EFFECT OF INTRATHECAL HEAVY BUPIVACAINE WITH DEXMEDETOMIDINE AND INTRATHECAL HEAVY BUPIVACAINE WITH FENTANYL IN LOWER ABDOMINAL AND GYNAECOLOGICAL SURGERIES

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ABSTRACT

Objective: Spinal or epidural anesthesia techniques provide the best method of anesthesia for lower abdominal and lower limb surgeries. Small doses of adjuvants administered spinally provide profoundly prolonged segmental analgesia with good post-operative pain relief. The objective of the present study is to evaluate the efficacy of dexmedetomidine (10 µg) versus fentanyl (25 µg) as an adjuvant added to bupivacaine in spinal anesthesia for patients undergoing lower abdominal and gynecological surgeries and assessment of duration of post-operative analgesia.

Methods: Hospital-based randomized double-blind controlled study conducted in tertiary teaching hospital of Kakinada and Rajahmundry. The period of study is February 2013–July 2018. Patients were divided into two groups of 25 each. In the first group, dexmedetomidine was added as adjuvant to bupivacaine whereas in the second group fentanyl was added as an adjuvant to bupivacaine. The visual analog scale used to assess the analgesic effect. Time at which the rescue analgesic given was noted which gives the duration of post-operative analgesia.

Results: Results were analyzed in both groups. The software used for statistical analysis was GraphPad for windows 10.0.5. Continuous variables were analyzed with student t-test and analysis of variance. Post-operative analgesia duration is significantly prolonged in the dexmedetomidine group with a mean 308.64 ± 12.50 compared to fentanyl group where the mean is 253.12 min± 14.30. There is a statistically significant difference ($p < 0.0001$) between the two groups.

Conclusion: Intrathecal dexmedetomidine supplementation to spinal bupivacaine seems to be a good alternative to intrathecal fentanyl since it produces prolonged post-operative analgesia with minimal side effects and excellent quality of spinal analgesia.

Keywords: Spinal anesthesia, Adjuvants, Post-operative analgesia, Visual analog scale, Intrathecal route.

INTRODUCTION

Most commonly used technique for lower abdominal surgeries is spinal anesthesia, as it is very economical and easy to administer [1]. While giving spinal anesthesia, various adjuvants have been used generally to reduce the intraoperative visceral and somatic pain, thereby providing prolonged post-operative analgesia. Dexmedetomidine has been in use as an adjuvant along with local anesthetics to provide analgesia during and after the period of spinal analgesia. The cost of general anesthesia, the skill and specialized equipment needed for its administration coupled with an indifferent supply of anesthetic gases and drugs and lack of monitoring equipment especially in peripheral areas in a country like India made regional anesthetic techniques as choice because they are relatively inexpensive and easy to administer.

The spinal route has gained immense popularity in surgeries involving lower abdominal and gynecological procedures. Spinal anesthesia provides profound muscular relaxation, which is ideal for intra-abdominal and gynecological procedures decreasing intraoperative blood loss and consequent complications [2]. It is currently believed that spinal or epidural anesthesia techniques provide the best method of anesthesia for lower abdominal and lower limb surgeries in patients having poor ventilatory performance.

New trends in the subarachnoid block are the use of adjuvants [3], which reduce the nature of complications as well as to improve the anesthetic effects. These solutions cause analgesia of different duration with variable latent periods and different dissemination times under clinical conditions. The solutions can be chosen for various procedures depending on the time of analgesia needed, the dermatomes which require to be anesthetized and also the depth of analgesia required.

Various adjuvants that can be added to local anesthetics and administered intrathecally are fentanyl, dexmedetomidine, clonidine, benzodiazepines, etc. The main objective of using spinal adjuvant is to obtain a reduction in dose of spinal anesthetic that results in effective analgesia with fewer side effects [4]. Small doses of adjuvants administered spinally provide profoundly prolonged segmental analgesia with good post-operative analgesia.

Dexmedetomidine is now being used adjuvant along with spinal anesthesia and is a highly selective α_2-agonist. It provides a good quality of intraoperative and prolonged post-operative analgesia with minimal side effects. Reports from earlier human studies suggest that intrathecal 10 µg dexmedetomidine would produce more post-operative analgesic effect along with bupivacaine in spinal anesthesia with very few side effects. The objective of the present study is to compare the efficacy of intrathecal bupivacaine with dexmedetomidine and intrathecal bupivacaine with fentanyl in patients undergoing lower abdominal and gynecological surgeries.

