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Document heading doi: 10.21276/apjhs.2019.6.2.23 **Research Article**

A Study to Compare the Effect of Intrathecal 0.5% (Heavy) Bupivacaine With Dexmedetomidine (5µg) and Intrathecal 0.5% (Heavy) Bupivacaine With Fentanyl (25µg) For Lower Abdominal and Gynecological Surgeries

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Abstract

Background: It is an established fact that regional anesthetic techniques especially through spinal route form an imperative for countries like India owing to their cheaper const, safety profile and ease of administration. Moreover, in lower abdominal and gynecological surgeries, they provide good muscle relaxation, higher success rate coupled with avoidance of multiple drugs. Aims and Objectives: The purpose of the study is to evaluate the efficacy of Dexmedetomidine (5µg) versus Fentanyl (25µg) as an adjuvant added to Bupivacaine in spinal anaesthesia and also to assess various hemodynamic parameters and side effects caused by them.Material and Methods: The current prospective study was conducted over a period of nineteen months from March 2017 to September 2018 at Government Medical College and Hospital, Anantapuramu and include a total of 50 cases were studied. Standard methods were used for recording as well as analysis of data.Observations and inference: It is observed in the study that that Intrathecal Dexmedetomidine produces early onset of sensory blockade significantly at 1.95±0.44 mins compared to Fentanyl at 2.89±0.42 mins and prolongs the duration of postoperative analgesia significantly up to 304.68 ±25.43 mins compared to Fentanyl where it is 253.12 ± 14.30 mins with desirable sedation and without significant side effects. Conclusion: It can be concluded from the study that intra the cal Dexmedetomidine is an ideal choice over Fentanyl for regional anesthesia.

Keywords: Bupivacaine, Dexmedetomidine, Fentanyl, Intrathecal, Lower Abdominal and Gynecological surgeries.

Introduction

The cost of general anaesthesia, the skill required to its practice, specialized equipment needed for its administration coupled with an indifferent supply of anesthetic gases/drugs and lack of monitoring equipment especially in peripheral areas in a country like India made regional Anesthetic techniques as an imperative choice because they are relatively inexpensive and easy to administer. The popularity of regional anaesthetic techniques especially through spinal route, being advised and practiced, owing to their safety profile when compared to the side effects associated with general anesthesia.

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The beauty of spinal anesthesia is that provides profound muscle relaxation, easy to administer, high success rate, rapid spread, avoids high doses of multiple drugs and above all the patient will be awake and cooperative. It also forms an established form of anesthesia for lower abdominal and gynecological techniques inpatients having poor ventilatory performance[1,2].

Aims and Objectives

The aims and objectives of current study are

1. To evaluate the efficacy of Dexmedetomidine (5µg) versus Fentanyl (25µg) as an adjuvant added to Bupivacaine in spinal anaesthesia
2. Assessment of the difference of various parameters including onset, duration and level of sensory blockade, onset of motor blockade,

duration of post-operative analgesia, changes in hemodynamic parameters if any and any other noticeable side effects.

Materials and Methods

The current study is a prospective randomized, controlled and double blinded study carried out at Government Medical College and General Hospital, Anantapuramu from March 2017 to September 2018 after obtaining clearance from Institutional Ethics Committee and included 50 patients in two groups (Dexmedetomidine and Fentanyl) by using ASA grade I and II physical status, aged between 18-60yrs, belonging to both sexes undergoing lower abdominal &gynecological surgeries. Patients who refused to be a part of study, those who fall under >ASA-III criterion, patients with infection, hypertensives and those who are dependent on opioids are excluded from the study. All the data obtained from the study are recorded in a pretested proforma, systematically tabulated and analyzed by appropriate statistical tools usingSSPS for windows 10.0.5. Continuous Variables were analyzed with student' s t-test, Analysis of variance (ANOVA). Fischer's F-test, Levine's test for equality of variance, Pearson correlation as appropriate. In student's t-test we have applied one sample t-test, independent sample t-test, paired sample t-test. Other parameters were analyzed by descriptive statistics as appropriate.

During preoperative visit patient's detailed history, general physical examination and systemic examination were carried out. Basic demographic data like age, sex, height and weight were recorded.

