Original research article

To evaluate the onset and duration of sensory and motor block and also to assess for any hemodynamic changes

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Abstract

Background: Spinal anesthesia is the easiest and most affordable anesthesia available for infra-umbilical surgeries. However, due to the lower dose of anesthetic agent required to induce, it doesn't provide adequate analgesia during the postoperative period. Various adjuvants have been tried to avoid intraoperative visceral and somatic pain. Fentanyl is an opioid that has been used previously as a neuralgic adjuvant. Dexmedetomidine is a new, highly selective alpha 2 agonist drug that has a lesser side effect profile than opioids and gives better analgesia.
Methods: A comparative controlled trial was done in Government General Hospital, Guntur on 70 patients. They were divided into two groups. One group received 15 mg of 0.5% Levobupivacaine (Isobaric) +25 µg Fentanyl 0.5ml. while the other group received 15 mg of 0.5% Levobupivacaine (Isobaric) +5 µg Dexmedetomidine (made into 0.5ml with normal saline). Various parameters were compared like demographic details and the duration for sensory block and motor block. Time to achieve maximum sensory block and motor block. Time required for rescue analgesia and side effects profile.
Results: Patients in Dexmedetomidine + Levobupivacaine group (BD) hada rapid onset of sensory block and motor block, shorter Time for Maximum sensory block and motor block, longer Time at which rescue analgesia was required, and a less painful experience.
Conclusion: Intrathecal dexmedetomidine administration has a longer motor and sensory block, and reduced demand of analgesics when compared to Fentanyl.
Keywords: Fentanyl, anesthesia, analgesics, sensory block and motor block

Introduction

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Relieving pain both intraoperatively and post-operatively is the main aim of anesthesia [1]. For lower abdominal surgeries, spinal anesthesia is preferred as it is very safe, economical, and easy to administer [2]. It also reduces autonomic, somatic, and endocrine responses, making it an effective treatment for acute operative pain [3]. A common problem during lower abdominal surgeries under spinal anesthesia is visceral pain, nausea and vomiting [3].

Previously, hyperbaric bupivacaine (which is a racemic mixture of its enantiomers, dextrobupivacaine, and levobupivacaine) 0.5% was the only drug used for spinal anesthesia. Cardiotoxicity is caused by the dextro enantiomer, whereas the pure S (-) enantiomer of Levobupivacaine, has been shown to have less central nervous system and cardiovascular toxicity [4-6]. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with a relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period [3].

Drugs including opioids, magnesium sulfate, vasopressors, and α_2-adrenergicagonists (dexmedetomidine and clonidine) have been tried extensively as an adjuvant to local anesthetic, and provide post-operative pain relief, decrease the dosage of local anesthetic and give hassle-free experience to both patient and operating team during operative and post-operative period [4]. Amongst opioids, fentanyl is a potent µ opioid receptor agonist with improved analgesia over morphine. 10-15µg of fentanyl, demonstrates a sparing effect on the requirement of levobupivacaine while maintaining excellent clinical efficacy with a less hemodynamic variation. However, intrathecal opioids can cause some side effects such as itching, urinary retention, nausea and vomiting as well as respiratory depression [7].

Dexmedetomidine (Dex), a new selective α2-agonist, as an adjuvant to local anesthetics has significant analgesic, sympatholytic, and sedative properties. Due to its high selectivity towards α2-adrenergic receptors (α2-AR) than other alpha-2 agonists (like clonidine), it has sedative and analgesic effects in supraspinal and spinal sites and also has an antinociceptive impact on both visceral and somatic pain. Intrathecal administration of this drug has shown to have better sedative and analgesic action than opioids without the side effects profile of opioids. More importantly, this drug does not cross the placenta significantly (0.77 maternal/fetal index), which confirmed its safety in cesarean delivery. However, some studies have reported that intrathecal injection of Dex is frequently associated with some side effects, such as a decrease in heart rate and blood pressure [8]. Due to the paucity of studies comparing these two neuralgic adjuvants, this study was done to evaluate the effect of adding fentanyl or dexmedetomidine to hyperbaric levobupivacaine and comparing it with the control group.

Aim and Objectives of the Study

This study aims to compare the onset and duration of the sensory and motor block as well as postoperative analgesia provided by intrathecal fentanyl 25μg and dexmedetomidine 5μg when used as an adjuvant to 15mg (3ml) of 0.5% Isobaric Levobupivacaine in Infra umbilical surgeries.

