

Low Dose Fentanyl and Dexmedetomidine as Adjuvants to Intrathecal Hyperbaric Bupivacaine in Lower Limb Surgeries: A Correlative Study

Geeta Kanithi¹, Prasad Rao Kaluvala², Krishna Rao Maremanda³, Damera Seshi Kumar⁴

¹Additional Professor, Department of Anesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

²Associate Professor, Department of Anesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

³Assistant Professor, Department of Anesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

⁴Postgraduate, Department of Anesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

Abstract

Background: The research goal to evaluate the speed of onset and duration of analgesia, motor blockade time, intraoperative hemodynamic alterations, and post-operative period in Fentanyl 25 µg group and Dexmedetomidine 5 µg intrathecally delivered group both given with Hyperbaric Bupivacaine 0.5%.

Material and Methods: At Anesthesiology and Intensive Care, Nizams Institute of Medical Sciences, Hyderabad, Telangana, India, 60 patients undergoing elective lower limb surgery under spinal anaesthesia participated in a randomised trial from 01-06-2017 to 31-04-2018. Patient groups were divided. Group D, 30 patients received 5 µg intrathecal dexmedetomidine. Group F, 30 patients got 2.5 ml bupivacaine and 25 µg intrathecal fentanyl after written, informed permission was given. Postoperative sensory blockade, motor blockade, and pain score using a visual analogue pain scale, and side effects were noted. Spss 18 and r 3.2.2 were used for statistical analysis and study used descriptive and inferential statistics. Categorical data are shown as percentages (%) and continuous data as mean sd. The 5% threshold of significance is analyzed.

Results: Two groups had similar sensory and motor block onset. Dexmedetomidine's sensory blockage lasted longer than Fentanyl's (430.50+25.84 minutes). Dexmedetomidine's motor blockage lasted longer than Fentanyl's (401.50+22.37 minutes). Systolic blood pressure, mean arterial pressure, and pulse rate fell significantly between groups at different time intervals. These changes reacted to treatment and are clinically inconsequential. Dexmedetomidine patients requested analgesics earlier than Fentanyl patients (283.67+34.74 mins). Dexmedetomidine extended analgesia. The study found few side effects.

Conclusion: Intrathecally given Bupivacaine coupled with dexmedetomidine produces longer-lasting sensory and motor blockade in lower limb procedures. Dexmedetomidine provides postoperative analgesia. Both drugs sustain hemodynamics. Dexmedetomidine or fentanyl have no side effects.

Keywords: Fentanyl, Dexmedetomidine, Spinal anaesthesia, Haemodynamic parameters.

Corresponding Author: Dr. Damera Seshi Kumar, Postgraduate, Department of Anesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

Introduction

Spinal anaesthesia is the method of choice when it comes to regional anaesthesia since it is simple to administer, it is cost-effective, and it results in a speedy onset of anaesthesia as well as total muscular relaxation. Intrathecal local anaesthetic is administered with the intention of achieving appropriate sensory and motor blockage, which is required for all lower limb and some lower abdomen surgical procedures. The type of intrathecal local anaesthetic that is used the most often is called hyperbaric bupivacaine. Bupivacaine has had a variety of adjuvants added to it in order to extend the duration of the block.^[1,2] They boost the effectiveness of local anaesthetics and make it possible to use lower doses of the medication. As an adjuvant, fentanyl, which is an opioid agonist, along with the intrathecal α 2-agonists clonidine and dexmedetomidine are utilised.

Fentanyl is predominantly an agonist of the receptor and has a stronger analgesic effect than morphine, petridine, and alfentanil. Action on the receptor at the supraspinal location causes analgesia. The activation of the central nucleus, which is dosage and infusion rate dependent, causes a drop in heart rate and blood pressure. It decreases SVR, slows A.V. conduction, lengthens the R-R interval, the A.V. node refractory period, and the duration of the purkinje fibre action potential.^[2-4] When given intravenously, fentanyl is 100 times more strong than morphine, but intrathecally, it is just 4 times as potent. The spinal cord is exposed to morphine more than Fentanyl does, which accounts for the 25 times lower dosage potency of Fentanyl. When compared to morphine, it has less rostral distribution and is a less hydrophilic opioid, which results in less respiratory depression. Fentanyl has a very low integral exposure within the spinal cord due to its enormous volume of distribution in the spinal cord and epidural region. Given that the majority of the fentanyl dose is lost into the epidural space, adding vasoconstrictors would only slightly improve spinal cord exposure.

