Original Research Article

Comparative evaluation of intrathecal dexmedetomidine and clonidine as an adjuvant to bupivacaine in gynaecological surgeries

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A R T I C L E   I N F O

A B S T R A C T

Background: Spinal anaesthesia is commonly used in gynaecological surgeries, with Bupivacaine being the most commonly used anaesthetic. Bupivacaine, on the other hand, has a shorter duration of action.
This clinical study was conducted to evaluate the behaviour of intrathecal clonidine and dexmedetomidine as an adjuvant to bupivacaine in augmenting block characteristics in patients undergoing gynaecological procedures.
Materials and Methods: A randomised controlled trial was conducted to compare intrathecal Dexmedetomidine and Clonidine as adjuvant to Bupivacaine in gynaecological surgeries. A total of 200 patients were divided into 100 groups, each randomly assigned to one of two groups, and intrathecal medication was administered according to the group assigned. The onset and duration of sensory and motor blockade, the highest level of sensory blockade, analgesia duration, and side effects were all evaluated.
Results: Although the time of onset of sensory and motor block in the Dexmedetomidine group was comparable to the Clonidine group, the two-segment regression time was higher in the Dexmedetomidine group as compared to the Clonidine group. The motor block onset according to Bromage grade-3 was 4.1 ± 1.1 minutes and 4.42 ± 1.2 minutes among Dexmedetomidine and Clonidine groups. Throughout the perioperative period, the central tendency values of mean arterial pressures and heart rate remained consistent in both groups.
Conclusion: Postoperative analgesia planning and management start from pre-anaesthetic evaluation. So, the analysis revealed that when combined as an intrathecal adjuvant with bupivacaine, dexmedetomidine not only provides better postoperative pain relief than clonidine but also a significantly longer sensory and motor block with preserved hemodynamic stability and lack of sedation.

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1. Introduction

The most commonly used block for lower abdominal, perineum, and lower limb surgery is spinal anaesthesia. Many adjuncts, such as fentanyl, ketamine, tramadol, neostigmine, magnesium sulphate, and others, have been used to extend the analgesic effect of local anaesthetics. Adjuvants used for spinal anaesthesia and local anaesthetics improve the quality of anaesthesia and require less analgesia during the postoperative period. The most common complaint among patients who have undergone surgeries is inadequate pain relief. Inadequate postoperative pain relief may significantly increase recovery time, postoperative complications, and extended hospitalization.[1,2]

Persistent acute postoperative pain is often caused by processes such as inflammation, chronic infection, tumour persistence, and recurrence.[3,4] The release of inflammatory mediators further causes the activation of peripheral

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nociceptors, which transmit nociceptive information to the Central Nervous System. Substance P and calcitonin are also released, causing vasodilation and extravasation leading to nociceptive pain sensations. [5,6]

Clonidine is one of oldest α adrenergic agonists, with an affinity predilection of 200:1 for α-2 versus α-1 receptors, respectively. Clonidine has been shown to significantly increase the duration of anaesthesia produced by hyperbaric or isobaric bupivacaine with good safety profile. [7] Clonidine, as a selective partial α-2 adrenergic agonist, is being evaluated as an adjuvant to intrathecal local anaesthetics without any clinically significant side effects. [8,9]

Dexmedetomidine, like clonidine, is also a highly selective α-2 agonist with a higher affinity for the α-2 receptor and is routinely used as an intravenous sedative drug. Dexmedetomidine exhibits a higher specificity of 1620:1 (α-2: α-1) than Clonidine 220:1. [10,11] Dexmedetomidine functions by inhibiting the release of substance-P from the spinal cord. [12,13] Previous studies have shown that using dexmedetomidine as an intrathecal adjuvant during the perioperative period results in substantially superior and long-lasting intraoperative and postoperative analgesia. [12,14]

In this study, the block characteristics of intrathecal dexmedetomidine and clonidine as adjuvants to bupivacaine in gynaecological surgeries were compared.

