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Original Research Article

Comparison between intrathecal hyperbaric bupivacaine-fentanyl and intrathecal hyperbaric bupivacaine-saline in patients undergoing appendicectomy: A clinical study

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Abstract

Aim and Objectives: To compare the effects of intrathecal Bupivacaine-Fentanyl (25 µg) combination with that of intrathecal Bupivacaine-Saline combination in patients undergoing Appendicectomy under spinal anaesthesia with regard to, Characteristics of sensory block, Duration of motor block, Quality of surgical anaesthesia, Haemodynamic and respiratory changes, Adverse Effects, if any.

Methods: A total of 60 patients aged between 20 to 40 years of either sex belonging to ASA Grade I & II posted for elective Appendicectomy under Spinal Anaesthesia were selected randomly for the study during the period starting from December 2021 to November 2022, at Department of Anesthesia & Critical Care, Dr B.R Ambedkar Medical College, Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka, India. The Study was approved by the Hospital Ethical Committee.

Results: The incidence of intraoperative complications was compared in both the groups. The addition of Fentanyl to intrathecal Bupivacaine did not produce any significant cardiovascular changes (Bradycardia, Hypotension). Respiratory depression was not observed in either of the groups. Nausea & vomiting was seen in 16.6% of the patients in group BS as compared to 3.5% in Group BF. The incidence of pruritus was higher in Group BF but none of the patients required any medication. Postoperative analgesia was assessed by the VNRS score. A significantly lower VNRS score (superior pain relief) was observed in Group BF with average duration of analgesia being 5 hours. The patients were followed up for 24 hours and showed no neurological sequelae.

Conclusion: We conclude that the addition of 25mg of preservative free Fentanyl to hyperbaric Bupivacaine administered intrathecally to a patient undergoing Appendicectomy provides improved quality of surgical anaesthesia, haemodynamic stability and significant post- operative analgesia with minimal side effects. However, the study needs to be conducted on a larger population for further evaluation.

Keywords: Bupivacaine-Saline, fentanyl, analgesia, intraoperative complications

Introduction

Pain, now regarded as the '5th vital sign' causes stimulation of sympathetic nervous system & subsequent tachycardia, increased stroke volume & increased cardiac workload. Hence, of the many roles performed by the modern anesthesiologist, alleviation of pain intra-operatively and post-operatively assumes paramount priority & necessity [1]. Pain is a multi-dimensional experience, comprising of a sensory & an affective component & the lower abdominal surgeries have a very high affective component. Visceral pain is characterized by an

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unspecific, diffuse, dull aching pain that tends to radiate. Additionally, it is accompanied by a sense of malaise, and when it is severe, it causes powerful autonomic phenomena. Along with pain, one may also experience other unpleasant sensations like choking or a feeling of a full stomach.

In some instances, the pain arising from viscera is referred to the skin and other somatic structures at considerable distance from the diseased viscus. Adequate stimuli that provoke visceral pain include spasm of smooth muscles of hollow viscera, contraction of gastrointestinal tracts, sudden distension, stretching of these structures, inflammation of the lining of the hollow viscera, chemical or mechanical stimuli applied to the inflamed mucous membrane of these structures and traction, compression or twisting of the mesentry or blood vessels [2]. Of all the surgeries performed, lower abdominal surgeries form a sizeable portion and Appendicectomies form a considerable number. Neuraxial block for Appendicectomy has been increasingly popular. Spinal anesthesia is commonly employed for Appendicectomy. Spinal anaesthesia is preferred to epidural anesthesia because it takes less time to perform, faster in onset, provides consistent and reliable block and excludes risk of aspiration. Some patients complain of pain when the appendix is retracted or the mop is put in the abdomen.

Many studies have shown that the addition of opioids to intrathecal local anaesthetic improves the quality of surgical anaesthesia and post-operative analgesia. Since their introduction into clinical practice in 1979 by Wang *et al*., intrathecal opioids have grown significantly in popularity in a variety of clinical settings, either used alone as the only anesthetic agent or in conjunction with a local anesthetic [3]. The initial opioid used intrathecally was morphine. However, because of the slower uptake, longer duration of action, higher CSF concentration, and rostral spread of the opioid, it was linked to side effects like respiratory depression, nausea, and vomiting. The use of more recent synthetic opioids like Fentanyl, Sufentanil, and Alfentanil was brought into focus by these factors.

Fentanyl, a highly lipophilic drug has rapid uptake & shorter duration of action with low CSF concentration with limited rostral spread of the drug & hence lesser deleterious effects as compared to Morphine. Segmental analgesia induced by spinal administration of Fentanyl has a role in the management of a wide variety of surgical & non-surgical painful conditions & it has been used successfully to treat intraoperative & postoperative pain [4, 5]. The use of newer opioids in spinal anaesthesia as a potent adjuvant to local anaesthetic has gained widespread popularity since it provides excellent, reliable and safe pain relief to the patients undergoing surgeries. The present study is aimed at evaluating the efficacy of intrathecal Fentanyl as an adjuvant to intrathecal Bupivacaine in patients undergoing Appendicectomy.

Materials and Methods

A total of 60 patients aged between 20 to 40 years of either sex belonging to ASA Grade I & II posted for elective Appendicectomy under Spinal Anaesthesia were selected randomly for the study during the period starting from December 2021 to November 2022, at Department of Anesthesia & Critical Care, Dr B.R Ambedkar Medical College, Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka, India. The Study was approved by the Hospital Ethical Committee.

Inclusion criteria

- Patients of either sex aged between 20-40 years.
- ASA grade I & II patients.