Medetomidine's active ingredient and isomer is dexmedetomidine. Mivazerol, clonidine, and to a lesser extent. Dexmedetomidine can react with α 2 nonadrenergic imidazoline receptors, hence it is not a pure 2 adrenoceptor agonist. An anti-arrhythmogenic and central hypotensive effect is mediated by imidazoline receptor activation. It's likely that imidazoline receptors play a role in some of the effects of α 2 adrenoceptor agonists. Researchers have employed 3, 5, and 10 g of intrathecal dexmedetomidine in a few dose-finding experiments on humans with positive outcomes, sustained hemodynamic stability, and no drowsiness. Increased motor block duration, which may not be suitable for mobile procedures, is a disadvantage of spinal blocks that also contain dexmedetomidine.^[4,5]

When taken as an adjuvant, fentanyl, which is a lipophilic μ -receptor opioid agonist, extends the period of time that a spinal block is effective. When administered intrathecally, the α 2 adrenoceptor agonist dexmedetomidine greatly lengthens the period of time that a spinal block is effective. It has a selectivity ratio of α 2/ α 1 that is eight times more than that of clonidine. It has been proven that administering intrathecal dexmedetomidine to animal models has analgesic effects.^[5,6]

Dexmedetomidine is a novel highly selective α 2-agonist that is currently being tested for its potential use as a neuraxial adjuvant. This is due to the fact that it maintains stable hemodynamic conditions, offers high-quality intraoperative and postoperative analgesia for a longer period of time, and has a low risk of adverse effects.^[6,7]

Patients in intensive care units (ICUs) who are receiving mechanical ventilation are eligible to receive dexmedetomidine as a short-term sedative that has been approved by the Food and Drug Administration (FDA). In the current investigation, fentanyl and dexmedetomidine were compared with regard to the effectiveness of their use as adjuvants to subarachnoid block.^[8,9]

Material and Methods

At Anesthesiology and Intensive Care, Nizams Institute of Medical Sciences, Hyderabad, Telangana, India, 60 patients undergoing elective lower limb surgery under spinal anaesthetic participated in a randomised trial from 01-06-2017 to 31-04-2018. The institutional ethics committee gave its approval to the project. Patient groups were split into two. Patients in Group D (30) received 2.5 ml of hyperbaric bupivacaine and 5 µg of intrathecal dexmedetomidine. Patients in Group F (30) received 2.5 ml of hyperbaric bupivacaine and 25 µg of intrathecal fentanyl.

The circulatory, pulmonary, and central nervous systems were all thoroughly examined before any anaesthesia was administered to all of the patients, and the spine was checked for deformity and infection. The patient gave written, fully informed consent. Baseline values for the following parameters were recorded: heart rate, systolic, diastolic, mean arterial pressure, and spo₂. Using a visual analogue pain scale, the assessment of sensory blockade, assessment of motor blockade, postoperatively, and the pain score were all recorded. When the VAS was greater than 3 or at the patient's request, intravenous paracetamol was administered as a rescue analgesic. It was noted how frequently negative symptoms including respiratory depression, hypotension, pruritis, nauseousness, vomiting, and shivering occurred.

In order to do the statistical analysis, SPSS 18 and R environment ver. 3.2.2 were used. In the current study, descriptive and inferential statistical analysis was completed. Results for categorical data were shown as percentages (%) while results for continuous data were shown as Mean SD. The 5% level of significance is used to determine significance.

Inclusion criteria

1. Patients of any gender.
2. Individuals with ASA Grades I and II
3. Individuals between the ages of 18 and 60

Exclusion criteria

1. ASA Grade-III and Grade-IV cases.
2. Persons who should not have central neuraxial blockade
3. Individuals taking alpha blockers,
4. Individuals with serious concomitant illnesses, such as ischemic cardiovascular disease, hypertension, renal impairment, and severe liver problem.

RESULTS

Table 1: Age distribution

Age in years	Fenta group F	Dexmed group D	Total
<20	1(3.3%)	4(13.3%)	5(8.3%)
20-30	10(33.3%)	3(10%)	13(21.7%)
31-40	10(33.3%)	6(20%)	16(26.7%)
41-50	5(16.7%)	5(16.7%)	10(16.7%)
51-60	2(6.7%)	5(16.7%)	7(11.7%)
61-70	2(6.7%)	7(23.3%)	9(15%)
Total	30(100%)	30(100%)	60(100%)
Mean ± SD	36.70±12.87	44.53±17.59	40.62±15.79
Test	Student t test		
P - value	0.101		
Inference	Not significant		

Group D patients were 44.53±17.59 and Group F 36.70±12.87. Two groups had similar ages.

Table 2: Gender distribution

Gender	Fenta Group F	Dexmed Group D	Total
Female	8(26.7%)	11(36.7%)	19(31.7%)
Male	22(73.3%)	19(63.3%)	41(68.3%)
Total	30(100%)	30(100%)	60(100%)
Test	Chi-Square Test		
p-value	0.405		
Inference	Not Significant		

Groups F and D had similar gender distributions.

Table 3: ASA grade distribution in two groups

ASA Grade	Fenta	Dexmed	Total
I	22(73.3%)	24(80%)	46(76.7%)
II	8(26.7%)	6(20%)	14(23.3%)
Total	30(100%)	30(100%)	60(100%)
Test	Chi-Square Test		
p- value	0.542		
Inference	Not Significant		

Groups F and D had similar ASA grade distributions.

Table 4: BMI (kg/m²) distribution.