2. Materials and Methods

A randomized control study was done among patients undergoing gynaecological surgeries with a subarachnoid block at a tertiary care hospital. The study duration was two years. The institutional scientific and ethical committees approved the study.

A total of 200 female patients of ASA 1/II and age group of 30 to 60 years with no comorbidities and posted for gynaecological surgeries (abdominal hysterectomy, vaginal hysterectomy, tubal ligation, laparotomy for ovarian mass/cyst, cystocele repair, vault repair, sling surgeries) of duration not > 3 hrs were included in this study. Patients taking drugs for long-term illness, pregnant women, obese people, people with a history of spine abnormalities or past spine surgeries, and people with blood disorders were excluded from the study. Additionally, patients with known allergies to the trial medications or local anaesthetics were also excluded from the participation.

A table of random numbers was used to divide the patients into two groups at random. Group BD: N = 100, Dexmedetomidine 10 μg and hyperbaric Bupivacaine 0.5%. Group BC: N =100, Clonidine 45 μg and hyperbaric Bupivacaine 0.5%. The drugs were given along with Bupivacaine intrathecally. Normal saline was used to dilute the Group BD and BC volumes to 3.5 ml.

Following pre-anaesthetic evaluation, the patients were fasted overnight the day before surgery. An intravenous line was placed in the pre-operative procedural room prior to surgery, and all patients were given 10 to 20 ml per kg body weight of ringer lactate over 15 to 25 minutes. Meanwhile, baseline ECG, oxygen saturation, and non-invasive blood pressure measurements were taken. All patients were given spinal anaesthesia under all aseptic precautions using 25 or 26 G Quincke Babcock spinal needles in the lateral position in L3-L4. The time of subarachnoid block was considered as the study's zeroth time; subsequent measurements were taken only from the zeroth time. The anaesthesiologists performing the block recorded the intra-operative data and an anaesthesia resident followed the patients post-operatively until discharged from the post-anaesthesia care unit (PACU). Both were blind to the group to which the patient was allocated. The level of sensory and motor blockades in either case was assessed intra-operatively at 5,10,15, 20 and 30 min, and then every 15 min until discharge from the PACU. For sensory, pinprick sensation by 25 G sterile hypodermic needle was used from the onset of block and dermatomes were tested every one minute for the first 5 minutes and then at 5 min interval till it is fixed. The motor level was assessed according to the modified Bromage scale: [15] Bromage 0, the patient is able to move the hip, knee and ankle; Bromage 1, the patient is unable to move the hip, but is able to move the knee and ankle; Bromage 2, the patient is unable to move the hip and knee, but is able to move the ankle; Bromage 3, the patient is unable to move the hip, knee and ankle. The times to reach the T6 dermatome, the highest dermatomal level (peak sensory level), a two-dermatome regression and regression to the S1 dermatome were recorded. The Ramsay sedation scale assessed the sedation of intraoperative and postoperative every 10 minutes throughout the surgical procedure. From the time of the block, HR, mean arterial blood pressure (MAP) and oxygen saturation were monitored and recorded every 5 minutes for 30 minutes; then at 15min up to 120 min and at 30 min interval thereafter till end of surgery and in PACU till 2 hrs. Ephedrine and Atropine were administered intravenously in the proper doses if there were any hemodynamic abnormalities during the perioperative period, such as bradycardia or hypertension.

Pain was assessed every 1hr until discharge from the PACU using a 100-mm visual analogue score (VAS: 0—100) till first six hrs or need of first rescue analgesia. Rescue doses of analgesics (VAS > 30/100) were recorded. The rescue analgesics consisted of intravenous paracetamol and tramadol. Patients who developed intra-operative or post-operative nausea or vomiting were recorded.

SPSS 21 version was used to do the statistical analysis. Results were expressed as the means and standard deviations, medians and ranges, or numbers and percentages. A chi-square test was used to compare the categorical data between the two groups, and a student

t-test was used to determine the significance of research parameters on a continuous scale between two groups. Throughout, two-tailed p values were utilised, and a p value of 0.05 was considered statistically significant. A sample size of 100 patients per group was determined using power analysis (α error 0.05; β error 0.80) to detect a 30-minute increase in the time of two-dermatome sensory regression.