Exclusion criteria

- Patients with hepatic & renal disorders; • Patients with cardio-respiratory disorders.
- Individuals with ASA Grade III or higher.
- People who are hypersensitive to local anesthetics.
- Patients taking pain-modifying medications.
- People who take aspirin while taking anticoagulants.
- People who have skin infections in the lumbar region.

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- Patients who already have spinal or neurological disorders or who have a gross spinal abnormality.

Results

A comparative study of 60 patients undergoing Appendicectomy under Spinal Anaesthesia randomized into 2 groups with 30 patients in Group BS (Bupivacaine- Saline) & 30 patients in Group BF (Bupivacaine-Fentanyl) is undertaken to assess the quality of surgical anaesthesia, haemodynamic parameters & the complications between the 2 groups.

Table 1: Drug administration

Group	No. of patients	Drug administered
BS	30	3cc (15mg) of Inj Bupivacaine 0.5% heavy + 0.5cc of Normal Saline.
BF	30	3cc (15mg) of Inj Bupivacaine 0.5% heavy + 0.5cc (25µg) of preservative free Fentanyl

Table 2: Age Distribution

Age (Years)	BS(n=30)	BF(n=30)
21-25	12	10
26-30	6	11
31-35	6	6
36-40	6	3
Range(years)	21-40	21-39
Mean ± SD	28.5333 ± 6.21862	28.1 ± 5.12835
'p' value	0.7722	
Remarks	Not significant	

Table 2 showing the age-wise distribution in both the groups BS and BF. It was observed that the minimum age was 21 years & maximum age was 40 years, mean age group in group BS was 28.53 ± 6.21 years and was 28.1±5.12 years in group BF with p value 0.772 (p>0.05) found to be not significant.

Table 3: Basic characteristics of the Study

Basic Characteristics		Group BS	Group BF	Remarks
Number of patients		30	30	-
Age in years (Mean ± SD)		28.5333 ± 6.21862	28.1 ± 5.12835	Age matched samples with p=0.7722
Height in cms (Mean ± SD)		156.5667 ± 5.37352	157.033 ± 8.8336	Height matched samples with p=0.808
Weight in Kgs (Mean ± SD)		59.7 ± 5.3765	58.76667 ± 7.82429	Weight matched samples with p=0.5753
Sex	Male	15 (50%)	13(43%)	Sex matched samples with p=0.605

Table 3 showing the basic characteristics of the study. Sex distribution was found to be equal in group BS and in group BF 13(43%) male patients & 17(57%) female patients. The p value was observed to be 0.772 & was found to be statistically not significant.

The mean height in group BS was 156.56 ± 5.37 cms and 157.03 ± 8.8 cms in group BF with p value being 0.808 and found to be statistically not significant.

The mean weight in group BS was 59.7 ± 5.37 kgs and 58.76 ± 7.82 kgs in group BF with p value being 0.57 and found to be statistically not significant.

Table 4: Comparison of study parameters between the two groups

Study parameters	Group BS	Group BF	p value	Remarks
Onset of sensory block (minutes)	2.6667 ± 0.71116 (1-4)	2.9 ± 0.71197 (2-4)	0.1287	Not significant
Onset of T6 blockade (minutes)	4.83333 ± 0.74664 (4-6)	4.66667 ± 0.6608 (3-5)	0.305	Not Significant

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Duration of Sensory block (minutes)	94.666 ± 14.0155 (80-109)	160 ± 22.44085 (137-183)	<0.001	Very Highly Significant
Onset of motor block (minutes)	6.6 ± 1.03724 (5-8)	6.56667 ± 1.0063 (5-8)	0.913	Not Significant
Duration of motor block (minutes)	145.1667 ± 16.78892 (128-162)	150.5 ± 15.33252 (177-210)	0.201	Not Significant
Duration of analgesia (minutes)	148.33333 ± 12.8876 (135-162)	292 ± 20.19730 (271-313)	<0.001	Very Highly Significant

Results are presented in Mean ± SD (Min-Max)

Table 4(a): Onset of Sensory Blockade

Onset of Sensory Blockade				
Group	**Range (minutes)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(1-4)	2.6667 ± 0.71116	0.1287	Not Significant
BF	(2-4)	2.9 ± 0.71197		

The Table 4(a) and Figure – 24 show the time of onset of sensory blockade. In group BS, the mean onset time was 2.6 ± 0.7 minutes (Range 1-4 mins). In group BF, the mean onset time was 2.9 ± 0.7 minutes (Range 2-4 mins). The p value was observed 0.1287 (p>0.05) and hence statistically not significant.

Table 4(b): Onset of T6 Blockade

Onset of T6 Blockade				
Group	**Range (mins)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(4-6)	4.83333 ± 0.74664	0.305	Not Significant
BF	(3-5)	4.66667 ± 0.66089		

The Table 4(b) shows the time of onset of sensory blockade at T6 level. In group BS, the range for onset of sensory blockade was 4-6 minutes with mean onset time being 4.83 ± 0.7 minutes. In group BF, the range for onset of sensory blockade was 3-5 minutes with mean onset time being 4.66 ± 0.66 minutes. The p value was observed 0.305 (p>0.05) and hence statistically not significant.

Table 4(c): Comparison of maximal sensory blockade between two groups

Maximal Sensory Blockade	Group BS	Group BF	p value
T6	13 (43.3%)	7(23.3%)	0.1322
T5	13 (43.3%)	10(33.33%)	
T4	4 (13.3%)	13(43.33%)	

p value obtained by Fischer Exact test.