BMI (kg/m ²)	Fenta	Dexmed	Total
<18.5	2(6.7%)	1(3.3%)	3(5%)
18.5-25	12(40%)	19(63.3%)	31(51.7%)
25-30	13(43.3%)	9(30%)	22(36.7%)
>30	3(10%)	1(3.3%)	4(6.7%)
Total	30(100%)	30(100%)	60(100%)
Test	Fisher Exact Test		
p-value	0.348		
Inference	Not Significant		

Two groups had similar BMI distributions.

Table 5: Perioperative heart rate.

Heart rate (bpm)	Fenta	Dexmed	Total	P value
Base line	91.87±12.45	87.90±11.42	89.88±12.01	0.204
5 mins	91.33±14.88	82.40±13.60	86.87±14.83	0.018*
10	88.03±14.59	73.67±11.16	80.85±14.78	<0.001**
15	87.80±15.15	78.40±14.46	83.10±15.43	0.017*
20	83.77±14.14	74.53±9.22	79.15±12.72	0.004**
25	82.90±12.49	73.13±8.70	78.02±11.75	0.001**
30	82.27±14.46	71.03±9.04	76.65±13.23	0.001**
45	82.27±14.28	72.73±9.66	77.50±13.01	0.004**
60	79.83±9.85	71.83±7.48	75.83±9.57	0.001**
90	82.43±12.70	74.23±10.45	78.33±12.25	0.008**
120	82.53±13.40	75.53±8.85	79.03±11.80	0.020*
150	83.33±10.96	74.37±9.23	78.85±11.02	0.001**
180	85.63±10.76	75.10±9.29	80.37±11.29	<0.001**

Student t test (Two tailed, independent)

Dexmedetomidine reduces heart rate compared to fentanyl at 5,10,15,20,25,30,45,60,90,120,150, and 180 minutes.

Table 6: Perioperative SBP

SBP(mm Hg)	Fenta	Dexmed	Total	P value
Base line	125.92±15.59	124.43±12.29	125.18±13.94	0.581
5 mins	119.97±17.43	116.63±11.25	118.30±14.64	0.382
10	116.73±14.45	111.03±10.91	113.88±13.02	0.090+
15	114.60±11.51	108.10±10.95	111.35±11.61	0.029*
20	111.83±10.69	105.83±8.20	108.83±9.92	0.018*
25	110.90±9.12	98.87±25.68	104.88±20.04	0.019*
30	113.20±10.67	103.87±9.08	108.53±10.89	0.001**
45	111.27±10.75	103.67±7.63	107.47±10.00	0.003**
60	112.77±10.01	104.27±7.39	108.52±9.72	<0.001**
90	112.03±11.06	105.27±6.25	108.65±9.54	0.005**
120	114.27±9.11	106.47±6.27	110.37±8.70	<0.001**
150	117.37±9.04	105.53±6.25	111.45±9.75	<0.001**
180	123.13±11.41	106.73±6.22	114.93±12.30	<0.001**

Student t test (Two tailed, independent)

In the dexmedetomidine group, systolic blood pressure falls significantly at 15,20,25,30,45,60,90,120,150, and 180 minutes.

Table 7: Comparison of diastolic bloodpressure

DBP(mm Hg)	Fenta	Dexmed	Total	P value
Base	76.87±7.67	75.10±7.80	75.98±7.72	0.380
5 mins	70.60±9.53	70.07±8.66	70.33±9.03	0.821
10	68.40±8.40	69.50±7.02	68.95±7.69	0.584
15	68.30±7.44	67.90±6.60	68.10±6.98	0.826
20	69.00±7.27	67.67±7.36	68.33±7.29	0.483
25	68.83±8.00	67.67±8.14	68.25±8.02	0.578
30	68.50±8.47	66.93±7.62	67.72±8.03	0.454
45	67.97±8.05	64.57±7.22	66.27±7.77	0.090+
60	69.33±7.78	65.37±6.68	67.35±7.46	0.038*
90	70.20±6.77	66.23±6.66	68.22±6.95	0.026*
120	69.90±6.90	66.80±7.40	68.35±7.26	0.099+
150	71.43±6.26	67.93±6.58	69.68±6.61	0.039*
180	71.63±7.37	67.73±6.18	69.68±7.02	0.030*

Student t test (Two tailed, independent)

In the dexmedetomidine group, diastolic blood pressure falls significantly at 60,90,150, and 180 minutes. except at 5,15,20,25,30,45-minute intervals.