3. Results

The current study had Groups BD and BC comparable, and there was no significant difference between the two groups in terms of basic demographic and anthropometric characteristics. (Table 1)

Table 2 demonstrated that the onset of sensory and motor block was nearly comparable(3.2 ±0.7min vs 2.92 ±0.5min) in both the Dexmedetomidine group (BD) and Clonidine group (BC). The two-segment regression took more time in the Dexmedetomidine group compared to the clonidine group. The total time required for two segment regression was 139±10 minutes and 107±13minutes, respectively, which was statistically significant. Similarly, the onset of the motor block based on Bromage grade 3 was 4.1 ±1.1minutes and 4.42 ±1.2minutes among Dexmedetomidine and Clonidine groups and this was non-significant. Over the course of the perioperative and postoperative periods, the mean arterial pressure and heart rate data were consistent.

According to the Ramsay scale, the sedation score for both groups was lower and restricted to grade 3. In comparison to the Clonidine group, the period for postoperative analgesia was much longer in the Dexmedetomidine group. (534 ±28min vs 349 ±36min). The rescue analgesia was rarely used in the Dexmedetomidine group compared to the Clonidine group. The patients were hemodynamically stable in both groups, and there were no side effects. Throughout the intraoperative and post-operative periods, the mean values of mean arterial pressure and HR were comparable between the two groups (Figures 1 and 2). None of the patient experienced respiratory distress at any point of time. All patients had SpO_2 levels greater than 96% at all times and did not require additional oxygen in the PACU.

Mean VAS Scores postoperatively at 1 and 2 hr postoperatively was non-significant and patient complained of no significant pain. VAS score in BD and BC group at 3 hr was 1.45 ±0.35 vs 2.03 ±0.55 and it was statistically significant and remained significant up till 6th hour postoperatively where mean VAS score was 2.76 ±0.73 in Group BD and was 3.46 ±0.50 which was significant with p value <0.0001.
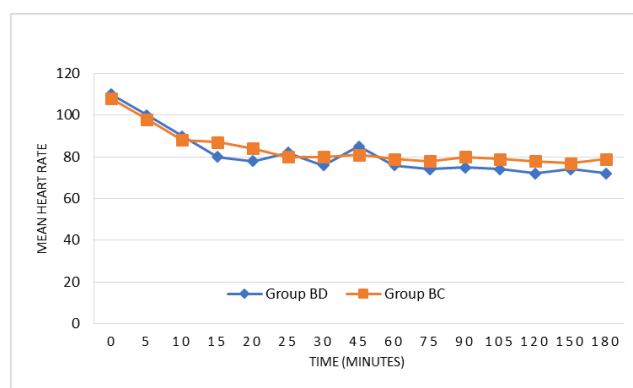

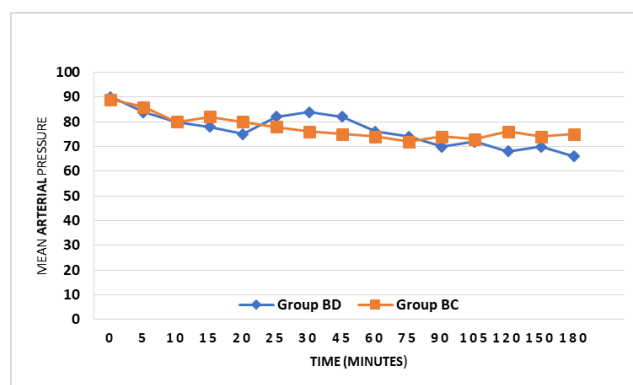**Fig. 1:** Heart rate values versus time

Fig. 2: Mean arterial pressure versus time

4. Discussion

Pain relief is one of the primary goals of anaesthesia. Because of their technical skill and pharmacological knowledge, anaesthesiologists are in a paradigmatic position to treat pain during the intraoperative and postoperative period. The goal of good postoperative analgesia is to produce perennial, long-lasting, continuous effective analgesia with minimal side effects. Spinal anaesthesia is used for the majority of gynaecological surgeries. The results of using hyperbaric Bupivacaine alone in terms of analgesia quality during the postoperative period are unsatisfactory. As a result, adjuvant-like dexmedetomidine and clonidine, combined with intrathecal bupivacaine, provide a reliable and predictable method for prolonging the duration of anaesthesia with prolonged postoperative analgesia.