METHODS

Study design
The study was a randomized, double-blind and controlled study of the effect of intrathecal bupivacaine with dexmedetomidine and intrathecal bupivacaine with fentanyl in patients undergoing lower abdominal and gynecological surgeries.

Source of data
This study was carried out in the department of anesthesiology of a tertiary care teaching hospital of Kakinada and Rajahmundry from February 1, 2013, to July 31, 2018, for a period of 5 1/2 years.

Ethical statement
The study proposal was presented in front of the Institutional Ethics Committee. The study was approved by the Institutional Ethics Committee. The Ethics Committee Approval number is IRBC/RMC/176/02/12/176.

Method of collection of data
A total number of 50 patients, 25 in each group undergoing lower abdominal and gynecological surgeries were selected for study; patients were allocated randomly to each group by lottery method. Patients were taken in to study after taking written informed consent.

Patients belonging to both the sexes and age 18–60 years of the American society of Anesthesiologists (ASA) Grades I and II are included in the study. Patients with hepatic or renal dysfunction, having a history of sensitivity to these two drugs, or those having a local infection at the site of injection or were excluded from the study. At the end of the study, all data are compiled and statistically analyzed using diagrammatic representation, descriptive data presented as mean±standard deviation (SD), continuous data are analyzed by paired student "t" test and analysis of variance (ANOVA).

During pre-operative visit patient's detailed history, general physical examination and systemic examination were carried out. Basic demographic data such as age, sex, height, and weight were recorded. During the pre-anesthetic check-up, linear visual analog scale (VAS) was explained to all patients using a 10 cm scale. All the patients were premedicated with Inj. Midazolam 0.05 mg/kg I.M 45–60 min before the procedure.

Procedure
The pulse rate, blood pressure, and respiratory rate were recorded before starting the case. Peripheral venous cannulation was done with 18G IV cannula and all the patients were preloaded with 10 ml/kg of Lactated Ringer's solution. The patients were placed in either right or left the lateral position or in sitting position and under strict aseptic precautions, lumbar puncture was carried out in midline using 25G Quincke–Babcock's needle through L3-L4 interspace.

After the appearance of cerebrospinal fluid, the drug was injected into the subarachnoid space according to their group and was turned to the supine position. Group A, n=25 were given 2.5 ml (12.5 mg) of 0.5% hyperbaric bupivacaine with 10 μg dexmedetomidine. Group B, n=25 were given 2.5 ml (12.5 mg) of 0.5% hyperbaric bupivacaine with 25 μg of fentanyl.

Vital signs such as pulse rate, blood pressure, respiratory rate, and SPO_2 were monitored every 1 min in the first 3 min, every 3 min up to 30 min and every 10 min until the end of the procedure and were noted in the pro forma.

Level of sensory block was assessed by pinprick, and the onset of the blockade was noted. Intraoperatively no narcotics or analgesics were administered, and if administered, the patients were excluded from the study.

In both the groups, the time of injection was recorded as zero hour, and the following parameters are observed intraoperatively. They are the onset of sensory blockade, onset of motor blockade, and post-operative analgesia duration. The side effects during the course of anesthesia were observed and recorded.

If there was any fall in blood pressure, intravenous fluids were rushed, and if the fall was more than 30% below, the baseline value Inj. Ephedrine was given in titrated doses. If the pulse rate was <60/min, Inj. Atropine 0.6 mg I.V was given. If the respiratory rate was below 10/min, respiratory depression was diagnosed. Side effects such as headache, nausea, vomiting, pruritus, urinary retention, and respiratory depression are noted in both the groups. At the end of surgery, the patient was shifted to post-operative ward. Patients were monitored at 30 min, 1 h, 2 h, 4 h, 8 h, 12 h, and 24 h postoperatively, and VAS scores were noted along with vital parameters.

The time at which rescue analgesic was given is noted which is taken as duration of post-operative analgesia. Rescue analgesic used was Inj. Tramadol 100 mg i.m. Rescue analgesia was administered when the VAS score was more than 4 in the post-operative period.

