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Comparison of two different doses dexmedetomidine as an adjuvant to bupivacaine in sub-arachnoid block for abdominal hysterectomies: A randomized double blinded study

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ABSTRACT

Background: Abdominal hysterectomy is often a long duration procedure and warrants intense pain relief in the post-operative period. Dexmedetomidine when added to bupivacaine in subarachnoid block prolongs the duration of surgical anaesthesia, decreases blood loss and prolongs duration of post-operative pain relief. **Aims and Objective:** To compare two different doses dexmedetomidine as an adjuvant to bupivacaine in sub-arachnoid block in abdominal hysterectomy surgeries. **Materials and Methods:** 60 patients of age group 30-60 years posted for elective abdominal hysterectomies under American Society of Anaesthesiologists (ASA) physical classification I or II were randomly allocated into 2 groups of 30 each. Group A received 5 micrograms (μg) of dexmedetomidine along with 3.5 ml of 0.5% bupivacaine in sub-arachnoid block. Group B received 10 μg of dexmedetomidine along with 3.5 ml of 0.5% bupivacaine in sub-arachnoid block. Changes in blood pressure, heart rate, respiratory rate, oxygen saturation, ephedrine consumption, blood loss, duration of sensory block, duration of motor block and duration of analgesia were compared between two groups. **Results:** There was no significant difference in change in heart rate, respiratory rate, oxygen saturation, duration of sensory block, duration of motor block between two groups. Patients in group B had significant decrease in blood pressure, blood loss and significant increase in ephedrine consumption compared to Group A. The duration of analgesia was also prolonged in group B compared to Group A. **Conclusion:** Dexmedetomidine in dose of 10 μg is a better adjuvant to bupivacaine in sub arachnoid block for abdominal hysterectomy surgeries.

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INTRODUCTION

Abdominal hysterectomy is one of the major gynaecological procedures which often may take a long duration and also associated with significant blood loss. Subarachnoid block is a safe and cost effective alternative to general anaesthesia in patients subjected for abdominal hysterectomy as it avoids polypharmacy and unwanted side effects such as post operative nausea and vomitting.[1,2] Hyperbaric bupivacaine is being used safely in sub-arachnoid block for abdominal hysterectomy but with limited duration of sensory block, motor block and post operative analgesia. Adjuvants like fentanyl, morphine, clonidine, dexmedetomidine, magnesium, midazolam are used to prolong the duration of sensory block, motor block and analgesia in sub-arachnoid block. Alpha adrenergic blockers like clonidine and dexmedetomidine, compared to other adjuvants effectively prolong the duration of block

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and post-operative analgesia.[3] Among alpha adrenergic agonists dexmedetomidine compared to clonidine is a safe and effective alternative when used as an adjuvant to bupivacaine.[4]

Studies done using different doses of dexmedetomidine have proven that 5 μg and 10 μg are safe doses when used in sub arachnoid block. These doses were associated with minimal hemodynamic alterations. Various studies conducted to determine the optimum dose of dexmedetomidine in sub-arachnoid block for lower abdominal surgeries concluded that dexmedetomidine in dose of 10 μg is a safe and effective dose when used as an adjuvant with bupivacaine.[5, 6, 7] Post operative analgesia is very crucial in abdominal hysterectomies as it helps in early mobilization and decreased incidence of complications such deep vein thrombosis and thrombo embolism. Hence previous studies emphasized more on duration of analgesia and anaesthesia. We have designed this study to analyze the effect of sub-arachnoid dexmedetomidine in hemodynamics and its associated decrease in blood loss during abdominal hysterectomy since blood loss and eventual blood component transfusion is associated with a multitude of complications.

MATERIAL AND METHODS

This study was conducted in a 1000 bedded multispecialty tertiary teaching hospital from August 2016 to November 2016 after getting institute's scientific and ethical committee approval. 60 patients under age group 30-50 years posted for elective total abdominal hysterectomy surgeries for fibroid uterus, categorized in ASA physical classification I or II were randomly allocated into two groups of 30 each using lot method. Exclusion criteria included patient refusal, coagulopathies, local site infection and patients under ASA physical classification III and IV. As the study involves blood loss estimation, patients with hemoglobin less than 10 g/dl were excluded from the study. During pre-operative assessment we have explained the study procedures to the patients and obtained informed consent.

We have selected the sample size based on our aim to compare the effect of two doses of intrathecal dexmedetomidine in total abdominal hysterectomy surgeries. We have compared duration of surgical anaesthesia, post-operative pain relief and total blood loss. We have used Statistical Analysis System (SAS) version 9.0 statistical software to determine the sample size. A sample size of n=30 was arrived for a significance level of 0.05 (α=5%) and a power of 80%. Blinding was done using sealed envelope technique to prevent observer bias.