Clonidine has been the subject of the majority of clinical experience with intrathecal $\alpha 2$ adrenoreceptor agonists.[7–9,16] The intrathecal dose of dexmedetomidine chosen for our study was based on previous human studies in which no neurotoxic effects were observed.[17,18]

Shagufta Naaz et al.[19] used $10\mu g$ dexmedetomidine intrathecally as an adjuvant to hyperbaric Bupivacaine, they found that there was significant prolongation of analgesia

Table 1: Showing the demographic and anthropometric distribution among dexmedetomidine and clonidine groups

Variable	Group BD (Dexmedetomidine)	Group BC (Clonidine)	P value
Age (in Years)	35.2 ± 2.5	38.2 ± 2.9	0.691
Weight (in Kg)	55.2 ± 1.2	59.6 ± 1.2	0.502
Height (in metre)	5.4 ± 0.2	5.5 ± 0.3	0.518
ASA I: II	20: 7	21: 8	0.742
Duration of Surgery (min)	150 ± 40	146 ± 45	0.723

Table 2: Showing the block characteristics among dexmedetomidine and clonidine groups

Variable	Group A (Dexmedetomidine)	Group B (Clonidine)	P value
Onset of Sensory Block (min)	3.2 ± 0.7	2.92 ± 0.5	>0.05
2 Segment Regression time (min)	139 ±10	107 ± 13	<0.001
Onset of Motor Block According to modified Bromage 3 (min)	4.1 ±1.1	4.42 ±1.2	>0.05
Time of Sensory regression to S1(min)	370 ± 32	295 ± 38	<0.001
Regression to Bromage 0 (min)	397 ± 20	274 ± 27	<0.001
Time of Rescue analgesia (min)	534 ± 28	349 ± 36	<0.0001

Table 3: Mean VAS score among dexmedetomidine and clonidine groups

Variable Mean +/- SD postoperatively	Group A (Dexmedetomidine)	Group B (Clonidine)	P value
1st hr	0	0	NS
2nd hr	0.47 ± 0.49	0.52 ±0.37	0.152
3rd hr	1.45 ± 0.25	2.03 ± 0.55	<0.001
4th hr	1.6 ± 0.43	2.33 ± 0.55	<0.001
5th hr	2.23 ± 0.37	2.85 ±0.71	<0.001
6th hr	2.76 ± 0.73	3.46 ± 0.50	<0.0001

with no side effects. Vidhi Mahendru et al.[20] did a double-blind controlled comparative study using intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine. Their study was very much similar to our study but it involved both sex and limited to lower limb surgeries only. In their study they used 12.5 mg bupivacaine plus 5μg dexmedetomidine and 30μg of clonidine. The mean age was between 35 to 37 years and weight distribution was 63 to 69 kgs among the groups and height varied from 168 to 170 cms., and this was found to be not significant. This was comparable to our study in terms of height, weight and age (all insignificant, p>0.05). The average duration of surgery in the study done by Vidhi Mahendru's et al.[11,20] varied from 93.8 to 110.8 min with standard deviation of 32 to 36 min among the groups and was competitively less than our study (130 ±30min and 125 ±30min among the dexmedetomidine and clonidine group, respectively).