Table 8: Comparison of mean arterial pressure

MAP (mm Hg)	Fentanyl	Dexmed	Total	P value
Base line	92.97±7.49	91.57±6.04	92.46±7.05	0.429
5 mins	87.10±10.09	85.53±6.75	86.32±8.55	0.483
10	84.47±8.33	83.33±5.73	83.90±7.11	0.542
15	83.80±6.64	81.37±6.60	82.58±6.68	0.160
20	83.33±6.28	80.43±6.17	81.88±6.34	0.076+
25	82.80±6.60	78.03±10.73	80.42±9.15	0.043*
30	83.33±7.12	79.17±6.38	81.25±7.02	0.020**
45	82.40±6.87	77.60±5.90	80.00±6.80	0.005**
60	83.83±6.41	78.33±5.72	81.08±6.63	0.001**
90	84.13±5.72	79.23±5.26	81.68±5.98	0.001**
120	84.67±5.57	79.93±5.41	82.30±5.94	0.001**
150	86.80±5.39	80.50±4.75	83.65±5.96	<0.001**
180	88.87±6.89	80.60±4.24	84.73±7.04	<0.001**

Student t test (Two tailed, independent)

Table 9: Comparison of spo2%

SpO2%	Group FFenta	Group DDexmed	Total	P value
Base line	98.97±0.85	99.03±0.67	99.00±0.76	0.737
5 mins	100.00±0.00	100.00±0.00	100.00±0.00	-
10	100.00±0.00	100.00±0.00	100.00±0.00	-
15	100.00±0.00	100.00±0.00	100.00±0.00	-
20	100.00±0.00	100.00±0.00	100.00±0.00	-
25	100.00±0.00	100.00±0.00	100.00±0.00	-
30	100.00±0.00	100.00±0.00	100.00±0.00	-
45	100.00±0.00	100.00±0.00	100.00±0.00	-
60	100.00±0.00	100.00±0.00	100.00±0.00	-
90	100.00±0.00	100.00±0.00	100.00±0.00	-
120	100.00±0.00	100.00±0.00	100.00±0.00	-
150	100.00±0.00	100.00±0.00	100.00±0.00	-
180	100.00±0.00	100.00±0.00	100.00±0.00	-

Student t test (Two tailed, independent)

Both groups had similar SPO2 distributions.

Table 10: Highest sensory level distribution in two groups

Highest Sensory Level	Group FFenta	Group DDexmed	Total
T10	20(66.7%)	20(66.7%)	40(66.7%)
T8	10(33.3%)	9(30%)	19(31.7%)
T6	0(0%)	1(3.3%)	1(1.7%)
Total	30(100%)	30(100%)	60(100%)
Test	Fisher Exact Test		
p-value	1.000		
Inference	Not Significant		

Table 11: Comparison of study variables

Variables	Group F Fenta	Group D Dexmed	Total	p value	Inference
Time for 2 segment regression	81.67±12.82	123.00±13.46	102.33±24.58	<0.001**	S
Injection to onset of sensory blockade (mins)	3.60±1.76	3.42±1.81	3.51±1.77	0.692	NS
Duration of sensory blockade(mins)	168±14.77	430.50±25.84	299.25±133.99	<0.001**	S
Onset of motor blockade(mins)	4.57±1.72	4.63±1.83	4.60±1.76	0.885	NS
Duration of motor blockade(mins)	139.83±14.41	401.50±22.37	270.67±133.25	<0.001**	S
Time to rescue analgesia	151.00±13.80	283.67±34.74	217.33±71.84	<0.001**	S

Student t test (Two tailed, independent)

Table 12: No. of post OP analgesia distribution

No. of Post op analgesia	Fenta	Dexmed	Total
1	0(0%)	5(16.7%)	5(8.3%)
2	0(0%)	17(56.7%)	17(28.3%)
3	14(46.7%)	8(26.7%)	22(36.7%)
4	9(30%)	0(0%)	9(15%)
5	7(23.3%)	0(0%)	7(11.7%)
Total	30(100%)	30(100%)	60(100%)
Test	Fisher Exact Test		
p-value	<0.001**		
Inference	Significant		

Table 13: Incidence of adverse effects

	Fenta (n=30)	Dexmed (n=30)	Total (n=60)	P value	Inference
Nausea	1(3.3%)	1(3.3%)	2(3.3%)	1.000	NS
Vomiting	1(3.3%)	0(0%)	1(1.7%)	1.000	NS
Bradycardia	0(0%)	1(3.3%)	1(1.7%)	1.000	NS
Test	Chi-Square/Fisher Exact Test				

DISCUSSION

In comparison to 25 mg of intrathecal fentanyl, 5 mg of dexmedetomidine added to spinal bupivacaine prolonged the sensory and motor block. Over Fentanyl, Dexmedetomidine provided better analgesia. One of the most important advancements in pain management has been the identification of opioid receptors as well as the development of intrathecal, epidural, and nonopioid adjuvant delivery systems. To prolong and improve the quality of intrathecal

local anaesthetics, drugs such as opioids, ketamine, clonidine, and neostigmine are added. Their usage is restricted by nystagmus, pruritus, urinary retention, respiratory depression, hemodynamic instability, nystagmus, nausea, and vomiting. Local anaesthetics' extended motor and sensory block is made possible by intrathecal α_2 adrenoreceptor agonists. Intrathecal α_2 adrenoreceptor agonists and local anaesthetics may have an additive or synergistic effect. Local anaesthetics shut down sodium channels, and α_2 agonists bind to dorsal horn neurons and C-fibers. By preventing the release of C-fiber transmitters and hyperpolarizing dorsal horn neurons, analgesia is induced. Strong analgesic effects are produced by local anaesthetics and α_2 adrenoreceptor agonists. By attaching to dorsal horn α_2 adrenoreceptor agonists, spinal anaesthetics can prolong the duration of a motor block.^[9,10]