After shifting the patient to operating room, an 18 gauge intravenous (i.v.) cannula was placed in the forearm and monitors such as pulse oximeter, electrocardiogram and noninvasive arterial blood pressure cuff were placed. The patient was placed in right lateral recumbent position and the skin over lower back was disinfected with 5% povidone iodine solution and draped with sterile linen. After identifying the L3-L4 interspinous space, the skin site was infiltrated with 2 ml of 2% lignocaine. Patients in group A received 5 micrograms (μg) of dexmedetomidine along with 3.5 ml of 0.5% bupivacaine in sub-arachnoid block. Patients in group B received 10 μg of dexmedetomidine along with 3.5 ml of 0.5% bupivacaine in sub-arachnoid block. In our study we used Quincky Babcock type spinal needle of size 25 G (standard wire gauge) for performing sub-arachnoid block. The spinal needle was inserted in L3-L4 interspinous space to obtain a cerebrospinal fluid tap. After confirming the proper placement of the needle by aspiration of cerebrospinal fluid, the drug was injected. Success of the block was assessed with the onset of sensory block using the pinprick test. Parameters such as heart rate, mean arterial blood pressure, oxygen saturation (spo_2) were monitored and recorded at 5 minutes intervals. Duration of sensory blockade, motor blockade, total ephedrine consumption, blood loss and post operative analgesia were recorded by blinded qualified anaesthesiologists.

Blood loss was estimated based on the techniques recommended by previous studies.[8] We have weighed all the dry as well as wet abdominal pads and gauze pieces before and after use in surgical field using a sterile electronic weighing machine. The difference of weight was calculated. The blood loss estimation was done with this difference of weight. 1 ml of blood is equivalent to 1 gram by weight.[9] Intra-operatively blood transfusion was done based on standard maximum allowable blood loss (MABL) and not on target haemoglobin.

Statistical analysis

It was performed using Statistical Package for Social Sciences (SPSS) version 22.0 software for windows (SPSS Inc, Chicago, USA). Changes in heart rate, mean arterial pressure, spo_2 over time between two groups were analyzed using Levene's test for equality of variances. Duration of sensory blockade, motor blockade, total ephedrine consumption, total blood loss and post operative analgesia were compared between two groups using Student's 't' test. A 'p' value of ≤ 0.05 was considered statistically significant.

RESULTS

We have conducted this study with 60 patients, divided into two groups of 30 each and used their data for statistical

analysis. There were no statistically significant differences regarding mean age, weight, and ASA classification in the two study groups.

There was no statistical significance in mean age between two group (Table 1).

There was statistically significant decrease in mean heart rate in Group B compared to Group A ('p' value = 0.0003 [<0.05]) (Table 2).

There was statistically significant decrease in mean of mean blood pressure in Group B compared to Group A ('p' value = 0.0078 [<0.05]) (Table 3).

There was no statistically significant changes in mean Spo_2 in Group B compared to Group A ('p' value = 1.000 [>0.05]) (Table 4).

There was no statistically significant difference in duration of sensory blockade between two groups. ('p' value = 0.6936 [>0.05]) (Table 5).

Table 1: Mean age of study group

Group	N	Mean	S.D	S.E.M	P value
Group A	30	46.3	14.5700	2.6601	0.1140
Group B	30	41.6	6.7190	1.2267	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 2: Change in mean heart rate (beats per minute) over time between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	77.600	9.5217	1.7384166	0.003
Group B	30	68.200	9.3307	1.7035450	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 3: Change in mean of mean blood pressure (mm of Hg) over time between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	84.700	10.6387	1.9423520	0.0078
Group B	30	78.300	6.9736	1.2730898	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 4: Change in Spo_2 (%) over time between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	99.300	1.0222	0.1866273	1.000
Group B	30	99.300	1.2077	0.2204948	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

There was no statistically significant difference in duration of motor blockade between two groups. ('p' value = 0.1044 [>0.05]) (Table 6).

There was statistically significant prolongation of post-operative analgesia in group B compared to group A. ('p' value = 0.0038 [<0.05]) (Table 7).

There was statistically significant increase in total ephedrine consumption in group B compared to group A. ('p' value = 0.0069 [<0.05]) (Table 8).

There was statistically significant decrease in blood loss in group B compared to group A. ('p' value = 0.002 [<0.05]) (Table 9).

There was statistically significant but clinically insignificant and manageable decrease in heart rate and blood pressure in group B compared to group A. There was statistically significant increase in ephedrine consumption in group B

Table 5: Comparison of duration of sensory blockade (minutes) between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	351.500	63.4381	11.5821595	0.6936
Group B	30	358.500	73.1690	13.3587706	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 6: Comparison of duration of motor blockade (minutes) between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	305.500	62.0532	11.3293125	0.1044
Group B	30	336.500	82.1285	14.9944527	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 7: Comparison of duration of post-operative analgesia (minutes) between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	459.000	68.7299	12.5481412	0.0038
Group B	30	515.500	75.9917	13.8741228	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 8: Comparison of total ephedrine consumption (milligrams) between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	4.800	5.3201	0.9713129	0.0069
Group B	30	9.000	6.2533	1.1416912	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

Table 9: Comparison of total blood loss (milliliter) between two groups

Group	N	Mean	S.D	S.E.M	P value
Group A	30	354.000	144.6625	26.29154165	0.002
Group B	30	180.500	72.3229	13.15429458	

N: Number of patients in the group, S.D: Standard deviation, S.E.M: Standard error of mean

compared to group A. But the total blood loss in group B was significantly low compared group A. Moreover there was significant prolongation of duration of post operative analgesia in group B compared group A.