The level of maximal sensory blockade was studied in both the groups. In group BS, 13 patients (43.3%) achieved blockade upto T6 & 13 patients (43.3%) achieved blockade upto T5 and 4 patients (13.3%) achieved upto T4 level. In group BF, 7(23.3%) patients achieved blockade upto T6 level, 10 (33.3%) patients achieved upto T5 & 13 patients (43.3%) upto T4 level. The p value obtained was 0.1322 and was statistically not significant.

Table 4(d): Duration of sensory block

Duration of sensory block				
Group	**Range (minutes)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(80-109)	94.666 ± 14.0155	<0.001	Very Highly Significant
BF	(137-183)	160 ± 22.44085		

The Table 4(d) showing the duration of sensory blockade. In group BS, the range was 80-109

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minutes with mean duration of sensory blockade being 94.6 ± 14.01 minutes. In group BF, the range was 137-183 minutes with mean duration of sensory blockade being 160 ± 22.4 minutes. The p value was observed to be < 0.001 and hence statistically very highly significant.

Table 4(e): Onset of motor block

Onset of motor block				
Group	**Range (mins)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(5-8)	6.6 ± 1.03724	0.913	Not Significant
BF	(5-8)	6.56667 ± 1.0063		

The Table 4(e) showing the onset of motor block. In group BS, the range was 5-8 mins with mean onset time for motor blockade being 6.6 □ 1.03 mins. In group BF, the range was 5-8 mins with mean onset time for motor blockade being 6.56 □ 1.00 mins. The p value was 0.913 which was statistically not significant.

Table 4(f): Duration of motor blockade

Duration of motor blockade				
Group	**Range (minutes)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(128-162)	145.1667 ± 16.78892	0.201	NS
BF	(131-171)	150.5 ± 15.33252		

The Table 4(f) showing the duration of motor block. In group BS, the range was 128-162 minutes with mean duration of motor blockade being 145.16 ± 16.78 minutes. In group BF, the range was 131-171 minutes with mean duration of motor blockade being 150.5 ± 15.33 minutes. The p value was observed to be 0.201 and hence statistically not significant.

Table 4(g): Duration of analgesia (mins)

Duration of analgesia(mins)				
Group	**Range (mins)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(135-162)	148.33333 ± 12.88767	<0.001	VHS
BF	(271-313)	292 ± 20.19730		

The Table 4(g) showing the duration of analgesia. In group BS, the range was 135- 162 mins with mean duration of analgesia being 148.33 ± 12.88 mins. In group BF, the range was 271-313 minutes with mean duration of analgesia being 292 ± 20.19 mins. The p value was observed to be < 0.001 and hence statistically very highly significant.

It was observed in our study that all the patients in both the groups (BS & BF) were awake and alert (grade 0 – no sedation). Hence, this parameter was not comparable & statistically not significant.

Table 5: Comparison of Intraoperative Discomfort between the two groups

Study Period (mins)	**Group BS Intraoperative discomfort Score**				**Group BF Intraoperative discomfort Score**			
	0	1	2	3	0	1	2	3
0	30	0	0	0	30	0	0	0
2	30	0	0	0	30	0	0	0
4	30	0	0	0	30	0	0	0
6	30	0	0	0	30	0	0	0
8	30	0	0	0	30	0	0	0
10	30	0	0	0	30	0	0	0
12	30	0	0	0	30	0	0	0
14	30	0	0	0	30	0	0	0

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16	29	0	1	0	30	0	0	0
18	29	1	0	0	30	0	0	0
20	29	1	0	0	29	1	0	0
25	30	0	0	0	30	0	0	0
30	30	0	0	0	30	0	0	0
35	30	0	0	0	30	0	0	0
40	30	0	0	0	30	0	0	0
45	30	0	0	0	30	0	0	0
50	30	0	0	0	30	0	0	0
55	30	0	0	0	30	0	0	0
60	30	0	0	0	30	0	0	0
65	30	0	0	0	30	0	0	0
70	30	0	0	0	30	0	0	0
75	30	0	0	0	30	0	0	0
80	30	0	0	0	30	0	0	0
85	30	0	0	0	30	0	0	0
90	30	0	0	0	30	0	0	0
p value Remark	0.308 Not Significant							

Table 5 showing intraoperative discomfort score between the two groups. It was observed that the scores were comparable in both the groups. In group BS, 3 patients on the whole complained of intraoperative discomfort of which 2 patients had Grade 1 & one patient had Grade 2 discomfort. In group BF, one patient had Grade1 discomfort. The p value was 0.308 & hence statistically not significant. It was observed in our study that the patients in Fentanyl group had lesser incidence of intraoperative discomfort.

Table 6: Comparison of Heart Rate between two groups

Study period	Group BS		Group BF		'p' value
	Mean	SD	Mean	SD	
0 minutes	78.83	09.60	78.70	12.01	0.963
2 minutes	78.43	09.72	78.90	12.79	0.873
4 minutes	78.00	10.13	78.27	12.99	0.929
6 minutes	78.67	10.08	77.97	11.46	0.803
8 minutes	79.00	09.38	78.53	11.16	0.860
10 minutes	78.97	09.24	79.33	10.46	0.888
12 minutes	79.53	10.52	79.70	09.12	0.947
14 minutes	80.43	10.69	79.13	09.67	0.623
16 minutes	80.47	11.39	78.43	10.24	0.469
18 minutes	80.07	11.37	77.57	10.13	0.372
20 minutes	81.00	12.77	78.07	10.00	0.327
25 minutes	81.33	12.49	77.23	09.71	0.161
30 minutes	80.17	12.14	77.67	10.56	0.398
35 minutes	79.87	11.21	78.23	09.77	0.548
40 minutes	79.13	11.75	79.27	10.77	0.962
45 minutes	80.00	12.31	77.33	11.64	0.392
50 minutes	80.90	11.34	77.90	11.35	0.310
55 minutes	81.07	11.39	78.80	10.91	0.434
60 minutes	79.77	11.81	79.07	10.71	0.811
65 minutes	81.90	10.58	78.63	11.48	0.256
70 minutes	81.77	09.47	79.63	10.51	0.411
75 minutes	81.67	09.52	79.93	11.48	0.525
80 minutes	82.33	09.27	79.83	12.47	0.382
85 minutes	81.50	08.00	80.50	12.14	0.708
90 minutes	82.20	08.21	81.23	11.35	0.706