The Primary objective is to evaluate the onset and duration of sensory and motor block and also to assess for any hemodynamic changes.

The Secondary objectives are to Determine the time duration for rescue analgesia and compare the Safety profile of the two mixtures (adverse effects like hypotension, bradycardia,
respiratory depression and PONV).

Materials and Methods

A prospective controlled comparative clinical study was conducted in the Department of Anesthesia, Guntur medical college, from January 2022 to December 2022 in Government General Hospital, Guntur.

Inclusion Criteria

Patients aged between 20-60 yrs, with ASA PS 1 & 2, who are posted for elective infraumbilical surgery and have given consent, were included in this study.

Exclusion Criteria

Patients who have not given consent, or are aged > 60yrs and < 20yrs, or have spinal deformities, or have contraindications to spinal anesthesia, or have ASA PS 3,4 & 5 or have been posted for emergency procedures, or have a history of allergy to any of the drugs used in this study, were excluded from the study.

A total number of 70 patients who are going to be posted for infra umbilical surgeries in Government General Hospital, Guntur, were divided randomly into 2 groups:

Groups

BF (n=35): 15 mg of 0.5% Levobupivacaine (Isobaric) + 25 μg Fentanyl 0.5ml.

BD (n=35): 15 mg of 0.5% Levobupivacaine (Isobaric)+ 5 μg Dexmedetomidine (made into 0.5ml with normal saline).

The following parameters were noted:

- The onset of sensory and motor blockade
- The maximum amount of sensory blockage achieved and the time taken to achieve it.
- The maximum degree of motor blockage achieved and the time taken to achieve it.
- The total length of sensory and motor blockage.
- The time when the first rescue analgesic was required was recorded.
- Total surgical time, analgesia, and side effects were recorded.
- During surgery and the perioperative phase, the vitals of all patients were monitored.

Data analysis was done using SPSS V 16 software. Qualitative data was expressed in frequencies and percentages and Quantitative data in mean and standard deviation. Nonparametric statistics i.e. Chi-square test/Fisher's exact test was used to find the significant association between the two qualitative variables. Unpaired t-test was used to find the statistical significance between quantitative variables. A p-value of <0.05 was considered statistically significant.

Results

Table 1: Medication difference

	Fentanyl + Levobupivacaine group (BF)	Dexmedetomidine + Levobupivacaine (BD)	
Mean age	45.51± 8.80	43.65 ± 8.82	P= 0.88; Not significant
Mean height (in cm)	164.17 ± 6.93	163.51 ± 5.30	P = 0.63; Not significant
Mean weight (in kg)	59.74 ± 9.15	60.05 ± 4.86	P = 0.79; Not significant
% of patients belonging to ASA Grade I	45.7%	51.4%	
% of patients belonging to ASA Grade II	54.3%	48.6%	

The mean age, weight, and height of the Fentanyl + Levobupivacaine group (BF) and Dexmedetomidine + Levobupivacaine (BD) group were similar.
The following figure shows the distribution of various surgical procedures performed.