Statistical analysis
The software used for statistical analysis was GraphPad for windows 10.0.5. Continuous variables were analyzed with student t-test, ANOVA. Other parameters were analyzed by descriptive statistics as percentages. At the end of the study, all data are compiled and statistically analyzed using diagrammatic representation, descriptive data presented as mean±SD, continuous data are analyzed by paired student "t" test and ANOVA.

OBSERVATION AND RESULTS

Results were analyzed in both the groups based on various parameters such as age, sex, ASA grade, types of surgery, onset of sensory and motor blockade, post-operative analgesia duration, and side effects experienced in both the groups.

Age distribution
Age distribution in Group A was from 18 to 60, whereas the age distribution in Group B was 19–60. The mean age in Group A was 39.96 with SD 11.46, whereas in Group B it was 39.32 with SD 11.27.

Table 1 shows age distribution. Both groups were comparable in terms of age distribution.

Sex distribution
Table 2 shows sex distribution. Both groups were comparable in terms of sex distribution.

Surgical procedures
Table 3 shows types of surgical procedures. Both groups are comparable with respect to the types of surgical procedures.

Table 1: Age distribution in Group A

Age in years	Group A
18–30	6
31–45	11
46–60	8
Total	25
Mean±SD	39.96±11.46

SD: Standard deviation

Table 2: Sex distribution in various groups

Sex	Group A	Group B	Total
Male	14	13	29
Female	11	12	21
Total	25	25	50

ASA grade

Table 4 shows the distribution of ASA grade. Both the groups are similar with respect to ASA Grade as well as are evident by the statistics below.

Intraoperative parameters

Onset of sensory blockade

Fig. 1 shows the difference in onset of sensory blockade between two groups. The onset of sensory blockade was faster in Group A (dexmedetomidine group) compared to Group B (fentanyl group). The onset of the blockade in dexmedetomidine group is with a mean of 1.98 min with a standard deviation of 0.27 compared to fentanyl group where it was 2.78 min with a standard deviation of 0.26 which is significant statistically with p<0.01.

Onset of motor blockade

Fig. 2 shows the difference in onset of motor blockade between two groups. The onset of motor blockade was faster in Group A (dexmedetomidine group) compared to Group B (fentanyl group). The onset of the blockade in dexmedetomidine group is with a mean of 4.68 min with a standard deviation of 0.31 compared to fentanyl group where it was 5.72 min with a standard deviation of 0.58 which is significant statistically with p<0.01.

Post-operative analgesia duration

Fig. 3 shows the difference in duration of post-operative analgesia. Post-operative analgesia duration is taken as the time from spinal injection to the time of administering rescue analgesic in the post-operative period. This is significantly prolonged in dexmedetomidine group with a mean value of 308.64 min with a standard deviation of 12.50 min compared to fentanyl group where it is 253.12 min with a standard deviation of 14.30. The statistical analysis by "t" test showed that there is a statistically significant difference.

The association is highly significant statistically with p<0.001

Side effects

Table 5 shows the incidence of side effects in two groups. The side effects most commonly observed are hypotension and bradycardia, which are seen commonly with regional anesthesia. Respiratory

depression, which is a feared side effect of opioids, is not observed in any patient belonging to either group. Pruritis is observed in two cases of fentanyl group which resolved spontaneously without any need for medication. Urinary retention is not observed as the patients are routinely catheterized. Nausea and vomiting were not observed in any patient in either group.

DISCUSSION

This study deals with the efficacy of dexmedetomidine 10 μg combined with 0.5% hyperbaric bupivacaine in providing post-operative analgesia compared to the fentanyl 25 μg combined with 0.5% hyperbaric bupivacaine, in lower abdominal surgeries by the intrathecal route. Both fentanyl and dexmedetomidine improved the quality of intraoperative analgesia and diminished the risk of supplementation of general anesthesia.

Fentanyl is an opioid analgesic generally used for pain relief together with other medications for anesthesia. It is 100 times more potent than morphine. Intrathecally, fentanyl exerts its effect by combining with opioid μ receptors in the dorsal horn of the spinal cord and may have
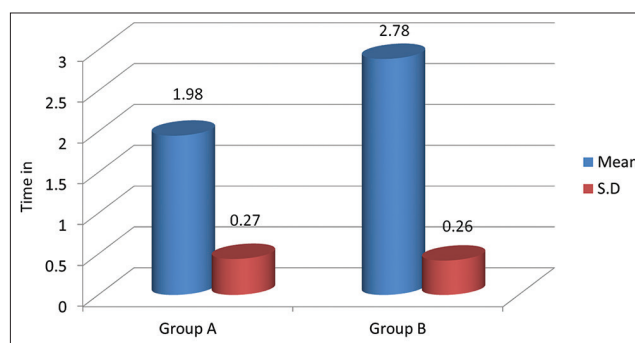
Table 3: Surgical procedure used in various groups