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Table 6 (a): Comparison of Heart Rate between two groups

Comparison of Heart Rate between two groups				
Group	**Range (minutes)**	**Mean ± SD**	**'p' value**	**Remarks**
BS	(69-91)	80.2800 ± 10.5752	(p=0.628)	Not Significant.
BF	(67-90)	78.7938 ± 10.9952		

Results are presented in Mean ± SD (Min-Max)

We observed in our study that there was no significant inter-group difference with regards to heart rate. The p value was 0.628 which was not statistically significant. The addition of Fentanyl to intrathecal Bupivacaine did not produce any significant changes in heart rate.

Table 7: Comparison of Systolic BP (mm Hg) between two groups

Study period	Group BS		Group BF		'p' value
	Mean	**SD**	**Mean**	**SD**	
0 minutes	123.50	10.54	121.90	08.70	0.524
2 minutes	122.67	09.95	123.43	09.97	0.769
4 minutes	117.97	13.00	124.20	09.75	0.040
6 minutes	116.97	12.92	125.00	10.59	0.011
8 minutes	118.17	11.98	124.37	11.69	0.047
10 minutes	118.43	13.17	123.87	11.40	0.090
12 minutes	120.17	11.97	123.83	11.04	0.223
14 minutes	120.43	11.23	124.23	10.19	0.175
16 minutes	119.97	10.89	123.60	10.47	0.193
18 minutes	121.27	11.63	121.70	11.75	0.887
20 minutes	121.00	10.48	121.70	11.64	0.807
25 minutes	122.37	10.63	120.23	13.44	0.497
30 minutes	121.30	10.84	119.33	13.17	0.529
35 minutes	120.13	10.92	120.47	11.78	0.908
40 minutes	119.30	12.15	118.60	10.70	0.814
45 minutes	120.10	11.37	120.03	09.04	0.979
50 minutes	120.47	10.97	120.87	08.44	0.875
55 minutes	119.80	09.98	119.83	10.96	0.991
60 minutes	121.43	08.79	120.63	11.46	0.763
65 minutes	122.37	08.34	119.10	11.37	0.209
70 minutes	123.40	08.82	118.33	11.70	0.063
75 minutes	124.30	07.84	120.10	10.62	0.087
80 minutes	124.33	07.52	120.03	09.93	0.064
85 minutes	124.30	07.77	120.07	09.86	0.070
90 minutes	124.23	09.10	119.43	08.40	0.038

Table 8: Comparison of Diastolic BP (mm Hg) between two groups

Study period	Group BS		Group BF		'p' value
	Mean	**SD**	**Mean**	**SD**	
0 minutes	81.50	11.99	82.50	09.97	0.727
2 minutes	81.33	11.33	83.47	09.87	0.439
4 minutes	80.30	11.42	83.53	10.97	0.269
6 minutes	80.30	12.25	83.30	10.47	0.312
8 minutes	80.97	12.14	84.30	10.56	0.262
10 minutes	80.30	12.42	82.70	10.44	0.421
12 minutes	80.00	11.78	83.67	09.94	0.197
14 minutes	80.07	11.14	83.67	10.17	0.196
16 minutes	79.33	11.09	82.90	10.57	0.207
18 minutes	79.77	10.69	82.90	10.09	0.248
20 minutes	80.17	11.75	82.03	10.15	0.514

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25 minutes	79.47	10.69	81.70	09.85	0.404
30 minutes	79.97	11.27	81.60	09.63	0.549
35 minutes	79.63	10.87	79.83	09.81	0.941
40 minutes	79.87	11.39	79.47	09.71	0.884
45 minutes	81.10	10.87	81.20	08.79	0.969
50 minutes	81.00	11.69	81.50	09.38	0.856
55 minutes	80.73	10.99	80.50	09.96	0.933
60 minutes	81.13	11.47	82.00	10.14	0.757
65 minutes	80.73	10.84	82.60	10.05	0.491
70 minutes	79.96	09.79	81.93	11.15	0.470
75 minutes	78.86	10.04	82.47	10.08	0.170
80 minutes	79.50	10.30	82.33	10.21	0.290
85 minutes	79.77	10.73	82.77	10.28	0.273
90 minutes	79.87	10.72	82.47	09.41	0.322