Dexmedetomidine is an effective and secure therapeutic adjunct because it is eight times more specific and selective than Clonidine. Opioid receptors were identified in the CNS in 1971. These receptors were discovered in the spinal cord's posterior horn in 1977. Intrathecal opioid effectiveness is based on bioavailability. Medullary penetration is influenced by molality, ionisation, and lipophilicity. Morphine absorbs more slowly than fentanyl and meperidine. They more tightly connect neural tissue. Clearance is determined by vascular absorption and neuraxis diffusion. The cerebello-medullary cistern's arachnoid granulations absorb the drug there, particularly morphine. The vertebral vasculature of the location reabsorbs lipophilic substances. Analgesia during and after surgery is increased by neuraxial opioids and local anaesthetics. Highly hydrophilic opioids like morphine are efficient in relieving pain before and after surgery, but their use is constrained by their rostral intrathecal dispersion. An opioid with a quick intrathecal onset is fentanyl. Safer than morphine, it is a frequent addition to hyperbaric bupivacaine. Intrathecal fentanyl may produce serotonin syndrome, as well as itching, nausea, and vomiting.^[10,11]

Sixty patients, 18–60 years old, of either sex, with ASA Grades I and II were randomly split into two groups (n=30). Randomness was produced by computers. Both Group D and Group F got 3 ml of hyperbaric Bupivacaine 0.5% along with 5 g of dexmedetomidine and 25 g of fentanyl, respectively. To achieve subarachnoid block, 3.5 ml were given to each group. The dexmedetomidine intrathecal dose used in this study was based on earlier human research that had no neurotoxic side effects. Intrathecal hyperbaric bupivacaine was used with 25 micrograms of fentanyl in 1995 by BN Biswas et al and Khanna MS et al. In our investigation, hyperbaric bupivacaine was combined with 25 micrograms of fentanyl. A high drug concentration at 2-adrenoreceptors in the spinal cord is attained by intrathecal injection of 2-adrenergic agonists, which inhibits C and A delta fibre conduction, raises potassium conductance, and intensifies local anaesthetic conduction block.^[11,12]

Al-Mustafa MM et al. noted that bupivacaine spinal anaesthesia was prolonged by intravenous dexmedetomidine. Dexmedetomidine bolus and 0.5g/kg/hr doses were required. The total dose of dexmedetomidine administered intrathecally ranges from 3 g to 15 g. Lower doses are possible with intrathecal administration since it is more accurate. Intrathecal dexmedetomidine was also used in our experiment. Lipophilic opioids lengthen the sensory block without lengthening the motor block or the duration of recovery. Patients undergoing laparoscopic surgery who were randomly assigned to receive either low dose hypobaric lidocaine (25 mg) with 25 g intrathecal fentanyl or plain hyperbaric lidocaine (75 mg) experienced less hypotension, required less I.V. propofol plus alfentanil supplementation, and recovered more quickly. For postoperative analgesia and the restoration of pulmonary function, spinal opioids are preferred by Ballantyne et al. above intermittent intramuscular opioids, PCA with intravenous opioids, intercostal block, or interpleural analgesia.^[12,13]

Intrathecal administration was used in our study. Age, body mass index, and height did not significantly differ across groups. Each group operated similarly. In order to prevent intraoperative and postoperative variations, all groups used the same parameters. Here are the

study's findings. Two-segment regression, sensory blockade, motor block, duration of motor block post-operative analgesia, hemodynamic stability, and adverse drug reactions. The sensory blockade began in Group F at 3.60 ± 1.76 minutes and in Group D at 3.42 ± 1.81 minutes. Both groups did not differ statistically. Dexmedetomidine and Fentanyl were used as adjuvants to isobaric Bupivacaine by Al Ghanem et al. (2009), and they discovered no difference in onset time ($P = 0.95$). Similar onset periods were observed when 5 g of dexmedetomidine and 25 g of fentanyl were used as adjuvants to hyperbaric bupivacaine by Gupta et al. (2011). In Group D, the motor blockade began at 4.63 ± 1.83 and in Group F, at 4.57 ± 1.72 . In terms of statistics, the groups did not differ.^[13,14,15]

Similar onset periods were observed when 5 g of dexmedetomidine and 25 g of fentanyl were used as adjuvants to hyperbaric bupivacaine by Gupta et al. (2011). Total sensory recovery in the current study took 168 ± 14.77 minutes in Group F and 430 ± 25.84 minutes in Group D. Group D suffered persistent sensory deprivation. difference that is statistically significant Longer than Fentanyl, dexmedetomidine promotes sensory blocking. The motor recovery time for Group F was 139.83 ± 14.41 minutes, compared to 401.50 ± 22.37 minutes for Group D. The motor blockade was lengthier in Group D. difference that is statistically significant More motor obstruction is induced by dexmedetomidine than by fentanyl.^[15-17]

