

Comparison between Dexmedetomidine and Clonidine as an Adjuvant to Spinal Anesthesia in Abdominal Hysterectomy

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Abstract: ***Introduction:** Newer α -2 agonist agents have opened a new chapter in prolongation of duration of neuraxial block and postoperative analgesia. **Material and Methods:** Sixty adult patients of ASA grade I-II were randomly divided into two groups of thirty each. Group Dexmedetomidine and group Clonidine. All patients received hyperbaric bupivacaine 0.5% (heavy) 15 mg intrathecally with dexmedetomidine 10 μ g and with clonidine 15 μ g respectively (30 each). Sensory block, motor block, intra-operative hemodynamic changes, two segment regression and total duration of analgesia was assessed. **Result and Conclusion:** Onset time of sensory and motor block was shorter in group D compared to group C. Two segment regression time was significantly higher in group D (100.67 \pm 17.798 min) as compared to group C (71.167 \pm 23.44 min). Total duration of analgesia was significantly prolonged in group D (97.73 \pm 27.43 min) as compared to Group C (32.33 \pm 21.96 min). Heart rate and mean arterial pressure remained at lower level in both groups but was not statistical significant. It can be concluded that though both clonidine and dexmedetomidine prolonged duration of sensory and motor block of bupivacaine, dexmedetomidine is better in terms of longer duration of action.*

Keywords: Dexmedetomidine, Clonidine, Hyperbaric Bupivacaine 0.5% (H), Spinal Anaesthesia.

1. Introduction

The sole essence of anaesthesia is pain relief. Ever since the introduction of local anesthetics, physicians have investigated different methods of using them. Spinal anaesthesia has emerged as an important technique, with simplicity, effectiveness, safety and a successful history since late nineteenth century. To improve the effect and duration of spinal anesthesia, various drugs are used as an adjuvant to hyperbaric bupivacaine.^[1, 2]

Dexmedetomidine & Clonidine both are α -2 agonist drugs. Clonidine is an α -2 adrenergic receptor agonist with a 200:1 ratio of α -2: α -1 receptor while Dexmedetomidine is a selective, specific, potent α 2 – adrenergic agonist with a 620:1 ratio of α -2: α -1 receptor. Dexmedetomidine showed protective or growth promoting properties in tissues, including nerve cells from cortex and has a neuroprotective effect similar to methylprednisolone in spinal cord injury when used intrathecally.^[3,4]

Clonidine has antihypertensive effects as well as the ability to potentiate the effect of local anesthetics. It can provide pain relief by an opioid-independent mechanism.^[5] Clonidine and Dexmedetomidine were added in present study to find out whether the addition of Clonidine or Dexmedetomidine to bupivacaine changes its efficacy and to find out any change in the quality of sensory and motor block. The aim of our study was to evaluate the efficacy and safety of intrathecal administration of Dexmedetomidine vs. intrathecal Clonidine as an adjuvant with 0.5% Bupivacaine (H) in abdominal hysterectomies.

Our objectives were to compare onset & duration of sensory analgesia, onset & duration of motor block achieved with the use of individual drug, hemodynamic changes, depth of sedation, side effects related to drugs under study, post-operative assessment of pain by VAS (Visual Analogue Scale).

2. Materials & Method

After approval of local institutional ethics committee, randomized double blind controlled study was carried out in 60 ASA I & II patients age between 30-60 years, weight between 35-80 kg, height between 140-170 cm. Patients willing to participate were included in the study. Patients scheduled for elective abdominal hysterectomy procedure were divided into two groups of thirty each and they were placed in Group C or Group D. Patients excluded from the study were patients with contraindications for spinal anesthesia, sensitivity to study drugs, recent onset of MI (<3 months), hypovolemic patient, patients with renal or hepatic impairment.

Group D: - Intrathecal injection of 15 mg of 0.5 % Bupivacaine (heavy) + 10 μ g Dexmedetomidine.

Group C: - Intrathecal injection of 15 mg of 0.5 % Bupivacaine (heavy) + 15 μ g Clonidine.

The total volume injected was 3.5 ml in both the groups.