Table 9: Comparison of Respiratory Rate (breaths / min) between two groups

Study period	Group BS		Group BF		'p' value
	Mean	SD	Mean	SD	
0 minutes	14.4	2.54	14.7	2.42	0.641
2 minutes	14.47	2.81	15.4	2.69	0.196
4 minutes	15.53	2.43	14.27	2.16	0.038
6 minutes	15.30	2.83	15.77	2.43	0.493
8 minutes	15.93	2.74	15.07	2.09	0.177
10 minutes	15.80	2.27	15.17	2.36	0.296
12 minutes	16.17	2.57	15.00	2.68	0.090
14 minutes	15.53	3.17	15.60	2.79	0.928
16 minutes	15.77	2.34	14.93	2.62	0.195
18 minutes	16.00	2.67	15.57	2.96	0.412
20 minutes	15.50	2.35	14.80	2.55	0.273
25 minutes	15.80	2.35	14.73	2.61	0.101
30 minutes	15.73	2.23	15.10	2.04	0.258
35 minutes	15.60	2.57	14.63	2.88	0.174
40 minutes	15.83	2.77	15.23	2.24	0.360
45 minutes	15.43	2.73	14.83	3.41	0.455
50 minutes	15.33	2.88	14.80	3.21	0.504
55 minutes	14.87	2.75	14.17	2.68	0.322
60 minutes	14.47	2.53	14.43	2.71	0.953
65 minutes	14.20	2.79	14.60	2.66	0.572
70 minutes	15.10	2.34	14.70	2.82	0.552
75 minutes	15.03	2.48	14.53	2.52	0.442
80 minutes	14.90	2.52	15.07	3.12	0.817
85 minutes	14.53	2.89	14.77	2.88	0.748
90 minutes	14.47	2.76	14.07	3.05	0.596

We observed in our study that there was no significant (p>0.05) intergroup difference between the two groups BS & BF with regards to systolic & diastolic blood pressure.
In our study we observed that there was no statistically significant difference between the two groups with regards to respiratory rate.

Table 10: Comparison of VNRS score between the two groups

Study period	Group BS				Group BF			
(Hrs)	Excellent	Good	Fair	Poor	Excellent	Good	Fair	Poor
2.5	13 (43.3%)	11 (36.6%)	6 (20%)	3 (10%)	30 (100%)	0	0	0
3.0	2 (6.6%)	8 (26.6%)	10 (33.3%)	10 (33.3%)	23 (76.6%)	7 (23.3)	0	0
3.5	-	1 (3.3%)	2 (6.6%)	10 (33.3)	9 (30%)	13 (43.3%)	8 (26.6%)	0
4.0	-	-	1 (3.3%)	1 (3.3%)	2 (6.6%)	15 (50%)	10 (33.3%)	3 (10%)

4.5	-	-	-	-	-	6 (20%)	11 (36.6%)	13 (43.3%)
5.0	-	-	-	-	-	1 (3.3%)	5 (16.6%)	10 (33.3%)
5.5	-	-	-	-	-	1 (3.3%)	5 (13.3%)	5 (16.6%)
6.0	-	-	-	-	-	-	2 (6.6%)	4 (13.3%)
6.5	-	-	-	-	-	-	2 (6.6%)	3 (10%)
7.0	-	-	-	-	-	-	2 (6.6%)	2 (6.6%)
7.5	-	-	-	-	-	-	-	4 (13.3%)

Table 10(a): Effectiveness of postoperative pain relief

Time for rescue analgesic in Hrs			p value
	Group BS	Group BF	
2.5	9	0	<0.001
3.0	20	0	<0.001
3.5	29	8	<0.001
4.0	30	13	<0.001
4.5	30	24	<0.05
5.0	30	29	>0.05
5.5	30	30	>0.05
6.0	30	30	>0.05
7.0	30	30	>0.05

Post-operative analgesia was quantified in all the patients using VNRS scale. As depicted in Table-14, at the end of 2.5 hours 13 patients (43.3%) in group BS had excellent analgesia as compared to 30 patients (100%) in group BF.

At 3 hours, 10 patients (33.3%) had good to excellent analgesia in group BS whereas all the patients (100%) in group BF had excellent analgesia.

At the end of 4 hours, one patient (3.3%) in group BS had fair analgesia and the rest of the patients required rescue medication. In group BF, 27 patients (90%) had excellent to fair analgesia and 3 patients (10%) requested rescue medication.

At the end of 7 hours all the patients (100%) in group BS had high VNRS scores (poor analgesia) whereas 2 patients (6.6%) in group BF had fair analgesia.

Table 11: Comparison of intraoperative complications

Complications	Group BS	Group BF
Bradycardia	3	2
Hypotension	5	2
Nausea & vomiting	5	1
Pruritus	1	9
Respiratory depression	0	0
Mean ± SD	2.8 ± 2.28035	2.8 ± 3.56371
p value	1.0	
Remarks	Not significant	

Table-15 showing the comparison of intraoperative complications between the two groups BS & BF.

3 patients (10%) in group BS had Bradycardia as compared to 2 patients (6.6%) in group BF. Bradycardia was treated with Inj. Atropine 0.6 mg IV.

Hypotension was observed in 5 patients (16.6%) in group BS. 2 patients (6.6%) in group BF had hypotension. Hypotension was treated appropriately.

Nausea & vomiting was noted in 5 patients (16.6%) in group BS and in 1 patient (3.3%) in group BF. Inj. Ondansetron 4mg IV was used to treat nausea & vomiting.

Pruritus was observed in 1 patient (3.3%) in group BS as compared to 9 patients (30%) in group BF. Inj. Pheniramine Maleate 45.4 mg IV was used to treat pruritus.

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Respiratory depression was not observed in any of the patients in both the groups.
Urinary retention could not be studied since patients were catheterized as part of surgical procedure.
The intraoperative complications were statistically comparable but not significant.

