesia and surgery. Uncontrolled post- operative pain resulting from any kind of surgery may produce a range of detrimental acute and chronic effects.

Spinal anaesthesia is the preferred regional anaesthetic technique because of technical ease, early onset and sure success of technique, but duration of anaesthesia and analgesia is limited.

Epidural anaesthesia, though demanding technically, has many advantages of providing anaesthesia for prolonged duration with repeated top-ups and also it is the preferred technique of choice for providing excellent post-operative analgesia. It contributes to intraoperative hemodynamic stability and has shown to reduce perioperative stress response thereby causing a decrease in complications and improving patients outcome. It helps in early mobilization by relieving postoperative pain, which decreases the incidence of thromboembolic events.

Bupivacaine, an amide type of local anaesthetic, has high potency, slow onset and long duration of action, is commonly employed for Epidural anaesthesia.

Dexmedetomidine is a selective Alpha-2-adrenoreceptor agonist with a α-2/α-1 (1620:1) selectivity. It has analgesic and sedative properties, when administered intrathecally, epidurally or intravenously as an adjuvant. Mostly used in ICU setups and awake neurosurgeries.

Clonidine is also alpha-2 receptor agonist acts on prejunctional and postjunctional adrenergic receptors.

Alpha-2 receptor agonists as adjuvants are known to increase both sensory and motor block of local anaesthetics and decrease the post-operative analgesic requirements and also causes augmentation of local anaesthetic which reduces the total dose of anaesthetic agents. Stable hemodynamic and decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacological agents.

This study was planned to compare analgesic effectiveness of Dexmedetomidine versus Clonidine as an adjuvant to Bupivacaine in epidural anaesthesia.

METHODS

The present study was conducted in Department of Anaesthesiology, SMS Medical College and attached group of hospitals, Jaipur to compare the analgesic effectiveness of Dexmedetomidine Versus Clonidine as an adjuvant to bupivacaine in epidural anaesthesia in patients undergoing Vaginal Hysterectomy.

60 patients of age group 35-60 years, weighing between 40-70 kgs and ASA grade I and II scheduled for vaginal hysterectomy under epidural anaesthesia were randomly selected and divided into 2 groups of 30 each.

Group A (n=30): Patients received 20 ml of solution consisting of 15 ml of 0.5% Bupivacaine plus Dexmedetomidine (1µg/kg body weight) diluted in normal saline to make total volume of 20 ml which was given in the epidural space.

Group B (n=30): Patients received 20 ml of solution consisting of 15 ml of 0.5% Bupivacaine plus Clonidine (2µg/kg body weight) diluted in normal saline to make total volume of 20 ml which was given in the epidural space.

A detailed pre-anaesthetic evaluation including history and a thorough general and systemic examination and all relevant investigations were done for all the patients.

After checking fasting status, informed written consent and PAC, intravenous access secured. Inj. Ringer lactate infusion started at rate of 10-15ml/kg//hr. Baseline haemodynamic parameters recorded. Inj. Ranitidine 1mg/kg + Inj. Metoclopramide 0.1 mg/kg was given 15 minutes prior to epidural administration of drug .

Under all aseptic precautions, in sitting position back of patient painted with povidone iodine solution. After that selected site draped with sterilized hole towel. Intervertebral space between L4-L5/L3-L4 vertebrae identified.

Lumbar epidural puncture performed with 18 G Tuohy needle in selected interspace. The identification of the epidural space was done with loss of resistance technique. After confirming the position of Tuohy needle, test dose of normal saline injected after that the titrated dose of 20 ml was given to the patient in epidural space .

Patient then put back in supine position. Sensory and motor block assessed every 2 minutes until the desired effect came.

INTRA-OPERATIVE MONITORING

The following parameters has been noted at specific time intervals (5,

10, 15, 20, 30 min and then every 15 mins till 90mins after that every 30 minutes till the completion of surgery).

A. Clinical parameter - Pulse rate, SpO2, Blood pressure, ECG
B. SENSORY BLOCK

The onset of sensory block was taken as the time from the epidural injection of the study drug to the time taken to attain maximum level of sensory block.

The level of sensory block was assessed after every 1 min after epidural injection of the study drug.

Grading of Sensory block

1. 0- Sharp pain.
2. 1- Touch sensation only.
3. 2- Not even touch sensation.