DISCUSSION

Abdominal hysterectomy is a common gynaecological surgical procedure done for conditions like fibroid uterus, dysfunctional uterine bleeding and uterine malignancy. This lower abdominal surgery is associated with significant blood loss and severe post-operative pain.[2] Total abdominal hysterectomies can be performed under general anaesthesia and regional anaesthesia.[1] Commonly performed regional anaesthetic techniques for lower abdominal surgeries are sub-arachnoid block and epidural analgesia. Regional anaesthetic techniques are cost effective, provide better post-operative pain relief, decreases intra operative blood loss and minimizes incidence of post operative vomiting.[10] Sub-arachnoid block compared to epidural anaesthesia are cost-effective and less time consuming.

Adjuvants like opioids, neostigmine, *a*2 adrenergic agonists, benzodiazepines and magnesium are used with hyperbaric local anesthetics to prolong the duration of surgical anaesthesia and post operative pain relief.[11-13] Among these adjuvants, *a*2 adrenergic agonists have lesser incidence of post operative nausea and vomiting.[14] Intrathecal *a*2- adrenergic agonists produces analgesia by, inhibiting the release of substance P, and hyperpolarizing post-synaptic dorsal horn neurons and there by inhibiting the release of C-fiber transmitters.[15] Clonidine and dexmedetomidine are commonly used *a*2 adrenergic agonists.[16] Intrathecal clonidine is known for severe hypotension and bradycardia.[17] Compared to clonidine, dexmedetomidine produces optimal hypotension which decreases blood loss during major abdominal surgeries like hysterectomies.[18,19] One study conducted with different doses of intrathecal dexmedetomidine (5 μg, 10 μg, 15 μg and 20 μg) as an adjuvant to assess duration of sensory block, motor block and duration of pain relief concluded that 5 μg and 10 μg are optimal doses.[5]

In this study we have compared two doses of dexmedetomidine 5 μg and 10 μg as an adjuvant to hyperbaric bupivacaine in sub arachnoid block for abdominal hysterectomies. Earlier studies have compared the duration of surgical anaesthesia and duration of post operative pain relief using intrathecal dexmedetomidine.[20] Dexmedetomidine causes decrease in blood loss which is secondary to hypotension. Since blood loss is one of the important complication in hysterectomy, in our study we wanted compare the blood loss in abdominal hysterectomies when two doses of intrathecal dexmedetomidine (5 μg and 10 μg) are used as adjuvants. We have fixed this dose based on previous studies.[6,7] We have chosen 60 patients with fibroid uterus planned for hysterectomy. Two groups of 30 each, group A and group B received 5 μg and 10 μg intrathecal dexmedetomidine respectively as adjuvants. Patients with dysfunctional uterine bleeding will be on hormonal therapy which increases bleeding during surgery. Hence we have excluded those patients from our study to prevent bias.

We have compared heart rate, blood pressure, spo_2, duration of sensory block, duration of motor block, duration of post operative analgesia, blood loss and total ephedrine consumption between two groups. There was no statistically significant difference in duration of sensory block and motor block between two groups. There was statistically significant decrease in heart rate (mean=68.2) and mean blood pressure (mean=78.3) in group B compared to group A which was clinically not significant and easily manageable. Ephedrine in increments of 5 mg was used to treat hypotension. There was statistically significant increase in ephedrine in group B (mean=9.0) compared to group A (mean=4.8) which again was clinically not significant. There was both statistically and clinically significant decrease in blood loss in group B compared to group A. There was also statistically significant prolongation of post operative pain relief in group B compared to group A. Dexmedetomidine in 10 μg dose significantly decreases blood loss during abdominal hysterectomy. In our study we have taken patients with fibroid uterus alone for analysis. In future studies, sub-arachnoid as well as epidural dexmedetomidine in different doses can be tried in patients with dysfunctional uterine bleeding and uterine malignancy planned for abdominal hysterectomy to decrease the surgical bleeding.

CONCLUSION

Dexmedetomidine in dose of 10 μg is a better adjuvant compared to dose of 5 μg when used along with hyperbaric bupivacaine in sub-arachnoid block. This dose significantly decreases blood loss without much compromise on hemodynamics and prolongs the duration of post-operative pain relief.

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Authors Contribution:
RKP - Concept and design of the study, preparation of the manuscript; **AR -** Collection of data, statistical analysis and reviewed the literature.

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