Table 12: Overall comparison between the Bupivacaine + Saline (Group BS) and Bupivacaine + Fentanyl (Group BF)

Study parameters	Group BS	Group BF	Clinical Significance	Statistical Significance
Onset of Sensory block(mins)	2.6667 ± 0.71116 (1-4)	2.9 ± 0.71197 (2-4)	Not significant	Not significant
Onset of T6 blockade (mins)	4.83333 ± 0.74664 (4-6)	4.66667 ± 0.6608 (3-5)	Not Significant	Not Significant
Duration of sensory blockade (mins)	94.666 ± 14.0155 (80-109)	160 ± 22.44085 (137-183)	Highly Significant	Very Highly Significant
Onset of motor blockade (mins)	6.6 ± 1.03724 (5-8)	6.56667 ± 1.0063 (5-8)	Not Significant	Not Significant
Duration of Motor Blockade (mins)	145.1667 ± 16.78892 (128-162)	150.5 ± 15.33252 (177-210)	Not Significant	Not Significant
Duration of Analgesia(mins)	148.33333 ± 12.8876 (135-162)	292 ± 20.19730 (271-313)	Highly Significant	Very Highly Significant
Intra operative discomfort score	3 (10%)	1 (3.3%)	Comparable	Not Significant
Heart rate (beats/min)	80.2800 ± 10.5752	78.7938 ± 10.9952	Stable	Not Significant
Systolic BP (mm Hg)	121.1352 ±10.512	121.3952±10.7224	Stable	Not Significant
Diastolic BP (mm Hg)	80.225±11.1864	82.2936±10.006	Stable	Not Significant
Respiratory rate(/ min)	15.2676±2.6124	14.8776±2.6632	Stable	Not Significant
Complications	14 (46.6%)	14 (46.6%)	Comparable	Not Significant

Discussion

It is important to provide adequate pain relief not only for humanitarian reasons but also to lessen the harmful effects of the endocrine, metabolic, and inflammatory reactions to pain. Post-operative pain may hence cause haemodynamic changes in a patient which may lead to increased cardiac workload, increased myocardial oxygen demand & increase the incidence of myocardial ischaemia. Post-operative pain also inhibits deep breathing & coughing leading to hypoxia, retention of secretions in the tracheo-bronchial tree which may lead to atelectasis. Therefore, adequate pain relief during and after surgery is central to the care of surgical patients.
Appendicitis is one of the most commonly encountered surgical ailments in our hospitals. Spinal anaesthesia is routinely employed for lower abdominal surgeries & particularly for Appendicectomies. It has definite advantages over other neuraxial techniques (Epidural anaesthesia, Combined Spinal Epidural). Spinal anesthesia is simple to administer, affordable, quick to take effect, reliable, promotes healthy muscle relaxation, and minimizes the risk of respiratory complications.
Some patients report unpleasant sensations like heaviness, pressure, squeezing, or choking when the vermiform appendix is handled or when the caecum is exteriorized, even though intrathecal local anesthetics have effectively blocked their sense of touch. The discovery of opioid receptors & the concurrent advances in narcotic pharmacology have opened newer horizons in pain management. One of the opioid receptors, kappa is primarily involved in the mediation of visceral pain observed as intraoperative discomfort (heaviness, squeezing or choking) during the procedure [6, 7]. Hence the use of an opioid as an adjuvant inhibits the nociceptive transmission mediated by the kappa receptors.
To synergise the analgesic effect of local anaesthetic several adjuvants have been used for many years. Benzodiazepines (Midazolam), anti-cholinesterases (Neostigmine), centrally

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acting α2 agonists (Clonidine) & opioids (Morphine, Fentanyl, Sufentanil) have been studied extensively & used in clinical practice as adjuvants to intrathecal Local anaesthetics. Ever since the use of intrathecal Morphine in 1979, spinal opioids have been consistently used in clinical practice. In small doses and concentrations with a lower chance of systemic side effects, neuraxial opioids offer good analgesia comparable to systemic administration. Modern lipophilic opioids like Fentanyl and Sufentanil have a higher potency, rapid uptake, short duration of action, low CSF concentrations, and limited rostral spread, which results in less frequently occurring respiratory depression and quicker recovery of motor function.

The present study is a randomized clinical comparative trial carried out on 60 patients undergoing Appendicectomy under Spinal Anaesthesia. A day prior to the surgery, a detailed pre-anaesthetic evaluation was done & written informed consent was obtained from all the patients. Patients with ASA Grade I & II were accepted for the surgery. All patents were pre-medicated with Tab. Diazepam 0.2 mg/kg per orally on the previous night of the surgery. The patients were randomly allocated to two groups (30 each); Group BS (control group) patients received 3cc of 0.5% hyperbaric Bupivacaine with 0.5 cc of Normal Saline & Group BF (study group) patients received 3cc of 0.5% hyperbaric Bupivacaine with 0.5 cc (25µg) of Fentanyl. During the intraoperative period, each patient's Heart rate, NIBP, respiratory rate & SpO2 were continuously monitored. Time of onset of sensory blockade, onset of T6 blockade, duration of sensory blockade, maximal sensory blockade, onset of motor block, duration of motor blockade, intraoperative discomfort, sedation score, duration of analgesia were noted. Side effects like nausea, vomiting, pruritus, respiratory depression were noted. During the postoperative period, analgesic efficacy was evaluated using the Verbal Numerical Rating Scale (VNRS) [1].

Demographic Parameters

The demographic parameters of the patients in the study were comparable. There was no statistical difference ($p>0.05$) among the groups in age, weight & height. The mean age in group BF is 28.1±5.1 years and in group BS is 28.53±6.1. The mean height of the patients is 157.033±8.83 cms & 156.56±5.37 cms in group BF and group BS respectively. The mean weight is 58.76±7.82 kgs in group BF and 59.7±5.37 kgs in group BS. The sex distribution among the study population was compared. The sex distribution in group BF is 13 Male-(43%) and 17 female – (57%) patients as compared to group BS which has equal sex distribution (Males-50%, Females-50%).