Patients were enrolled after taking informed consent. Patients were explained about Visual analogue scale preoperatively and in the operating room. Baseline vitals like Heart rate, respiratory rate, ECG, oxygen saturation, non-invasive blood pressure were recorded. All patients were preloaded with 10ml/kg ringer lactate.

Patients were placed in sitting position on the operation table. With strict aseptic precautions, midline approach subarachnoid block was achieved in L3-L4 space with 25G disposable Quincke spinal needle. Drug was injected after free flow and clear aspiration of CSF. Patients were immediately placed in the supine position with no tilt given to the table. The onset of sensory analgesia was tested by pinprick. Sensory anesthesia was defined as loss of sensation to pin-prick with 24G hypodermic needle. Time taken for achievement of sensory anesthesia at L1 after intrathecal injection was recorded. Sensory anesthesia was recorded

every 15 seconds initially for 5 minutes and then every minute for 15 minutes.

Time taken to achieve highest sensory level was noted. Time taken for onset of maximum motor blockade i.e. the time taken from the time of spinal to the time to achieve maximum grade of motor blockade was noted. Maximum grade of motor blockade achieved using modified Bromage score was also noted. Time to return of Modified Bromage score to zero was recorded.

Total duration of analgesia was defined as the time taken from the time of spinal anesthesia to the first request of rescue analgesia. Duration of motor blockade was defined as the time taken from the time of spinal anesthesia to the return of modified bromage score of grade 0. After intrathecal drug injection, hemodynamic data was recorded for every 2 minutes for first 5 minutes then every 5 minutes for next 60 minutes and then for every 10 minutes till the procedure was completed.

Hypotension (defined as a decrease in systolic blood pressure > 30% of the baseline value or systolic blood pressure < 90 mm Hg) was treated with intravenous boluses of 3 mg ephedrine. Bradycardia (defined as a decrease in heart rate of < 20% of baseline value or 50 beat/min) was treated with boluses of 0.6 mg atropine.

Visual Analogue Scale (VAS) was used for assessment of post-operative pain relief at 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, 240, 300 minutes. Patient was explained about Visual analogue scale preoperatively. When VAS score was 3 or > 3, Inj. Diclofenac 75 mg. IM was given as rescue analgesia.

Level of sedation was assessed by Ramsay Sedation Score.

3. Statistical Analysis

Quantitative data was analyzed by student 't' test. Nominal categorical data among study groups were compared using the chi-square test. P < 0.05 was considered to be statistically significant.

4. Observation and Results

In our study we found onset of sensory anesthesia at L1 was significantly early with Dexmedetomidine group (1.00 ± 0.0 min) as compared to Clonidine group (1.13 ± 1.64 min). No statistically significant difference in onset of time was seen between Dexmedetomidine and Clonidine groups ($p > 0.05$). We found that the spread of sensory block with intrathecal Dexmedetomidine was 100% at T4 level.

In our study the two segment regression time in Dexmedetomidine group was (100.67 ± 17.798 min) and Clonidine group (71.167 ± 23.44 min). Thus time for 2 segment regression was faster in Clonidine group as compared to Dexmedetomidine. The difference was statistically significant ($p < 0.05$).

Total duration of analgesia in Dexmedetomidine group (97.73 ± 27.43 min) as compared to Clonidine group (32.33 ± 21.96 min) was significantly higher in Dexmedetomidine

group ($p < 0.05$). The mean time for motor block Bromage grade 3 in Dexmedetomidine group was (2.2 ± 0.55 min) whereas in Clonidine group was (2.7 ± 0.63 min). The difference was statistically significant when study groups were compared ($p < 0.05$). The mean time for return of Bromage score to zero for Dexmedetomidine and Clonidine 247.43 ± 28.53 min and 168.83 ± 51.55 min respectively. Significantly high time was required in return of bromage score to zero in Dexmedetomidine group as compared to Clonidine group ($p < 0.05$) which was statistically significant.