Name of surgery	Group A	Group B
Hysterectomy	9	9
B/L hernioplasty	6	5
TURP	5	6
Others	5	5

Table 4: As a grade in two groups

Grade	Group A	Group B	Total
I	22	21	43
II	3	4	7
Total	25	25	50

Table 5: Side effects as seen in the two groups

Side effects observed	Group A	Group B
Headache	0	0
Nausea and vomiting	1	1
Respiratory depression	0	0
Hypotension	4	3
Bradycardia	9	6
Pruritus	0	2
Neurological deficits	0	0
Others	0	0

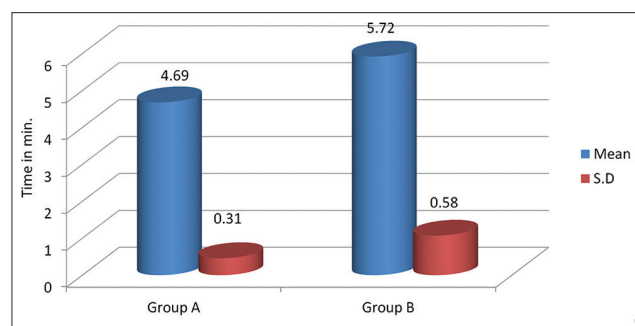**Fig. 1: Figure representing the onset of sensory blockade**

Fig. 2: Figure representing the onset of motor blockade

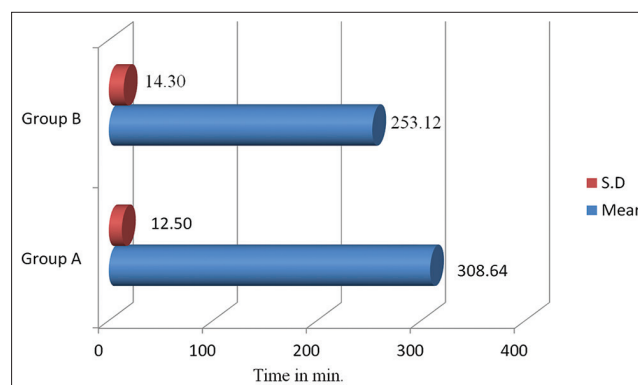**Fig. 3: The duration of post-operative analgesia**

a supraspinal spread and action [5]. Pain is frequently encountered during surgery on the female genital organs under spinal local anesthetics, intrathecal fentanyl when added to spinal local anesthetics reduces significantly visceral and somatic pain, and this analgesic effect has been proved by many studies [6].

Intrathecal fentanyl prolongs the duration of spinal anesthesia produced by bupivacaine and lignocaine, and this effect has been shown in obstetric and non-obstetric patients undergoing various surgeries [7]. The prolongation of the duration of spinal analgesia produced by intrathecal fentanyl is not a dose related [8].

Seewal *et al.* [8] found a significant improvement in the duration and quality of analgesia produced by intrathecal fentanyl and bupivacaine compared to intrathecal bupivacaine alone, meanwhile, the author found no further increase in the duration of analgesia when the dose of fentanyl was increased from 10 µg to 20, 30, or 40 µg. Kuusniemi *et al.* [9] reported that different durations of spinal anesthesia were related to different doses of spinal bupivacaine supplemented with 25 µg fentanyl in patients undergoing urological procedures.

In non-obstetric patients, studies demonstrated that a dose of 25 µg fentanyl for supplementation of spinal anesthesia produces the excellent quality of perioperative analgesia [10]. Based on the findings of the above studies, fentanyl in a dose of 25 µg was used for supplementation of spinal bupivacaine, which was found to be effective in the present study also.

Dexmedetomidine is a highly selective α_2-adrenoreceptor agonist approved as intravenous sedative and adjuvant to anesthesia. Dexmedetomidine when used intravenously during anesthesia reduces opioid and inhalational anesthetics requirements [11]. De kock *et al.* [11] recommended a dose of 15–45 µg clonidine for supplementation of spinal anesthesia since this dose effectively prolongs the duration of the spinal block with minimal sedation and side effects.