Onset of Sensory Blockade

In the present study, the mean time for the onset of sensory blockade in group BF is 2.9±0.71 minutes and in group BS is 2.66±0.71 mins. The 'p' value observed was 0.1287 which was statistically insignificant. So, the addition of Fentanyl to intrathecal Bupivacaine did not produce significant difference in the onset of sensory block. This observation correlates with the study by Catherine O Hunt *et al*. who documented the onset of sensory blockade as 3.5±1.0 mins.47 Techanivate *et al*. observed the onset time to be 2.0 ± 1.0 mins.1 Studies by Hunt *et al*. & Techanivate *et al*. also recorded no significant difference in the onset of sensory blockade on addition of Fentanyl to intrathecal Bupivacaine.

Onset of Sensory Blockade at T6 level

It was observed in our study that the mean onset time of sensory blockade to T6 level is 4.66±0.66 mins in group BF and 4.83 ± 0.76 mins in group BS with 'p' value of 0.305 being statistically insignificant. Techanivate *et al*. observed in their study that the time taken to achieve sensory blockade at T6 is 5 mins (5-10 mins range) in both the groups.1 Our study is consistent with Techanivate *et al*. who showed that there was no difference in the onset of sensory blockade to T6 in the control group and the Fentanyl group.

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Maximal Sensory Blockade

In group BF, 7(23.3%) patients achieved a block upto T6, 10 (33.3%) patients upto T5 and 13 patients (43.5%) upto T4. In group BS, 13(43.5%) patients achieved block upto T6, 13(43.5%) patients achieved block upto T5 and 4 patients achieved upto T4. The 'p' value was 0.1322 (p>0.05) and was statistically not significant. Our observation correlated with that of H. Singh *et al*. who demonstrated a higher level of sensory blockade with the addition of 25 µg Fentanyl to Bupivacaine (T7) as compared to Bupivacaine-Saline group (T8) [4].

Duration of Sensory Blockade

According to our observations, group BF's sensory blockade lasted significantly longer than group BF's. In group BF, the mean time of sensory blockade was 160 22.44 minutes, whereas in group BS, it was 94.6 14.01 minutes, with a 'p' value of 0.001, which is extremely highly significant. This finding is in line with H. Singh *et al*. findings, which showed that the sensory blockade lasted 9322 mins in the group receiving bupivacaine and fentanyl as opposed to 7418 mins in the group receiving bupivacaine and saline [4].

In the present study, we observed that the addition of intrathecal Fentanyl to Bupivacaine in comparison with Bupivacaine-Saline group did not produce any change in the onset of sensory block and the onset of sensory blockade to T6 level but prolonged the duration of sensory blockade significantly. The maximal sensory blockade achieved was higher with the Bupivacaine-Fentanyl group but was statistically insignificant.

Opioids and Local Anaesthetics exert their anti-nociceptive effect by different mechanisms. Fentanyl has an agonistic action on µ-receptors by opening K+ channels and reducing Ca++ influx resulting in inhibition of transmitter release. Bupivacaine acts mainly by blockade of Na+ channels in the axonal membrane. The potential synergism observed in Bupivacaine-Fentanyl is due to the combination of these individual effects.

Motor Blockade

In the current study, we found that the mean time for the onset of motor blockade in group BF was 6.51.006 mins and in group BS was 6.61.03. In terms of statistics, the "p" value obtained was 0.913 (p>0.05). With a 'p' value (p>0.05) that was not significant, the motor blockade lasted for 150.5 15.33 min in group BF and 145.16 16.7 min in group BS. This observation agrees with Hunt *et al*. assertion that intrathecally administered Bupivacaine-Fentanyl had no appreciable impact on the onset or duration of motor blockade [10]. They observed that the onset of motor blockade was 7.2 ± 2.68 mins in Bupivacaine-Fentanyl group and 4 ± 2 mins in Bupivacaine-Saline group with p value being statistically insignificant. The duration of motor blockade was 156 ± 77 mins in Bupivacaine-Fentanyl group and 126±32.86 mins in Bupivacaine-Saline group with p value being statistically insignificant.

Hunt *et al*. observed in their study that addition of 25 µg of Fentanyl in patients undergoing Caesarean Section did not produce any significant differences in the onset and duration of motor blockade. The onset time for motor blockade was 7.2 ± 2.683 mins and the total duration of motor blockade was 156 ± 77.46 mins. The results of our study are consistent with Hunt *et al*. with regards to onset and duration of motor blockade.

Duration of Analgesia

The mean duration of analgesia in group BF was 292±20.197 mins and in group BS was 148.33± 12.88 mins with 'p' value of <0.001 which is statistically very highly significant.

Our observation correlates with different workers who had observed significant prolonged duration of analgesia with intrathecal Fentanyl compared to the control group. Our finding concurs with Bohannon (1987) *et al*. who reported that injection of 20-40 µg of Fentanyl with LA intrathecally provided 4-5 hours of post-operative analgesia. Belzarena *et al*. (1992) documented that intrathecal administration of 25 µg Fentanyl provided post-operative analgesia for 305±89 mins which concurs with our observation of 292 ± 20.197mins.5 The results observed in our study correlate to the above mentioned studies.

Improved perioperative analgesia can be explained by a synergistic inhibitory action of

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Bupivacaine-Fentanyl combination on A-gamma and C fibers.