The effects of intrathecal Clonidine and Dexmedetomidine on 60 patients undergoing transurethral prostate or bladder tumour excision under spinal anaesthesia were examined by G.E. Kanazi, M.T. Aouad, et al. in 2006. There were 20 patients per group. Bupivacaine (12 mg) was given to Group B, hyperbaric (12 mg) bupivacaine (3 mg) was given to Group D, and clonidine (30 mg) was given to Group C. The timings of sensory and motor start and regression were noted. We also kept track of sedation and hemodynamic changes. In comparison to Group B, Groups D and C displayed earlier onset of motor block and longer sensory and motor regression periods. In Group D, the mean sensory regression to the S1 segment was 303 ± 75 min, in Group C it was 272 ± 38 min, and in Group B it was 190 ± 48 min (B vs.D and B vs.C, $P < 0.001$). It took 250 ± 76 minutes for Group D's motor block to regress to Bromage 0 (B vs. D and B vs. C, $P 0.001$). The commencement and regression times for groups D and C were comparable. Dexmedetomidine or clonidine added to bupivacaine spinal block results in a slower onset of motor block and a longer sensory and motor block than bupivacaine alone.^[17,18]

A double-blind controlled trial with 76 patients planned for vaginal hysterectomy, vaginal wall reconstruction, and tension-free vaginal tape was carried out in 2009 by Subhi M. Al-Ghanem, Islam M. Massad, et al. They investigated the onset, elapsed time, analgesia throughout surgery, and adverse reactions of intrathecal dexmedetomidine or fentanyl combined with 0.5% bupivacaine. Hemodynamic changes, adverse effects, and the onset time to the maximum degree of sensory and motor function were also noted. In comparison to group F, group D displayed longer sensory and motor block durations. Sensory regression took 274 ± 73 minutes in Group D and 179 ± 47 minutes in Group F. ($P 0.001$). In Group D, motor block regression to modified bromage-0 was 240 ± 60 min, and in Group F, it was 155 ± 46 min ($P 0.001$). T10 dermatome, peak sensory level, and modified bromage-3 motor block onset timings were comparable across the two groups.^[18,19]

In comparison to 25mg of fentanyl, 10mg of bupivacaine and 5mg of dexmedetomidine causes a longer motor and sensory block in female patients having vaginal reconstructive surgery. The effects of dexmedetomidine or fentanyl delivered intrathecally with 0.5% bupivacaine on hemodynamics, postoperative analgesia, and side effects were examined by Gupta R, Verma R, Bogra J, et al. in 2011. Patients who are ASA classifications I and II undergoing lower abdominal surgery. In group D ($n = 30$), patients received 12.5 mg of hyperbaric bupivacaine together with 5 g of dexmedetomidine, while in group F ($n = 30$), patients received 12.5 mg of hyperbaric bupivacaine along with 25 g of fentanyl. Patients on

dexmedetomidine exhibited longer sensory and motor block periods than those taking fentanyl (F). Sensory regression took 47.6+23 minutes in group D and 18.7+12 minutes in group F ($P < 0.001$). A modified Bromage 0 was reached in 42.1+21 minutes in group D and 149.18 minutes in group F ($P < 0.001$). When compared to fentanyl, intrathecal dexmedetomidine prolongs the duration of the motor and sensory block, maintains hemodynamic stability, and lessens the requirement for rescue analgesics within 24 hours. The Time to 2 Segment Regression for Group F was 81.67+12.82 minutes, whereas that for Group D was 123.00+13.46 minutes. The decline in Group D persisted longer. difference that is statistically significant These results were in line with those of Gupta R, Verma R, Bogra J, et al. (2011), who discovered that patients receiving Dexmedetomidine (120+22.2 mins) rather than Fentanyl (76 +20.3 mins) as adjuvants to hyperbaric Bupivacaine had a longer duration to 2 segment regression ($P = 0.001$). In our study, Group F had the earliest request for analgesics at 151.00+13.80 minutes, whereas Group D had the earliest at 283.67+34.74 minutes. Later, Group D asked for analgesics. difference that is statistically significant.^[19,20]

A randomised, double-blind trial on the analgesic effectiveness of intrathecally administered dexmedetomidine or dexmedetomidine combined with fentanyl was undertaken in 2012 by Mohamed AA, Fares KM, and Mohamed SA. Ninety patients received intrathecally either 10 mg of bupivacaine 0.5% (control group, $n = 30$), 10 mg of bupivacaine 0.5% plus 5 g of dexmedetomidine (dexmedetomidine group, $n = 30$), or 10 mg of bupivacaine 0.5% plus 25 g of fentanyl (dexmedetomidine+ group, $n = 30$). Hemodynamics, sedation level, pain intensity, when the first analgesic was requested, how many analgesics were used overall, and the initial 24-hour side effects were evaluated. The intraoperative heart rates of the dexmedetomidine and dexmedetomidine+ groups were lower than those of the control group ($P 0.05$). Additionally, there were no appreciable variations in postoperative hemodynamics or sedation levels between the dexmedetomidine group ($P 0.05$) and the dexmedetomidine+ group ($P 0.05$) compared to the control group in terms of intraoperative systolic and diastolic blood pressure.^[19,20]