Postoperatively sensory block was tested every 30 minutes.

Duration of sensory block was defined as the time taken for the sensory block to regress two segments lower than the maximum sensory level achieved.

C. MOTOR BLOCK

Onset of motor block Defined as the time taken from injection to motor block to reach maximum Modified Bromage score.

Offset of motor block was taken as Modified Bromage scale 6. Intensity of motor block - Modified Bromage Score :

Score Criteria

1. Complete block (unable to move feet or knees)
2. Almost complete block (able to move feet only)
3. Partial block (just able to move knees)
4. Detectable weakness of hip flexion while supine (full flexion of knees)
5. No detectable weakness of hip flexion while supine
6. Able to perform partial knee bend.

Total Duration of motor block – Assessed by using Modified Bromage score Duration of motor block was measured by the time elapsed from the 1 to the 6 Modified Bromage score.

D. ADVERSE EVENTS-

The following adverse events were noted and managed accordingly.

Hypotension, Bradycardia, Respiratory depression, nausea and vomiting.

Episodes of intra-operative hypotension were managed with colloids and if required with incremental doses of inj. Mephentermine 6 mg intravenously. Bradycardia was treated with 0.6mg of inj. Atropine intravenously. Intra- operative nausea was treated with inj. Ondansetron 4 mg and any pruritus was treated using anti-histaminics. Regular check-up of blood pressure, pulse rate, saturation were done at 2,5,10,15,30,60,75,90,120 min interval and post- operatively at 60 min until 6 hours, two hourly until the twelfth hour, four hourly in the next twelve hours.

POST-OPERATIVE ASSESSMENT

Vital parameters – Pulse Rate, NIBP, saturation were recorded at regular interval of 30 min for first 4 hours, once every 2 hours until the 8 hour and once every 4 hours for the next 16 hours.

Two segment regression time (time of regression of sensory block by two segments from the highest level attained).

Duration of analgesia – Analgesia duration was observed using Visual analogue score (VAS) .

Duration of effective analgesia (Time to First Rescue analgesia) was measured as time from the epidural drug administration to the patients VAS score > 3. Patient's VAS>3 and administration of rescue analgesia constituted the end point of the study. Patient was kept under observation for a total period of 24 hours for routine post-operative monitoring. The total number of analgesic doses required in post-operative period for 24 hours was also noted.

Sedation score - Post-operative sedation level was measured by using Five Point Sedation Scale and serially assessed at an hour interval starting from immediate postoperative period which considered as 0 hour in post-op monitoring.

STATISTICAL ANALYSIS

Analysis was done using SPSS version 20. Chi-square test was used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$.

Observations

The demographic profiles with regard to age and weight was comparable. The distribution as per ASA status was similar. The duration was surgery in both the groups was also similar and statistically insignificant.

Pre-induction heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, spo2 were comparable in both the groups with a statistically no significant difference between them ($p<0.05$).

Table 1: Mean time to achieve highest level of sensory block (min) and motor block (min)

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Sensory block (mins)	11.8	1.157	16.60	1.163	**< 0.05**
Motor block (mins)	15.70	1.264	21.73	1.552	**< 0.05**

Table shows the mean time to achieve highest level of sensory block, it was 11.8±1.157 min in group A and 16.60±1.163 min in group B, difference was statistically significant ($p<0.05$) and the mean time to achieve highest level of sensory block was earlier in group A.

Above table depicts the mean time to achieve highest level of motor block. It was 15.70±1.1264 min in group A and in group B it was 21.73±1.552 min. Difference was statistically significant ($p<0.05$).

Table 2: Total duration of Motor blockade (min)

	Group A	Group B
Mean	226.33	176.17
Std. Deviation	24.77	19.37
P value	0.001 (S)	

Table shows total duration of Motor Blockade of both groups. It was 226.33±24.77 minutes for Group A and for Group B 176.17±19.37 minutes. The difference was statistically significant (P value =0.001).