During the pre anaesthetic checkup, linear visual analogue scale (VAS) was explained to all patients using a 10cm scale. Informed consent was obtained from all the 50 patients after a detailed explanation of the procedure to be performed. All the patients were premedicated with Inj. Midazolam 0.05mg/kg I.M 45-60mins prior to procedure.

The pulse rate, blood pressure and respiratory rate were recorded before starting the case. Peripheral venous cannulation was done with 18 G 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 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 sub arachnoid space according to their group and were turned to supine position.

Group D, n=25 were given 2.5ml (12.5mg) of 0.5% Hyperbaric Bupivacaine with 5µg dexmedetomidine (made to 0.5 ml).Group F, n=25 were given 2.5ml (12.5mg) of 0.5% Hyperbaric Bupivacaine with 25 µg of Fentanyl (0.5 ml).

Vital signs such as pulse rate, blood pressure, respiratory rate and SPo2 were monitored everyone minute in the first three minutes, every three minutes up to thirty minutes and every 10 min till the end of procedure and were noted in the proforma.

Level of sensory block was assessed by pinprick and the onset of blockade was noted. Intra operatively 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 intra operatively: Onset of sensory blockade, Level (dermatomal) of sensory blockade, Onset of motor blockade, Quality of motor blockade by BROMAGE SCALE, 2-segment regression time, Degree of sedation (Wilson sedation scale), Duration of motor blockade which is taken as the time from injection to return of power to BROMAGE Grade 0.Side effects like headache, nausea, vomiting, pruritus, urinary retention and respiratory depression are noted in both the groups.

If there was any fall in blood pressure, intravenous fluids were rushed and if the fall was more than 30% below the base line value Inj. Ephedrine was given in titrated doses. If the pulse rate was less than 60 per minute, Inj. Atropine 0.6mg I.V was given. If the respiratory rate was below 10 /min respiratory depression was diagnosed**.**

At the end of surgery, the patient was shifted to postoperative ward. Patients were monitored at 30 min, 1 hour, 2 hours, 4 hours, 8 hours, 12 hours and 24 hours postoperatively, and VAS scores were noted along with vital parameters. The time at which rescue analgesic was given are noted which is taken as duration of postoperative analgesia. Rescue analgesic used was Inj. tramadol 100mg IM. Rescue analgesic was administered when the VAS score was more than 4 in the postoperative period.

Observations and Inferences

Results were analyzed in both the groups based on various parameters such as age , sex , weight , height , ASA Grade , types of surgery ,onset of sensory and motor blockade , highest sensory level reached, grade of motor blockade , two segment regression time , duration of motor blockade ,time for rescue analgesic (postoperative analgesia duration) and side effects experienced in both the groups.

Age wise distribution of cases: The age distribution in GROUP D was from 18-60 whereas the age distribution in GROUP F was 19-60. The mean age in GROUP D was 39.96 with SD 11.46 whereas in

GROUP F it was 39.32 with SD 11.27. Both groups were comparable in terms of age distribution. The same findings are depicted in table No.1 below.

Table No.1: Age wise distribution of cases

AGE	GROUP -D	GROUP- F
18-30	6	5
31-45	11	12
46-60	8	8
TOTAL	25	25
MEAN	39.96	39.32
STANDARD DEVIATION	11.46	11.27

Sex wise distribution of cases: when sex wise distribution of cases is considered, 14 males and 11 females were present in Group-D whereas 13 males and 12 females were preset in Group-F as depicted in table No.2. However, distribution of cases is not statistically significant.

Table No.2: Sex wise distribution of cases

Sex	GROUP -D	GROUP- F	Total
MALE	14	13	27
FEMALE	11	12	23
Total	25	25	50

Height and weight wise distribution of cases: As observed from the Table-3, No statistically significant differences is made out as for as height and weight of study subjects are concerned.The mean weights of patients in both the groups were comparable. There is no statistical significance between the groups with P value being 0.2064.The mean height in both groups was comparable as evident by the P value 0.5101 which is not significant statistically.