Intra-operative Discomfort

It was noted that 1 patient in group BF had Grade I discomfort in the first 20 mins from the commencement of surgery as compared to 3 patients in group BS wherein 2 patients had Grade I discomfort and 1 patient had Grade II discomfort in the first 20 mins. The intraoperative discomfort characterized by unpleasant sensations like heaviness, pressure, squeezing & choking observed in patients of both the groups did not necessitate anxiolytic medication and the patients were relieved by reassurance. The p value is > 0.05 which was statistically not significant but clinically comparable as the study group had lesser incidence of intraoperative discomfort.

Our observation concurs with Khanna *et al*. who reported higher incidence of intraoperative discomfort in Saline group (40%) than the Fentanyl group (20%) [8].

Sedation Score

The sedation score was assessed by Wilson scoring system. It was observed that the patients in both the groups were awake & calm (Grade 0) during the study period. Belzarena *et al*. studied that 83% of patients had the sedation score of grade 0 in the Fentanyl group as compared to 93.3% patients in saline group with no statistical difference between the two groups [5]. This observation concurs with our study.

Intraoperative Complications

2 (6.6%) patients in group BF and 3 patients (10%) in group BS had Bradycardia (HR<60) treated with Inj Atropine 0.6 mg IV.

Hypotension, which is defined as a fall in systolic blood pressure of more than 30% from the baseline reading, occurred in 2 patients (6.6%) in group BF and 5 patients (16.6%) in group BS. Treatment for hypotension was effective. No between-group differences that were statistically significant (p>0.05) were found. Numerous studies have shown that administering intrathecal fentanyl did not result in any appreciable changes to the cardiovascular system (Belzarena *et al*. 1992, Ben Hannou *et al*. 1998, Shende *et al*. Our findings are in line with those of Teoh *et al*., who found that preloading does not always prevent hypotension brought on by sympathetic block from spinal anesthesia with or without fentanyl [9].

It was observed in our study that there was no significant change in respiratory rate and was statistically insignificant (p>0.05). This correlates with the studies of Hunt *et al*., Bohannon *et al*. and Shende *et al*. [10].

Nausea and vomiting are a common side effect seen during visceral handling. 1 patient (3.5%) in group BF and 5 patients (16.6%) in group BS had nausea and vomiting with no significant intergroup differences (p>0.05). Gunnar Dahlgren *et al*. reported less intraoperative vomiting from their study of intrathecal Fentanyl (10 µg) with Bupivacaine.52 They documented that no patients complained of nausea and vomiting in the Fentanyl group as compared to 5 patients (25%) in the control group. Palmer *et al*. also reported decreased nausea & vomiting with Fentanyl & Lignocaine [11].

Pruritus was noted in 9 patients in group BF as compared to 1 patient (3.5%) in group BS with 'p' value being 0.0381 (p<0.05) and hence statistically significant. None of the patients did not require any treatment. Pruritus is the most common side effect of neuraxial opioids. Kristina *et al*. noted that pruritus was present in 22.5% of the patients in their study population which correlated with our study.58 Hunt *et al*. observed a significant increase in incidence of itching in 25 & 50 µg Fentanyl groups. Reuben *et al*. concurred with this observation when 50% patients complained of itching when they were administered high dose (50µg) Fentanyl while the incidence was only 20% in patients who received 10-40 µg of Fentanyl [12].

Our observation correlates with the results of Kristina *et al*., Hunt *et al*. & Reuben *et al*.

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Post-operative analgesia

The VNRS score was used to evaluate post-operative analgesia, with the patient verbally corresponding numbers 0 and 10 to "no pain" and "worst pain imaginable," respectively. The VNRS scores are further classified into 0 = Excellent analgesia, 1-3 = Good analgesia, 4- 6 = Fair analgesia & 7-10 = Poor analgesia when patient was supplemented with rescue analgesia.

In the present study, at the end of 2.5 hours no patient in group BF required rescue analgesia as compared to 9 patients (30%) in group BS. The p value (<0.001) is statistically highly significant.

At the end of 3 hours, no patients in group BF requested for rescue analgesia whereas 20 patients (66%) in group BS had higher VNRS scores with p value (<0.001) being statistically highly significant.

At the end of 4 hours, 13 patients (43.3%) in group BF had high VNRS scores requiring analgesic medication whereas all (100%) the patients in group BS required rescue medication.

We observed that the mean duration of post-operative analgesia in group BF was approximately 5 hours (maximum of 7 hours) as compared to 2.5 hours (maximum of 4 hours) in group BS.

Techanivate *et al*. observed in their study that the patients had higher VNRS scores in the saline group (23.3%) as compared to Fentanyl group (0%). They concluded that administration of intrathecal Fentanyl with Bupivacaine provided post-operative analgesia for 13.6 hours in comparison with 6.3 hours in Saline group. The prolonged duration observed by Techanivate *et al*. could be attributed to a higher dose of local anaesthetic used in their study (4 ml 0f hyperbaric Bupivacaine) as compared to 3ml used in our study [1]. Our observations are in concurrence with the study conducted by Techanivate *et al*.

Conclusion

Based on the results of the current study, we draw the following conclusions regarding the benefits of intrathecal administration of Fentanyl 25 mg in combination with 15 mg (3 cc) of 0.5% hyperbaric Bupivacaine over Bupivacaine and saline: Significant improvement in the surgical anesthesia's quality, hemodynamic stability, prolongation of post-operative analgesia, absence of respiratory depression, and minimal side effects.

We come to the conclusion that adding 25 g of preservative-free Fentanyl to hyperbaric Bupivacaine and administering it intrathecally to a patient undergoing an appendectomy improves the surgical anesthesia's quality, haemodynamic stability, and significant post-operative analgesia with few side effects. To provide a more thorough analysis, the study must be carried out on a larger population.

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Conflict of interest

None

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