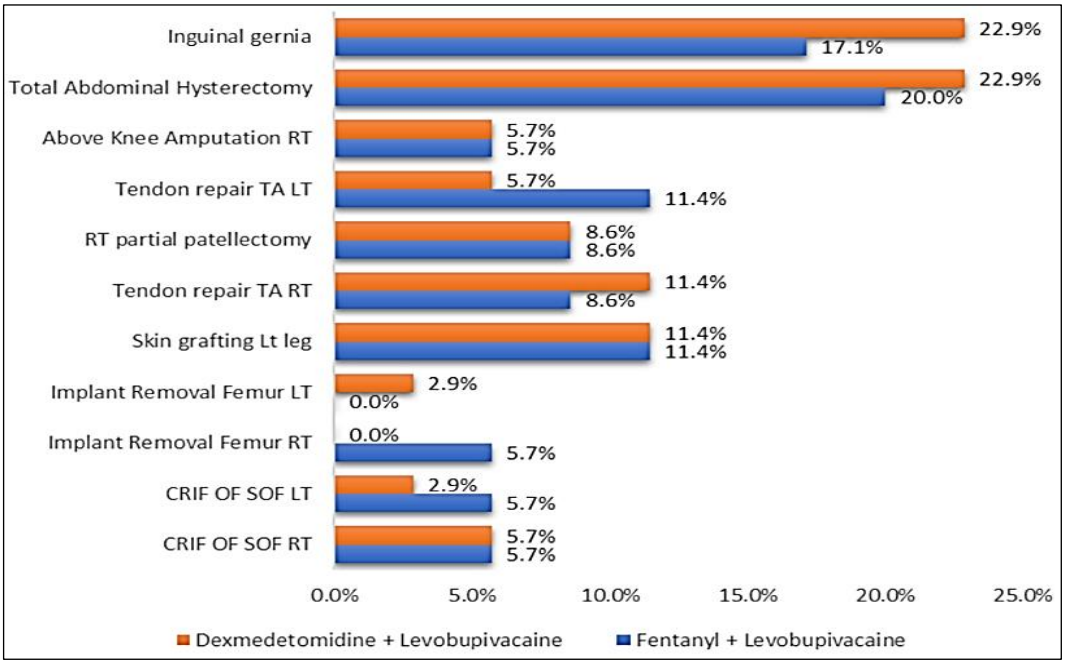

Fig 1: Distribution of various surgical procedures

Table 2: Data on medication for sensory and motor block

	Fentanyl + Levobupivacaine group (BF)	Dexmedetomidine + Levobupivacaine (BD)
The mean time for the onset of sensory block	7.17±0.89min	4.97 ± 0.80min
The mean time for maximum sensory block	13.05 ± 0.99min	8.31 ± 0.67min.
The mean time for the onset of motor block	9.48 ± 1.14min	6.45 ± 1.03min.
The mean time for maximum motor block	19.14 ± 1.62min	19.05 ± 1.47min.
The mean duration of surgery in minute	81.57±16.0	84.57±16.95.
The mean time for two-segment regression	106.71 ± 7.46min	195.28 ± 11.04min
Mean time for rescue analgesia	248.28 ± 24.90min	441.42 ± 19.87min.
The mean duration of regression to S1	243.71 ± 12.08min	389.85 ± 14.62min
The mean duration of regression to Bromage0	231.28 ± 12.20min	332.28 ± 14.26min

Side effects profile
Among the patients of group BF 8.6% of patients had bradycardia whereas in patients of group BD, 5.7% of patients each had bradycardia and hypotension.

- The mean VAS in patients of group BF was 3.48 ± 1.66 whereas the mean VAS in patients of group BD was 2.11 ± 0.90. The P value was <0.001, thus there was an increased VAS score in patients of group BF when compared with group BD.

Discussion
Major abdominal surgeries may be done by using regional (spinal or epidural) or general anesthesia. Epidural anesthesia reduces the perioperative stress response to surgery and improves surgical outcomes.

Epidural anesthesia and analgesia have become among the best-accepted techniques for lower abdominal & lower limb surgeries as it provides good sensory and motor blockade, retain adequate spontaneous respiration and provide hemodynamic stability during the intraoperative period. Epidural anesthesia gives the additional advantage of an indwelling epidural catheter by which further administration of analgesic doses for the postoperative period can be done.

Few individuals who were administered bupivacaine three decades ago experienced life-threatening arrhythmias that were resistant to therapy. This was due to the cardiotoxic 'R' form. Thus, the hunt for better, safer local anesthetic medicines began and the 'S' isomer of bupivacaine (levobupivacaine) which has far less cardiotoxicity was discovered. Levobupivacaine, the pure S (-) enantiomer of bupivacaine, due to its safety and superior pharmacokinetic properties is an emerging alternative to bupivacaine.

Ropivacaine and levobupivacaine are the newest local anesthetic medicines that have much-decreased cardiotoxicity compared to bupivacaine.

The regression of motor block occurs earlier than bupivacaine which makes it favorable for ambulatory surgery.

There have been few reports of levobupivacaine poisoning, and any toxic symptoms are typically reversible with minor treatment and have no fatal consequences. In anesthetic and analgesic practice, levobupivacaine and bupivacaine induce equivalent surgical sensory block but levobupivacaine has the benefit of creating less motor blockage.

Levobupivacaine has a wide range of applications in regional anesthetic techniques, including subarachnoid block, epidural anesthesia and analgesia, brachial plexus blocks, and local infiltration, due to its low cardiovascular and neurological toxicity. It is also being utilized for intraoperative anesthetic, labor analgesia, and postoperative pain management. In comparison to bupivacaine, both levobupivacaine, and ropivacaine are preferred in labor analgesia because they provide equivalent long-lasting analgesia, less motor block, and less toxicity.