Table No.3: Height and weight wise distribution of cases

Parameter	Weight in Kilograms		Height in Cms	
	Group-D	Group-F	Group-D	Group-F
Range	51-79	49-82	150-178	153-180
Mean	66.24	69.28	162.84	161.36
Standard deviation	7.70	9.03	7.80	7.97

Distribution of cases as per ASA criteria: Both the groups are similar with respect to ASA Grade as well as are evident by the statistics below. When chi squared the value is 0.166 with one degree of freedom withP value >0.05 indicating that there is no statistical significance. The findings are presented in Table No.-4 below.

Table No.4: Distribution of cases as per ASA Criterion

GRADE	GROUP -D	GROUP -F	Total
GRADE- I	22	21	43
GRADE- II	3	4	7

Total	25	25	50

Table No.5: Distribution of case as per the surgical procedures underwent by them

Distribution of cases as per the surgical procedures: The surgical procedures underwent by the subjects are presented in table No.5 below. The procedures underwent by the subjects are almost comparable.

SURGICAL PROCEDURE	GROUP D	GROUP F
HYSTERECTOMY	9	9
B/LHERNIOPLASTY&INCISIONAL HERNIA	6	5
TURP	5	6
OTHERS	5	5

Observations as to the intraoperative Parameters

1. **Sensory blockade**:Onset of sensory blockade was faster in Group D (Dexmedetomidine group) compared to Group F (Fentanyl group). Onset of blockade in Dexmedetomidine group is with a mean of 1.96 min with standard deviation of 0.27 compared to Fentanyl group where it was 2.76 min with standard deviation of 0.26 which is highly significant statistically with a P value of <0.0001(Table No.6).
2. **Onset of Motor blockade**:Onset of motor blockade was faster in Group D (Dexmedetomidine group) compared to Group F (Fentanyl group). Onset of blockade in Dexmedetomidine group is with a mean of 4.69 min with standard deviation of 0.31 compared to Fentanyl group where it was 5.72 min with standard deviation of 0.58 which is highly significant statistically with a P-value of <0.0001(Table No.6).

Table No-6: Onset of sensory and Motor blockades

Parameter	Onset of Sensory blockade		Onset of Motor blockade	
	Group-D	Group-F	Group-D	Group-F
Mean	1.96	2.76	4.69	5.72
Standard deviation	0.27	0.26	0.31	0.58
p-Value	**<0.0001**		**<0.0001**	

3. **Quality of Motor Blockade**: Quality of motor blockade assessed by BROMAGE scale was comparable among both the groups and is statistically not significant as indicated by the table below.
4. **Quality of sedation**: Level of Sedation was assessed in both the groups(Table No.7) by **Wilson sedation scale**. 3/5 Wilson sedation grade which is highly desirable in regional anesthesia is observed in 13 patients in Dexmedetomidine group compared to only 6 patients in Fentanyl group which is statistically significant.

Table No.7- Quality of sedation

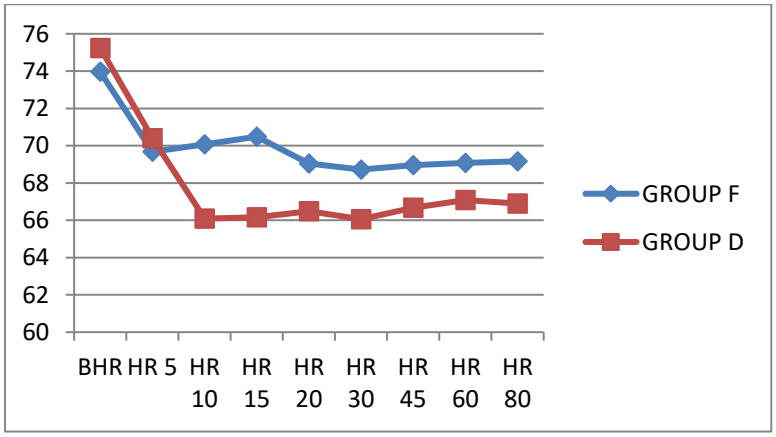
SEDATION GRADE	GROUP D	GROUP F
1	4	10
2	8	9
3	13	6
4	0	0
5	0	0