Table 1: Comparison between Group D and C patients according to various study parameters

	Group D	Group C	P value
Onset of sensory block	1 ± 0	1.13 ± 1.64	0.07
Onset of motor block	2.2 ± 0.55	2.7 ± 0.63	0.0005
Duration of sensory block	275.8 ± 31.984	196.667 ± 25.23	0.00000006
Total duration of motor block	247.43 ± 28.538	178.16 ± 25.67	0.0000000004
Two segment regression	100.67 ± 17.798	71.167 ± 23.44	0.00000036
Total duration of analgesia	10 ± 11.26943	10 ± 16.462	00000000000000.76

Significant difference in the VAS scores was observed between Dexmedetomidine and Clonidine which was statistically significant ($P < 0.05$).

Rescue analgesic Diclofenac 75mg was administered I.M at VAS scores of 3 or more. In our study, sedation score was assessed using Ramsay sedation score at regular intervals. 22(73%) patients in group C whereas 16 (53%) patients in group D had sedation score 2, while 12(40%) patients in group D and 4(13%) patients in group C had a sedation score of 1. 1 (3%) patient in group D and 3 (10%) patients in group C had sedation score 3. In group C, 1 patient had sedation score 4 whereas nil in group D. Sedation score was comparable with time period in both the groups.

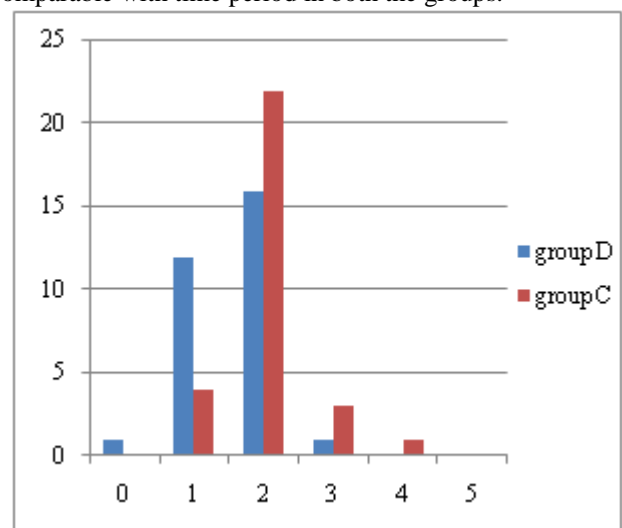


Figure 1: Ramsay sedation score in Group C and D patients

No difference in the pulse rate was observed between Dexmedetomidine and Clonidine ($p>0.05$).

We found that the mean SBP remained at lower levels from 20 min after drug administration till 45 min in dexmedetomidine and clonidine groups. But the overall systolic blood pressure changes were statistically insignificant in both the groups. Also change in mean systolic blood pressure at various intervals from baseline between two groups was statistically insignificant at majority of times ($p>0.05$). Overall diastolic blood pressure

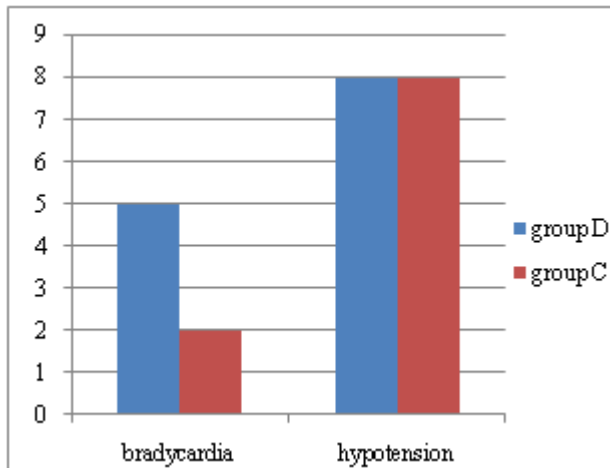


Figure 2: Bar diagram showing incidence of complications in Group C and D

5. Discussion

Early onset of sensory and motor block with Dexmedetomidine + Bupivacaine than Clonidine + Bupivacaine correlated with study of Subhi M Al-Ghanem [6] et al.