Various opioids have been used intrathecally like morphine, fentanyl, buprenorphine, and nalbuphine to fasten the onset and prolong the duration of sensory and motor blockade. Fentanyl is a lipophilic μ receptor opioid agonist. Intrathecal fentanyl as an adjuvant to local anesthetic has a rapid onset of action and significantly reduces visceral and somatic pain which has been proved in various studies. Though intrathecal fentanyl gives better quality analgesia and duration, it is also associated with significant pruritis.

Dexmedetomidine is a highly selective α_2 agonist, which has been used as a short-term sedative agent for mechanically ventilated ICU patients. Off late it has been used as a neuraxial adjuvant for cesarean section and labor analgesia because of its stable hemodynamics, potent intraoperative and prolonged post-operative analgesic properties.

A prospective controlled comparative study was done among 70 patients admitted for intra-umbilical surgeries in the department of anesthesia satisfying inclusion and exclusion criteria during the study period after obtaining informed consent.

All the 70 patients were classified into two groups:

Group BF: 35 patients received 15mg of 0.5% Levobupivacaine (Isobaric)+ 25μg fentanyl 0.5ml

Group BD: 35 patients received 15mg of 0.5% levobupivacaine (Isobaric) + 5μg dexmedetomidine (prepared into 0.5ml with normal saline).

The mean age, height, and weight observed in the present study are similar to the study done by Gupta *et al*., [9].

Table 3: The mean age, height and weight observed

	Present study	**Gupta *et al*.,**
Mean age	Group BF= 45.51 Group BD= 43.65	Group BF = 42.21 Group BD = 44.35
Mean height	Group BF =164.17 Group BD = 163.51	Group BF = 156 Group BD = 158.0
Mean weight	Group BF =59.74 Group BD = 60.05	Group BF = 64.42 Group BD = 65.13

The majority of patients in both groups had ASA Grade I (BF= 54.3%; BD = 51.4%). Srinivasa Rao *et al*., [10] had similar findings in their study (BF= 50%; BD = 50%).

Group BD had a statistically significant quicker onset of sensory block at T10, had achieved maximum sensory block in significantly lesser time and the majority of them attained maximum level of sensory block at T6 when compared to group BF. Bhure *et al*., [11] had similar findings in their study; however, the majority of the participants in group BD had achieved maximum sensory level at T8.

Table 4: Comparative data

	Present study	**Bhure *et al*., [11]**
The mean time of onset of sensory block at T10	Group BF=7.17 Group BD= 4.97 P value = < 0.0001	Group BF= 2.1 Group BD= 8.25 P value = < 0.0001
The mean time for maximum sensory block	Group BF=13.05 Group BD=8.31 P value = < 0.0001	Group BF=5.33 Group BD= 13.25 P value = < 0.0001
% of patients who had achieved the maximum level of sensory block at T6	Group BF=100% Group BD=100%	Group BF=72.5% Group BD=15%

The mean time for the onset of motor block in patients in group BF was 9.48 1.14 minutes, whereas the mean time for onset of motor block in patients in group BD was 6.45 1.03 minutes in this study. Because the p-value was 0.0001, there was a statistically significant difference in the time it took for patients in group BD to develop motor block when compared to patients in group BF. Srinivasa Rao *et al*., [10] had similar mean values in their study (BF- 9.87; BD- 9.57), but it was not statistically significant.
The mean time for the maximum motor block in the study was in accordance with a study done by Paul *et al*., [12]. However, Paul *et al*., had a statistically significant difference, with the group BD attaining quicker maximum motor block.
The mean time for surgery in Group BF was 81.57 ± 16.07min and for Group BD was 84.57 ± 16.95min.
The mean time for two-segment regression and mean duration of regression to Bromage 0 was significantly longer in patients of group BD when compared with patients of group BF. Rahimzadeh *et al*., [13] also observed similar statistically significant differences.