5. **Two segment regression time**: Two segment regression time was prolonged in Group D (Dexmedetomidine group) compared to Group F (Fentanyl group). Two segment regression time in Dexmedetomidine group is with a mean of 129.68 min with standard deviation of 8.75 compared to Fentanyl group where it was 81.16 min with standard deviation of 7.85 which is highly significant statistically with a P value of <0.0001.
6. **Duration of motor Blockade**(Table No.8):Duration of motor blockade was comparable in both groups. Duration of motor blockade in Dexmedetomidine group is with a mean of 233.88min with standard deviation of 14.74 compared to Fentanyl group where it was 158.24 min with standard deviation of 13.18 which is significant statistically with a P value of <0.0001.
7. **Postoperative duration of analgesia**: Postoperative analgesia duration is taken as the time from spinal injection to the time of administering rescue analgesic in the postoperative period. Postoperative analgesia duration 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 254.32 min with standard deviation of 12.15.(TableNo.8)

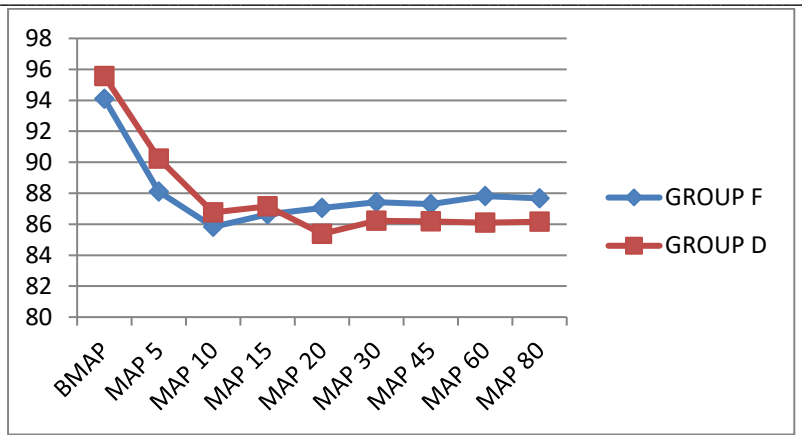
Table No.8- Duration of Motor blockade and Postoperative duration of analgesia

Parameter	Duration of motor blockade		Postoperative analgesia	
	Group-D	Group-F	Group-D	Group-F
Mean	233.88	158.24	308.64	254.32
Standard deviation	14.74	13.18	12.50	12.15
p-value	<0.0001		<0.0001	

8. **Side effects**: The side effects most commonly observed are hypotension &bradycardia which are seen commonly with regional anaesthesia. Respiratory depression which is a feared side effect of opioids is not observed in any patient belonging to either group. Pruritus is observed in two cases of Fentanyl group which resolved spontaneously without any need for medication.
9. **Hemodynamic monitoring**: Hemodynamic monitoring was done continuously throughout the procedure. Both groups are comparable in terms of blood pressure and pulse rate as evident from the Graph-1, Graph-2 and table No. below.



Graph-1: heart rate variations in test groups



Graph-2: Mean arterial pressure plotting

Table No.9- Mean blood pressure recordings at different time intervals

	GROUP F	GROUP D
BSBP	124.80±16.36	126.80±16.51
SBP5	112.40±9.26	120.40±16.95
SBP10	109.60±12.41	115.20±16.10
SBP15	111.60±8.50	112.40±17.15
SBP20	111.60±8.50	113.20±12.49
SBP30	112.80±8.93	114.40±11.58
SBP45	112.49±7.52	114.18±12.08
SBP60	112.98±8.43	113.89±12.88
SBP80	112.76±6.82	113.78±10.52
BDBP	78.80±7.81	79.20±8.12
DBP5	76.00±6.45	75.60±9.17
DBP10	74.08±6.45	72.40±9.26
DBP15	73.60±5.69	72.00±9.26
DBP20	74.80±5.86	72.40±7.23
DBP30	74.82±5.88	72.00±7.64
DBP45	74.68±5.67	72.12±7.57
DBP60	74.65±5.87	72.26±7.08
DBP80	74.86±5.38	72.16±6.93