Table 2 shows the block characteristics, time of rescue analgesia, and regression to Bromage zero (0) among dexmedetomidine and clonidine groups. The time taken for two segment regression was 139±10 minutes and 107 ±13minutes, respectively and was statistically significant (p<0.001). This was quite comparable with Vidhi Mahendru

et al.,[20] where the mean time of two segment sensory block regression was 147 ±21min in Group dexmedetomidine and 117 ±22min in Group clonidine (P > 0.0001). The time of sensory regression to S1 was more in the dexmedetomidine group as compared with the clonidine group (370 ±32min vs 295 ±38min, p<0.001). In line with study by Anandani DN et al.,[21] our investigation found that the mean onset time of motor blockage was faster in group dexmedetomidine as compared with the clonidine group (4.1 ±1.1min vs 4.42 ±1.2min). The regression time of motor block to reach modified Bromage zero (0) in our study was 397 ±20min (Group BD) and 274 ±27min (Group BC) and this was comparatively higher than the study of Vidhi Mahendru et al.[20] (275 ±25 min in dexmedetomidine, 199 ±26min in clonidine group). This difference can be easily explained by the higher doses of dexmedetomidine and clonidine used in our study. In a comparative study of dexmedetomidine and clonidine as an adjuvant to intrathecal bupivacaine in lower abdominal surgeries done by Ganesh M, and Krishnamurthy D,[22] the mean sensory onset in Group C (clonidine 30 μg) was 1.4 ±0.5 min, and in Group D (dexmedetomidine 3μg) was 1.2 ±0.4 min. This was found to be statistically significant and also quite fast in comparison to our study (3.2 ±0.7min vs 2.91 ±0.5min) as they used the lesser doses

of both adjuvants resulting in less change in baricity of bupivacaine and hence faster onset. However, mean sensory regression in their study by two segments in Group C was 136.7 ±10.7 min, and in Group D was 136.4 ±11.7min (p=1.0). While in our study it was more in dexmedetomidine group than clonidine group (139 ±10min vs 107 ±13min, p<0.001). This could be explained by the comparatively higher dose of dexmedetomidine in our study. Our results are more in consistent with Vidhi Mahendru et al.[20] where they observed that mean time of two segment sensory block regression was 147 ±21 min in Group BD, 117 ±22min in Group BC (P>0.0001).

In the various studies conducted by Grande et al.,[23] Chabra et al.,[24] and Abdelhamid et al.,[25] all found that group dexmedetomidine produced significantly longer durations of analgesia than group clonidine. These all studies are in consistent with our results for mean VAS score (534 ±28 min vs 349 ±36min). Kalso et al.[26] further argued that Dexmedetomidine has 10 times more affinity to the α-2 receptor than clonidine leading to better and prolonged analgesia, which can be seen in our study too. The fact that mean VAS scores in group BD were consistently lower than those of group BC also suggests that in the group BD, postoperative analgesia was of higher quality and required less rescue analgesia in PACU. These results of our investigation were similar to those of Abdelhamid et al.[25] and Ashraf Amin M et al.[27]

Dexmedetomidine or clonidine in combination with intrathecal bupivacaine did not significantly lower blood pressure during or after surgery in our patients. Intrathecal local anaesthetics lower blood pressure by blocking sympathetic outflow. The doses used for spinal anaesthesia usually result in a sympathetic block that is close to maximum. The near-maximal sympatholysis is not further impacted by the addition of a low dose of an α2-agonist to a high dose of local anaesthetics.[28] Small doses of adjuvants may also be responsible for the lack of sedation observed in any of the study groups.

5. Conclusion

Adjuvants are essential for improved intraoperative and postoperative analgesia.

This also reduces the need for rescue analgesia and has a higher patient acceptance rate. Our findings indicate that, the use of intrathecal dexmedetomidine as an adjuvant to bupivacaine may be a more appealing option than clonidine because its potent intrathecal anaesthetic and analgesic qualities and low risk of adverse effects. We also observed a longer lasting motor and sensory block, stable hemodynamic condition, and high patient satisfaction in the dexmedetomidine group. Dexmedetomidine is better than Clonidine as an adjuvant and must be used regularly in gynaecological surgeries.

6. Source of Funding

None.

7. Conflict of Interest

None.

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