When compared to the control group, dexmedetomidine and dexmedetomidine+ both decreased VAS ratings immediately after surgery and 12 hours later. The dexmedetomidine group (3.30 +0.87 hours, $P < 0.01$) and the dexmedetomidine+ group (5.41+1.23 hours, $P 0.01$) had significantly longer mean times before the first analgesic request than the control group (0.23+ 0.11 hours). Dexmedetomidine and dexmedetomidine+ groups consumed significantly less postoperative tramadol than the control group (310.0 + 12.08 mg). The investigation didn't uncover any significant adverse effects. After major abdominal cancer surgery, patients' postoperative analgesic quality and duration are enhanced by intrathecal administration of 5 g of dexmedetomidine. Fentanyl 25 mg intrathecal has no clinical advantage. According to Gupta et al., intrathecal Dexmedetomidine and Fentanyl improved the effectiveness of analgesics ($P 0.001$).

With less need for analgesics, Al-Mustafa et al. and Hala EA Eid et al. showed dose-dependent prolongation of the motor and sensory blockade. According to the study, Dexmedetomidine, when combined with intrathecal Bupivacaine, prolongs postoperative analgesia more than Fentanyl. Intrathecal Bupivacaine with Dexmedetomidine added improves postoperative analgesia and has a longer half-life than Fentanyl. blood pressure stability In comparison to fentanyl, dexmedetomidine lowers heart rate after 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, 150, and 180 minutes. Bupivacaine + Dexmedetomidine lowers mean arterial pressure more quickly (after 25 minutes) than Bupivacaine + Fentanyl. Bradycardia occurred in 1 patient in Group D without any discernible difference. To keep 100% SPO₂, O₂ (6 l/min) was administered to both groups while wearing a face mask. According to research by A.M. El-Hennawy, A.M. Abd-Elwahab, et al. (2009), caudal Bupivacaine significantly improved analgesia in children without creating significant hemodynamic

changes or side effects. When Catherin O. Hunt et al. studied intrathecal fentanyl with 10 mg of bupivacaine in 1987, they found no appreciable hemodynamic effects. In 1995, Singh et al. administered Fentanyl 25 mg and Bupivacaine 13.5 mg to urological patients. The cardiovascular characteristics of their patients were stable. Hemodynamics are unaffected when low dosages of Fentanyl, Dexmedetomidine, or Clonidine are combined with intrathecal Bupivacaine.^[20,21]

Our research supports it. The two main adverse effects of intrathecal α_2 agonists are bradycardia and hypotension. Brady cardia was only detected in one case of the Dexmedetomidine group in the current investigation. Since we combined high dose local anaesthetic with low dose intrathecal Dexmedetomidine and Fentanyl, these side effects were not severe. The near maximal sympatholysis of local anaesthetics was unaffected by these adjuvant concentrations. Nausea was reported by 1 patient on Dexmedetomidine and 1 patient on Fentanyl. One fentanyl patient passed out. Opioid intrathecal medications impair breathing. Without any respiratory depression, all of our patients kept their SpO₂ levels at 100%.^[21]

Variables In 1992, G. et al. examined the ventilatory effects of a number of intraethecal fentanyl dosages on elderly patients. They concluded that 50 g produced respiratory depression and advised 25 g as the only dose free from it. In this trial, pruritus—a frequent (49–100%) adverse effect of intrathecal Fentanyl—was not present. With the exception of the face, low doses of bupivacaine administered to intrathecal fentanyl reduce the incidence of pruritus from 95% to 36%. By reducing opioid receptor activity and increasing opioid binding to delta and kappa receptors, the combination of local anaesthetic and opioid may reduce pruritus. α_2 Adrenergic medications, according to Talke et al. and Maroof M et al., lessen shivering. No shivering was observed.^[21,22]

CONCLUSION

Intrathecally administered Bupivacaine combined with dexmedetomidine has been shown to produce longer-lasting sensory and motor blockage compared to intrathecal Bupivacaine administered with fentanyl in lower limb surgeries. An extended period of postoperative analgesia is provided with dexmedetomedine. Both of these medications help maintain steady hemodynamics. The addition of dexmedetomidine or fentanyl does not result in any notable adverse effects.

References

1. Dahlgren, G., Hultstrand, C., Jakobsson, J., Norman, M., Eriksson, E. W., & Martin, H. (1997). Intrathecal sufentanil, fentanyl, or placebo added to bupivacaine for cesarean section. *Anesthesia & Analgesia*, 85(6), 1288-1293.
2. Palmer, C. M., Van Maren, G., Nogami, W. M., & Alves, D. (1999). Bupivacaine augments intrathecal fentanyl for labor analgesia. *The Journal of the American Society of Anesthesiologists*, 91(1), 84-89.
3. Gupta, R., Verma, R., Bogra, J., Kohli, M., Raman, R., & Kushwaha, J. K. (2011). A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. *Journal of anaesthesiology clinical pharmacology*, 27(3), 339-343.
4. Grewal, A. (2011). Dexmedetomidine: new avenues. *Journal of anaesthesiology, clinical pharmacology*, 27(3), 297.
5. Al-Mustafa, M. M., Abu-Halaweh, S. A., Aloweidi, A. S., Murshidi, M. M., Ammari, B. A., Awwad, Z. M., ... & Ramsay, M. A. (2009). Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. *Saudi Med J*, 30(3), 365-70.
6. Routray, S., Ravi, K., & Mishra, D. (2015). Effect of Intrathecal Dexmedetomidine and Fentanyl as adjuvant to hyperbaric bupivacaine for orthopaedic lower limb and lower