Discussion

Provision of effective and adequate intra operative and postoperative pain relief is important not only for humanitarian reasons but also because of the deleterious effects of pain on various organ systems and negative impact on postoperative recovery. But unfortunately, it is often neglected and left to the discretion of the nurses and surgeons, most of the times. Both fentanyl and Dexmedetomidine improved the quality of intraoperative analgesia and diminished the risk of supplementation of general anesthesia. Fentanyl basically is a lipophilic μ-receptors agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of

spinal cord and may have a supra spinal spread and action [1,2]. 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 [3-5]. 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 [7-8]. The prolongation of the duration of spinal analgesia produced by intrathecal fentanyl is not a dose related phenomenon.

Seewal*et al.* [9] 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.* [6] reported that different durations of spinal anesthesia were related to different doses of spinal bupivacaine supplemented with 25 µg fentanyl in patients undergoing urology procedures. Hamber*et al.* [10] in a review article found that a dose of 20-30 µg fentanyl as adjunct to spinal anesthesia produces faster block onset time, improvedintraoperative analgesia and decrease incidence of intraoperative nausea and vomiting in obstetric patients.

In non-obstetricpatients' studies demonstrated that a dose of 25 µg fentanyl for supplementation of spinal anesthesia produces the excellent quality ofperioperative analgesia [11,12]. In present study fentanyl in a dose of 25 µg was used for supplementation of spinal bupivacaine.

Dexmedetomidine is a highly selective α2 - adrenoreceptor agonist approved as intravenous sedative and adjuvant to anesthesia. Dexmedetomidine when used intravenously during anesthesia reduces opioid and inhalational anesthetics requirements [13,14]. Axelson and Gupta found that alpha-2 receptor agonists are important as neuraxial adjuvants to improve the quality of preoperative and postoperative analgesia in high-risk patients and in ambulatory procedures. When clonidine ordexmedetomidine added to intrathecal local anesthetics, the regression of sensory and motor block increased dose-dependently, and postoperative analgesia was prolonged. (15)

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 [16], moreover, Kalso*et al.*[17] and Post *et al.*[18] reported a 1:10 dose ratio between intrathecal DEXEMEDETOMIDINE and clonidine in animals.

Clinical studies in surgical patients showed that intrathecal clonidine increases the duration of sensory and motor spinal block when added to spinal local anesthetics and this effect of clonidine is dose-dependent [19,20], and doses of more than 75 µgintrathecal clonidine is accompanied by excessive sedation, hypotension and bradycardia. De Kock *et al.* [21] recommended a dose of 15-45 µg clonidine for supplementation of spinal anesthesia since this dose effectively prolongs the duration of spinal block with minimal sedation and side effects. The clinical studies about the use of intrathecaldexmedetomidine in surgical patients are scarce in the literature.

Kanazi*et al.* [22] found that 3µg dexmedetomidine or 30 µg clonidine added to 13 mg spinal bupivacaine produced the same duration of sensory and motor block with minimal side effects in urologic surgical patients. From Kanazi study and animal studies, we assumed that 3-5 µgdexmedetomidine would be equipotent to 30-45 µgclonidine when used for supplementation of spinal bupivacaine. Intrathecaldexmedetomidine when combined with spinal bupivacaine prolongs the sensory block by depressingthe release of C-fibers transmitters and by hyperpolarization of pos-synaptic dorsal horn neurons [23,24].

Calasans-Maia et al. (25) investigated the effects of adding intrathecaldexmedetomidine to 0.5% levobupivacaine over motor block duration in pigs and found that intrathecaldexmedetomidine (0.1, 0.2, and 0.4 µg) prolonged the motor block duration. Motor block prolongation by α2 - adrenoreceptor agonists may result from binding these agonists to motor neurons in the dorsal horn of the spinal cord [26-28].Intrathecal α2 - receptor agonists have been found to have antinociceptive action for both somatic and visceral pain.

In the current study, the intrathecal dexmedetomidine and bupivacaine block has resulted in significantly less side effects than intrathecal fentanyl bupivacaine block. The most significant side effects reported about the use of intrathecal α2adrenoreceptor agonists are bradycardia and hypotension, in present study, these side effects were not significant probably because we used small dose of intrathecaldexmedetomidine which was confirmed by the findings of Kanazi report.