Two segment regression time and total duration of analgesia is higher in Dexmedetomidine group than Clonidine group. This result is in accordance with the study of Rampal Singh [7] et al in 2012. They concluded that though both Clonidine and Dexmedetomidine prolonged duration of sensory block of Bupivacaine, Dexmedetomidine is better in terms of longer duration of action. Hala E A Eid [8] et al in 2012 studied dose response study using intrathecal Dexmedetomidine 10mcg & 15 μ g in arthroscopic anterior cruciate ligament reconstruction surgery found that 10 μ g and 15 μ g of intrathecal Dexmedetomidine produces dose dependent analgesia and concluded that 15 μ g dose may be beneficial in patients undergoing prolonged lengthy complex surgical procedures.

Mean regression time to Bromage 0 motor block was significantly higher in Dexmedetomidine group than Clonidine group. This result correlated with study of G. E. Kanazi et al[9] in 2006.

Adjuvants have an additive or synergistic effect secondary to the different mechanisms of action of the local anesthetic and the α_2 -adrenoceptor agonist. The local anesthetic acts by blocking sodium channels whereas the α_2 -adrenoceptor agonist acts by binding to pre-synaptic C-fibers and post-

changes were statistically insignificant in both the groups. ($p>0.05$)

In our study we defined hypotension as a decrease of systolic B.P of more than 30% of baseline, 8 (27%) patients had hypotension in group C and group D. All the patients were treated with one dose of Inj. Ephedrine 3 mg IV each after treating with IV fluids.

Five (17%) patients in Dexmedetomidine group while two (7%) patients in Clonidine group had bradycardia and were treated with a single dose of Inj. Atropine 0.6mg IV.

synaptic dorsal horn neurons. Intrathecal α_2 -adrenoceptor agonists produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. This antinociceptive effect may explain the prolongation of the sensory block when added to spinal anesthetics.

We found that the change in mean heart rate at various intervals from baseline in both groups was statistically insignificant. This finding is in accordance with the study of G.E. Kanazi [9] et al. Rampal Singh et [7] al found 10/30 patients had hypotension in Clonidine group 9/30 patients in Dexmedetomidine group, 4/30 patients in Control group had hypotension which was not statistically significant. Also 6/30 patients in Clonidine group, 2/30 patients in Dexmedetomidine group, 4/30 patients in Control group had bradycardia which was not statistically significant.

Alpha-2 agonists stimulate alpha-2 receptor in brain and spinal cord and inhibit the neuronal firing, which leads to hypotension and bradycardia. All patients in our study were preloaded with 10ml/kg Ringers lactate. This could be the reason why even though patients had decrease in blood pressure, these findings were easily treatable and the results were not statistically significant.

In our study, sedation score was assessed using Ramsay sedation score at regular intervals. Sedation score was comparable with time period in both the groups.

The sedation effect of alpha-2 agonist is postulated to be in the locus ceruleus (a bilateral nucleus that contains many adrenergic receptors) in the brainstem. The locus ceruleus is also the origination site for the descending medullospinal adrenergic pathway, which is known to be a key mechanism in regulating nociceptive neurotransmission.

Our study VAS was at significantly lower levels in Dexmedetomidine group as compared to Clonidine group. Asharaf Amin Mohamed [10] et al in 2012 found that mean VAS score showed a significant reduction immediately postoperatively and at 12 hours postoperatively in Dexmedetomidine group than the control group.

Both Dexmedetomidine and Clonidine activates alpha 2-adrenoceptors in the spinal cord reducing transmission of nociceptive signals like substance P and produces analgesia. Kalso [11] A. reported that as compared to Clonidine, the affinity of Dexmedetomidine to alpha-2 receptors is ten times greater and a much more effective analgesic agent than Clonidine. The rescue analgesic Inj. Diclofenac 75mg

was administered intramuscularly at VAS scores more than 3. None of the patient in the present study required supplementation with General anesthesia.

6. Conclusion

Based on the results obtained of our study, we conclude that the supplementation of Bupivacaine spinal block with intrathecal Dexmedetomidine (10 μ g) and Clonidine (15 μ g) leads to significant faster onset of sensory block and motor block. They also prolong the duration of sensory and motor block than Bupivacaine alone. Dexmedetomidine a newer α -2 agonist seems to be an attractive adjuvant to spinal bupivacaine which provides longer duration of sensory and motor block and post-operative analgesia when compared to clonidine.

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