In a study conducted by Kanazi *et al.* [12] 3 µg dexamethasone (DXM) or 30µg clonidine along with spinal bupivacaine resulted in the same duration of sensory and motor block in urologic surgical patients and the side effects are very less. From Kanazi study and other animal studies, we assumed that 3–5 µg DXM would give equal results as 30–45 µg clonidine when used for supplementation of spinal bupivacaine.

Compared with clonidine, a α_2-adrenoreceptor agonist, the affinity of dexmedetomidine to α_2 receptors has been reported to be 10 times more than clonidine [12]. Moreover, Kalso *et al.* [13] and Post *et al.* [14] reported a 1:10 dose ratio between intrathecal dexmedetomidine and clonidine in animals.

Many studies in surgical patients showed that intrathecal clonidine increases the duration of the sensory and motor spinal block when added to spinal anesthesia and this effect of clonidine is dose-dependent [15], and higher doses of intrathecal clonidine are accompanied by excessive sedation, hypotension, and bradycardia. Intrathecal dexmedetomidine when combined with spinal bupivacaine prolongs the sensory block by depressing the release of C-fibers transmitters and by hyperpolarization of pos-synaptic dorsal horn neurons [16-18].

In the present study, the intrathecal dexmedetomidine and bupivacaine block have resulted in significantly less side effects than intrathecal fentanyl and bupivacaine block. The most significant side effects reported about the use of intrathecal α_2-adrenoreceptor agonists are bradycardia and hypotension, in the present study; these side effects were not significant probably because we used a small dose of intrathecal dexmedetomidine which was confirmed by the findings of Kanazi report.

Hypotension and bradycardia were more in the dexmedetomidine group than in the fentanyl group, but it did not reach a significant difference in

the present study. Pruritus reported after intrathecal fentanyl is around 40–70%, but it is very less comparatively in the present study.

Avoidance of respiratory depression in the patients who were administered dexmedetomidine was one of the most remarkable observations, and the evidence is similar to the earlier studies where researchers have found a complete absence of respiratory depression with the same drug [19]. In addition, we found that the onset of sensory block to reach T10 dermatome was shorter with the usage of dexmedetomidine in a dose-dependent manner [20]. Opioids as epidural adjuvants to LA improve the quality of the block and provide a dose-sparing effect [21].

In 2002, Dr. B.N.B *et al.* conducted a study on intrathecal opioids using intrathecal fentanyl with hyperbaric bupivacaine during cesarean delivery for post-operative analgesia. They concluded that intrathecal opioid fentanyl improves intraoperative anesthesia and reduced the demand for post-operative analgesia with good maternal satisfaction and fetal well-being.

From 1990 to 1996, Dr. Kenneth *et al.* conducted a study for 7 years regarding the safety and efficacy of intrathecal opioid analgesia for acute post-operative pain on 5969 surgical patients. They concluded that intrathecal opioids provided highly satisfactory post-operative analgesia and was rated by patients as being >85% effective during the first 24 h after surgery.

In 2008, Al-Mustafa *et al.* conducted a study on the addition of dexmedetomidine to intrathecal bupivacaine in urologic surgeries. They concluded that intrathecal dexmedetomidine when used as adjuvant to intrathecal bupivacaine-prolonged duration of spinal anesthesia and also reduced the need for post-operative analgesics. In 2010–2011, Dr. Hala *et al*. conducted a study on using intrathecal dexmedetomidine as an adjuvant to hyperbaric bupivacaine in lower limb surgeries. They concluded that dexmedetomidine significantly prolong anesthetic and analgesic effects of bupivacaine in a dose-dependent manner.

From the results of the present study and the previous studies conducted on dexmedetomidine and fentanyl, we can conclude that dexmedetomidine is more effective when added as an adjuvant to bupivacaine in spinal anesthesia.

CONCLUSION

Intrathecal dexmedetomidine supplementation to spinal bupivacaine seems to be a good alternative to intrathecal fentanyl since the first one produces prolonged post-operative analgesia and more suitable for surgeries that need quite long time. Minimal side effects and excellent quality of spinal analgesia are observed with dexmedetomidine.

AUTHORS' CONTRIBUTIONS

CONFLICTS OF INTEREST

SOURCE OF FUNDING

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