It is observed in the present study that hypotension was more in the Dexmedetomidine group than in the Fentanyl group, but it did not reach a significant difference. Meanwhile, hypotension occurred 25-30 min after spinal injection. 2 patients in the dexmedetomidine group and one patient in fentanyl group had mild episodes of hypotension in the PACU. Relativelybradycardia was more in Dexmedetomidine group than fentanyl group,but it did not proceedto a

significant difference. Pruritus after intrathecal fentanyl is reported to be 40-70% but it was only 8% in present study which can be explained by the fact that pruritus is a benign subjective symptom which is under reporting and usually need no treatment.

It is understood from the current study that demographic data comparing age, sex, height, and weight shows no statistically significant difference (P>0.05) among both the groups, so also the type of surgeries and ASA grade of patients in both groups were comparable and statistically not significant.

The mean time of onset of analgesia in group D was 1.96±0.27min and in group F was 2.76±0.26 mins. The statistical analysis by **"t" test**, showed that there is a statistically significant difference (P <0.0001**)** between the two groups. Theonset of motor blockade in Group D was 4.69 ± 0.31 min compared to Group F patients where it is 5.72 ± 0.58 min which is highly significant statistically with P value <0.0001.The highest level of sensory blockade and the degree of motor blockade assessed by Bromage scale were comparable among both the groups and statistically not significant.

Sedation level was assessed in both the groups by Wilson sedation scale. It is highly desirable to have the patient with mild to moderate sedation during regional analgesia which is Wilson sedation grade 3 which is seen in 13 patients in Dexmedetomidine group compared to only 6 patients in Fentanyl group. Two segment regression time was prolonged in Group D (Dexmedetomidine group) compared to Group F (Fentanyl group). Two segment regression time in Dexmedetomidine group is with a mean of 129.68 min with standard deviation of 8.75 compared to Fentanyl group where it was 81.16 min with standard deviation of 7.85 which is highly significant statistically with a P value of <0.0001.

Duration of motor blockade was comparable in both groups. Duration of motor blockade in Dexmedetomidine group is with a mean of 233.88 min with standard deviation of 14.74 compared to Fentanyl group where it was 158.24 min with standard deviation of 13.18 which is highly significant statistically with a P value of <0.0001. In a study RachanaJoshi et al (53)Dexmedetomidine significantly prolonged the duration of analgesia and duration of sensory and motor block as compared to intrathecal bupivacaine alone. It is taken as the time from spinal injection to the time of administering rescue analgesic in the post-operative period. The post-operative duration of analgesia in group D was 308.64 ± 12.50 mins and in group F was 254.32 ±12.15 mins. The statistical analysis by **"t" test**, showed that there is **a** statistically significant difference (P <0.0001**)** between the two groups. Our study results like onset of analgesia and duration of analgesia well correlated with Al- Ghanem SM, Massad IM, Al-Mustafa MMetal.[13] study results. Hemodynamic monitoring was done continuously throughout the procedure. Both groups are comparable in terms of blood pressure and pulse rate.

Conclusion

The study was undertaken to evaluate the role of Dexmedetomidine as an additive to Bupivacaine to increase the duration of analgesia postoperatively by Intrathecal route. The study group as divided into 2 groups of 25 patients each of both sexes ranging from 18- 60 years age group of ASA grade I and II, selected for lower abdominal & gynecological surgeries , using 5µg of Dexmedetomidine (made to 0.5 ml) with 0.5% Hyperbaric Bupivacaine 2.5 ml in study group intrathecally with control group 0.5% Hyperbaric Bupivacaine with 25 µg (0.5ml) of Fentanyl.

At the conclusion of study it has to be acclaimed thatIntrathecalDexmedetomidine produces early onset of sensory blockade significantly at 1.95±0.44 mins compared to Fentanyl at 2.89±0.42 mins and prolongs the duration of postoperative analgesia significantly up to 304.68 ±25.43 mins compared to Fentanyl where it is 253.12 ± 14.30 mins with desirable sedation and without significant side effects.

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