Table 3: Mean Sedation score for 24 hours post-operatively

Time (hrs)	Group A		Group B		p Value
	Mean	SD	Mean	SD	
0	2.20	0.407	2.03	0.183	0.04 (S)
1	2.00	0.0	1.47	0.507	0.04 (S)
2	1.07	0.254	1.00	0.00	0.001(S)
3	1.00	0.00	1.00	0.00	-
4	1.00	0.00	1.00	0.00	-
5	1.00	0.00	1.00	0.00	-
6	1.00	0.00	1.00	0.00	-
8	1.00	0.00	1.00	0.00	-
10	1.00	0.00	1.00	0.00	-
12	1.00	0.00	1.00	0.00	-
16	1.00	0.00	1.00	0.00	-
20	1.00	0.00	1.00	0.00	-
24	1.00	0.00	1.00	0.00	-

Above table shows sedation score in both groups for 24 hours post-operatively and it appeared that at 0, 1st, 2nd hour the sedation score was more for Group A patients than Group B patients. The difference was statistically significant.

Table 4: Comparison of Mean VAS score

Time (hr)	Group A	Group B	P value
0	**0**±0	**0**± 0	**-**
1	**0**± 0	**0**± 0	**-**
2	**1.17**± 0.112	**1.5**±0.212	**0.003 (S)**
3	**2.17**±0.12	**2.37**±0.100	**0.08 (S)**

4	**3.13**±0.010	**3.37**±0.016	**0.03 (S)**
5	**3.5**±0.017	**2.53**±0.006	**0.02 (S)**
6	**0.6**±0.110	**1.17**±0.12	**0.001 (S)**

Above table shows the mean VAS score. The mean VAS score for Group A at 2nd, 4th, 5th and 6th hour was 1.17 ±.112, 3.13±.010, 3.5±.017 and 0.6±.110 respectively. For Group B it was at 2nd, 4th, 5th and 6th hour was 1.5±.212, 3.37±.016, 2.53±.006, 1.17±.012 respectively. The difference in mean VAS Score between both the groups was statistically significant for the same hours mentioned above.

DISCUSSION

Epidural anaesthesia is most common regional anaesthesia technique used for intraoperative surgical anaesthesia as well as postoperative analgesia.

Vaginal hysterectomy is one of the least and minimally invasive types of hysterectomies and it has better outcomes and fewer complications compared to other types. The advantages of VH include less pain, rapid recovery, faster return to work, lower cost and lower morbidity.

Pain in the post-operative period is one of the major factors that prevent early recovery from anaesthesia and surgery. Uncontrolled post- operative pain resulting from any kind of surgery may produce a range of detrimental acute and chronic effects. The transmission of nociceptive stimuli from the periphery to the CNS results in neuroendocrine stress response resulting in increased sympathetic tone, increased catecholamine levels and catabolic hormone secretion which delays in the recovery.

The adjuvants, because of their analgesic properties and augmentation of local anaesthetic effects reduces the requirement of anaesthetic agents. Their use is known to increase both sensory and motor block of local anaesthetics and decrease the post- operative analgesic requirements.

Alpha-2 adrenoceptor agonists are routinely used as an adjuvant in regional anaesthesia due to its many desirable effects, like anxiolysis, analgesia, sedation, anaesthetic-sparing and peri-operative haemodynamic-stabilising effects.

Dexmedetomidine, a highly selective α-2 agonist with a relatively high ratio of α-2:α- 1 activity (1620:1 as compared to 220:1 for clonidine). Clonidine is also alpha-2 receptor agonist acts on prejunctional and postjunctional adrenergic receptors this study was planned to compare analgesic effectiveness of Dexmedetomidine versus clonidine as an adjuvant to Bupivacaine in epidural anaesthesia.

The present study was conducted in the department of Anaesthesiology, S.M.S. medical college and attached group of hospitals, Jaipur. 60 eligible female patients of age group 35-60 years, weighing between 40-70 kgs and ASA grade I and II scheduled for Vaginal hysterectomy under epidural anaesthesia were randomly selected and divided into 2 groups of 30 each.

Group A (n=30): Patients received 20 ml of solution consisting of 15 ml of 0.5% Bupivacaine plus Dexmedetomidine (1µg/kg body weight) diluted in normal saline to make total volume of 20 ml which was given in the epidural space.

Group B (n=30): Patients received 20 ml of solution consisting of 15 ml of 0.5% Bupivacaine plus clonidine (2µg/kg body weight) diluted in normal saline to make total volume of 20 ml which was given in the epidural space.