- abdominal procedures: A double blind control study. *Indian Journal of Clinical Anaesthesia*, 2(4), 204-8.
7. Eid, H. E., Shafie, M. A., & Youssef, H. (2011). Dose-related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *Ain Shams J Anesthesiol*, 4(2), 83-95.
 8. Gupta, R., Bogra, J., Verma, R., Kohli, M., Kushwaha, J. K., & Kumar, S. (2011). Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. *Indian journal of anaesthesia*, 55(4), 347.
 9. Mohamed, A. A., Fares, K. M., & Mohamed, S. A. (2012). Efficacy of intrathecally administered dexmedetomidine versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. *Pain physician*, 15(4), 339.
 10. Lawhead, R. G., Blaxall, H. S., & Bylund, D. B. (1992, November). α -2A is the predominant α -2 adrenergic receptor subtype in human spinal cord. In *The Journal of the American Society of Anesthesiologists* (Vol. 77, No. 5, pp. 983-991). The American Society of Anesthesiologists.
 11. Gertler, R., Brown, H. C., Mitchell, D. H., & Silvius, E. N. (2001, January). Dexmedetomidine: a novel sedative-analgesic agent. In *Baylor University Medical Center Proceedings* (Vol. 14, No. 1, pp. 13-21). Taylor & Francis.
 12. Murthy, T. V. S. P., & Singh, R. (2009). Alpha 2 adrenoceptor agonist-dexmedetomidine role in anaesthesia and intensive care: A clinical review. *Journal of Anaesthesiology Clinical Pharmacology*, 25(3), 267-272.
 13. Bajwa, S. J. S., Bajwa, S. K., Kaur, J., Singh, G., Arora, V., Gupta, S., ... & Goraya, S. P. S. (2011). Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. *Indian journal of anaesthesia*, 55(2), 116.
 14. Salgado, P. F., Sabbag, A. T., Silva, P. C. D., Brienze, S. L., Dalto, H. P., Módolo, N. S., ... & Nascimento Jr, P. (2008). Synergistic effect between dexmedetomidine and 0.75% ropivacaine in epidural anesthesia. *Revista da Associacao Medica Brasileira* (1992), 54(2), 110-115.
 15. Biswas, B. N., Rudra, A., Bose, B. K., Nath, S., Chakrabarthy, S., & Bhattacharjee, S. (2002). Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post-operative period. *Indian Journal of Anaesthesia*, 46(6), 469-472.
 16. Ozkardesler, S., Gurpinar, T., Akan, M., Koca, U., Sarıkaya, H., Olmez, T., & Elar, Z. (2008). A possible perianesthetic serotonin syndrome related to intrathecal fentanyl. *Journal of clinical anesthesia*, 20(2), 143-145.
 17. Khanna, M. S., & Singh, I. K. (2002). Comparative evaluation of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients. *Indian Journal of Anaesthesia*, 46(3), 199-203.
 18. Filos, K. S., Goudas, L. C., Patroni, O., & Polyzou, V. (1992). Intrathecal clonidine as a sole analgesic for pain relief after cesarean section. *The Journal of the American Society of Anesthesiologists*, 77(2), 267-274.
 19. Hunt, C. O., Naulty, J. S., Bader, A. M., Hauch, M. A., Vartikar, J. V., Datta, S., ... & Ostheimer, G. W. (1989). Perioperative analgesia with subarachnoid fentanyl-bupivacaine for cesarean delivery. *Anesthesiology*, 71(4), 535-540.
 20. Asokumar, B., Newman, L. M., McCarthy, R. J., Ivankovich, A. D., & Tuman, K. J. (1998). Intrathecal bupivacaine reduces pruritus and prolongs duration of fentanyl analgesia during labor: a prospective, randomized controlled trial. *Anesthesia & Analgesia*, 87(6), 1309-1315.
 21. Vaghadia, H., McLeod, D. H., Mitchell, G. E., Merrick, P. M., & Chilvers, C. R. (1997). Small-dose hypobaric lidocaine-fentanyl spinal anesthesia for short duration outpatient

- laparoscopy. I. A randomized comparison with conventional dose hyperbaric lidocaine. *Anesthesia & Analgesia*, 84(1), 59-64.
22. Ballantyne, J. C., Carr, D. B., deFerranti, S., Suarez, T., Lau, J., Chalmers, T. C., & Mosteller, F. (1998). The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesthesia & analgesia*, 86(3), 598-612.