Table 5: Comparative study

	Present study	**Rahimzadeh *et al*., [13]**
The mean time for rescue analgesia (in min)	Group BF= 248.28 Group BD=441.42 P value = <0.001	Group BF= 296.33 Group BD=496.63 P value = <0.001
The mean duration of regression to Bromage 0 (In min)	Group BF= 231.28 Group BD= 185.56 P value = <0.001	Group BF= 332.28 Group BD= 331.60 P value = <0.001
The mean time for two-segment regression (In min)	Group BF= 106.17 Group BD=195.28 P value = <0.001	Group BF= 329.83 Group BD=560.53 P value = <0.001

In group BD patients, 5.7% of them had bradycardia and 5.7% of them had hypotension. Whereas, in group BF, 8.6% of them had bradycardia. None of the patients in group BF had hypotension. Unlike the present study, Pocham *et al*., [14] observed that 16% of patients in Group BF had hypotension and none of them had bradycardia. The visual analog score of patients in group BF was significantly higher than that of patients in group BD. This indicated that Group BF patients had experienced a higher amount of pain than the other group.

Conclusion

In this study, we observed that the Dexmedetomidine + Levobupivacaine group (BD)had

- A rapid onset of sensory block.
- Shorter Time for Maximum sensory block.
- Quicker Onset of motor block.
- Shorter Time for Maximum motor block.
- A longer two Segment Regression time.
- Longer Time at which rescue analgesic is required.
- shorter duration of Regression time to S1.
- Shorter duration of regression to Bromage.
- Lesser painful experience.

Thus, we conclude that Dexmedetomidine + Levobupivacaine is more efficacious compared to the Fentanyl + Levobupivacaine combination.

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References

1. Jain S, Sharma G, Bafna U, Jain D, Meena S, Jetley P. A Comparative Study of Intrathecal Fentanyl

and Dexmedetomidine as Adjuvants to Hyperbaric Levobupivacaine 0.5% and Hyperbaric Levobupivacaine 0.5% Alone in Infraumbilical Surgeries. J Recent Adv Pain. 2016;2(2):44-48.
2. Brown DL. Spinal, Epidural and Caudal Anaesthesia. In: Miller's Anaesthesia. Miller RD, Erikssson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. 7th ed. Philadelphia: Churchill Livingstone Elsevier; c2010. p. 7.
3. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesth Clin Pharmacol. 2011;27:339-43.
4. Burlacu CL, Buggy DJ. Update on local anesthetics: focus on levobupivacaine. Ther. Clin. Risk Manag. 2008;4(2):381-92.
5. Sanford M, Keating GM. Levobupivacaine: a review of its use in regional anesthesia and pain management. Drugs. 2010;70(6):761-91.
6. Bajwa SS, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. J Anaesthesiol. Clin. Pharmacol., 2013, 29(4).
7. Kukanich B, Clark TP. The history and pharmacology of fentanyl: relevance to a novel, long-acting transdermal fentanyl solution newly approved for use in dogs. J Vet. Pharmacol Ther. 2012;35(2)3-19.
8. Khosravi F, Sharifi M, Jarineshin H. Comparative Study of Fentanyl vs Dexmedetomidine as Adjuvants to Intrathecal Bupivacaine in Cesarean Section: A Randomized, Double-Blind Clinical Trial. J Pain Res. 2020 Oct;13:2475-2482. Doi: 10.2147/JPR.S265161. PMID: 33116789; PMCID: PMC7548853.
9. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesth Clin Pharmacol. 2011;27(3):339-43.
10. Rao CS, Sujani K, Sudhakar NS. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine for infra-umbilical 80 surgeries. Journal of Evolution of Medical and Dental Sciences. 2015 Jan;4(6):962-8.
11. Bhure A, Jagtap N. A comparison of intrathecal dexmedetomidine and fentanyl as an adjuvant to isobaric levobupivacaine for lower limb orthopedic surgery. Indian J Clin Anaesth. 2019;6(1):89-96.
12. Paul A, Nathroy A, Paul T. A comparative study of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in lower limb surgeries. J Med Sci [serial online] [cited 2022 Jan 12]. 2017;37:221-6.
13. Rahimzadeh P, Faiz SHR, Imani F, *et al*., Comparative addition of dexmedetomidine and fentanyl to intrathecal bupivacaine in orthopedic procedure in lower limbs. BMC Anesthesiol. 2018;18:62. https://doi.org/10.1186/s12871-018- 0531-7.
14. Pocham V, Naik LG. A Prospective Randomized Double-Blind Study Comparing Intrathecal Dexmedetomidine and Fentanyl as Adjuvants to Bupivacaine in Infra Umbilical Surgeries. Int J Sci Stud. 2018;6(7):1-14.