The parameters studied included postoperative analgesia, hemodynamic stability, sensory and motor block characteristics, sedation property and perioperative adverse effects (if any).

The demographic profiles with regard to age and weight was comparable. The distribution as per ASA status was similar. The mean age was 50.63±8.231 years in group A and 46.77±7.205 years in Group B and the mean weight of patients was 54.30±5.553 in group A and 54.50±7.375 in Group B. ASA grade distribution was comparable in both the groups.

The mean duration of surgery was comparable in both the groups. It was 81.03±17.101 minutes in group A while 82.90±16.961 min in group B.

The mean time to reach highest level of sensory block in Group A was 11.80 ± 1.157minutes and in Group B was 16.60± 1.163 minutes. Mean time to achieve highest level of sensory block was earlier in group A as compared to group B. This was statistically significant (p value =0.001).

Results of this study coincides with study done by Safiya I Shaikh et al[1] (2016) they observed that epidural administration of dexmedetomidine (1µg/kg) fastens onset of sensory block as compared to clonidine (2µg/kg) as an adjuvant to 0.5% bupivacaine.

Shilpi Agarwal et al[2] (2015) also found that onset of sensory block was earlier in Dexmedetomidine group as compared to Clonidine group. Result of this study correlates with the above-mentioned study in terms of mean time to achieve highest level of sensory block.

20% cases of Group A achieved T4 sensory level while 6.7% cases in Group B achieved the T4 sensory level. In Group A 60% cases reached T6 sensory level while 73.3% patients in Group B achieved T6 sensory level. 20% cases of both the groups achieved T8 sensory level. Though the more cases of Group A achieved higher level of sensory block as compared to Group B but the difference in highest level of sensory block was comparable between both the groups and it was statistically insignificant.

Result of this study coincides with the result of study done by Safiya I Shaikh et al[1] (2016). They also reported that mean level of sensory block was higher in Dexmedetomidine group as compared to Clonidine group. The difference was statistically significant.

Similarly Anjana hazarika et al[3] (2020) also reported that mean level of sensory block was higher in Dexmedetomidine group as compare to Clonidine group . The difference was statistically significant.

The mean duration of two segment regression for Group A was 133.27± 5.206 minutes and for Group B was 126.20± 3.089 minutes. The mean duration of two segment regression was prolonged in group A as compared to group B and difference was statistically significant (p value= 0.001).

Result of this study was supported by study done by Anjana hazarika et al[3] (2020) . They concluded that the mean duration of two segment regression was prolonged in Dexmedetomidine group as compared to Clonidine group.

Results of this study coincides with the results of the study done by Satya Prasanna nayak et al[4] (2017). They also reported that the mean duration of two segment regression was significantly increased in Dexmedetomidine group as compared to Clonidine group.

The mean time to achieve highest degree of motor block for Group A was 15.70 ± 1.264 minutes and for group B mean time was of 21.73 ± 1.552 minutes. The mean time to achieve maximum degree motor block was earlier in group A as compared to group B and the difference was statistically significant in between both the groups (p value= 0.001).

Anjana hazarika et al[3] (2020) , also reported that the mean time to achieve maximum degree of motor block was shorter in Dexmedetomidine group as compared to Clonidine group. The result of this study coincides with above study.

Safiya I Shaikh et al[1] (2016) also observed shorter mean time to achieve maximum degree of motor block in Dexmedetomidine group as compared to Clonidine group. Their study also supports the result of this study.

Mean total duration of motor blockade for Group A was 226.33±24.77 minutes and for Group B was 176.17±19.37 minutes. The duration of motor block was longer in group A as compared to Group B and the difference in duration of motor block between both the groups was statistically significant (p value =0.001).

Result of this study supported the study done by Safiya I Shaikh et al[1] (2016). They also found that the mean duration of motor block was prolonged with Dexmedetomidine group as compared to Clonidine group.

Satya Prasanna nayak et al[4] (2017) also concluded that mean duration of motor block was significantly increased in Dexmedetomidine group

as compared to Clonidine group.

The result of this study correlates with the above mentioned study in terms of duration of motor block.

The mean sedation score for Group A at 0, 1st and 2nd hour was 2.20±0.407, 2.00±.00 and 1.07±.254 respectively while for Group B it was 2.03±0.183, 1.47±0.507 and 1.00±.000 respectively. Group A patients were comparatively more sedated at 0, 1st and 2nd hour than group B. The difference in sedation score at above mentioned time was statistically significant.

All the patients of both Groups were completely awake and not under any sedation after 2 hours post-operatively.

Similarly Shilpi Agarwal et al[2] (2015) also reported that more sedation occurred in Dexmedetomidine group as compared to clonidine group.

Safiya I Shaikh et al[1] (2016) also found that sedation was more in epidural Dexmedetomidine group in comparison to epidural Clonidine group as an adjuvant to 0.5% bupivacaine . The finding was similar to this study.

Mean VAS score was significantly lower in group A as compared to group B at 2nd, 4th, 5th, and 6th hour postoperatively. The difference was statistically significant as the P value was 0.003, 0.03, 0.02 and 0.001 respectively.

In Group A patients the mean time to first rescue analgesia was 359.97±11.473 minutes and in Group B mean time to first rescue analgesia was 310.27±34.455 minutes. The duration of analgesia was longer in group A as compared to group B. The difference was statistically significant (P value =0.001).

Result of this study is supported by the study done by Shilpi Agarwal et al[2] (2015).They observed longer mean time to first rescue analgesia with Dexmedetomidine group as compared to Clonidine group.

Study done by Anjana hazarika et al[3] (2020) , reported prolonged mean time to first rescue analgesia with Dexmedetomidine group as compared to Clonidine group.

Result of this study coincides with the result of study done by Safiya I Shaikh et al (2016). They compared epidural Dexmedetomidine and Clonidine with bupivacaine and also found that the duration of analgesia was more in Dexmedetomidine group as compared to Clonidine Group. Which resembles the results of this study.

The postoperative analgesia requirement was observed in both the groups for 24 hours post-operatively. The mean number of analgesic dose required to the patients of Group A was 2.07±0.365 and for Group B patients was 2.77±0.430. The difference in requirement of total number of rescue analgesia given in 24 hours post-operatively between both the groups was statistically significant (P value=0.001). It suggested that in Group A patients analgesic demand was less as compared to Group B.

All the studies reported that the duration of analgesia is prolonged in Dexmedetomidine group as compared to Clonidine group but no study has mentioned the total number of post-operative analgesic requirement in 24 hours.

Mean HR, Mean systolic blood pressure, Mean diastolic pressure and Mean Spo2 at baseline, intraoperative and postoperative time were comparable between Group A and Group B.

The difference between the groups was found to be statistically not significant ($p > 0.05$).

Anjana hazarika et al[3] (2020) also found that there was statistically no significant difference in mean HR and mean SBP and mean DBP in between both dexmedetomidine group and clonidine group. The results of the present study correlates with the above mentioned studies.

Shailesh et al[5] (2019) concluded that there was no statistically significant difference in haemodynamic parameters between both the groups.

Hypotension occurred in 6 patients of group A while 2 patients of group B. The difference in occurrence of hypotension was statistically insignificant (p=0.29).

Bradycardia was seen in 4 patients of group A and none of the patients in group B. The difference was statistically insignificant (p=0.29).

Nausea and vomiting occurred in 4 patient of group A and 3 patients of group B and the difference was statistically not significant (p=0.29).

In a study conducted by Anjana hazarika et al[3] (2020), they found hypotension was the most common adverse event in both the groups, although it was statistically insignificant. The result coincides with the results of present study.

Similarly the result of study done by Shilpi Agarwal et al[2] (2015) also supports the findings of present study.

CONCLUSION

It was concluded that Epidural Dexmedetomidine as an adjuvant to 0.5% bupivacaine provided longer duration of post-operative analgesia and significantly less requirement of total number of rescue analgesia in first 24 hours postoperatively, as compared to epidurally administered clonidine as an adjuvant to 0.5% bupivacaine.

It was also observed that block characteristics in terms of onset and duration of sensory and motor blockade was better in Dexmedetomidine group as compared to clonidine group.

Hence epidural Dexmedetomidine is a safe alternative to Clonidine as an adjuvant to 0.5% bupivacaine in terms of enhanced postoperative analgesia and less requirement of total number of rescue analgesics in first 24 hours post- operatively.

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