

## Post Operative Analgesic Efficacy of Intrathecal Fentanyl versus Tramadol as Adjuvant to Bupivacaine in Total Abdominal Hysterectomy

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### Abstract:

**Background:** Total abdominal hysterectomy is an infraumbilical surgery which is commonly done under subarachnoid block as it is easy to perform, economical and faster in onset. Duration of postoperative analgesia produced using local anesthetics alone is very limited, hence the use of adjuvants has become a necessity to improve the block characteristics and to enhance the duration of postoperative analgesia. Therefore, we decided to study the post operative analgesic efficacy of fentanyl and tramadol along with intrathecal bupivacaine.

**Materials and Methods:** 84 patients of ASA 1 and 2 physical statuses posted for elective total abdominal hysterectomy were included in the study and were randomized into 2 groups using computer generated chits.

Group F received 2.5ml of 0.5% bupivacaine heavy with 25mcg of fentanyl.

Group T received 2.5ml of 0.5% bupivacaine heavy with 25mg of tramadol.

These groups were compared for the following block characteristics like onset of sensory and motor blockade, duration of postoperative analgesia, hemodynamic variations and complications like sedation, nausea, vomiting, bradycardia, pruritis, urine retention etc.

**Results:** Mean duration of postoperative analgesia in group F was 274.88± 64.41 min and in group T was 186.31± 16.27 min with a p value of <0.001 making it significant. Hemodynamic variations and complications in both the groups were similar and were not clinically significant.

**Conclusion:** Postoperative analgesic efficacy of fentanyl group was superior when compared to tramadol group making it a better adjuvant in terms of postoperative analgesia. However, both tramadol and fentanyl groups showed similar hemodynamic profile and also complications which were not clinically significant making them the safe additives to intrathecal bupivacaine.

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### Introduction

Lower abdominal and lower limb procedures are commonly done under spinal anesthesia as it is easy to perform and the effect is immediate making it the preferred choice of anesthesia. Having advantages such as reduction in blood loss, protection against thromboembolic episodes and also helps us to avoid general anaesthesia which is associated with polypharmacy and generalized CNS depression.[1]

Local anaesthetics produce its clinical effect by blocking transmission of pain from nociceptive afferents by blocking the sodium channels. Bupivacaine when used alone for intrathecal injection has a disadvantage of limited duration of action [2]. Additives are used along with local anaesthetics to prolong the duration of sensory and motor blockade through syn-

ergistic effect. They also help in limiting the cumulative dose requirement of local anaesthetics and its dose dependent adverse effects on the cardiac and central nervous system [3].

Many local anesthetic adjuvants have evolved over time varying from opioids, alpha 2 agonists like clonidine, dexmedetomidine, dexamethasone, magnesium sulfate, neostigmine, midazolam etc each of it possessing varying degree of additive effect [3].

Fentanyl is a lipophilic opioid which acts on the  $\mu$  receptors located in the substantia gelatinosa of the dorsal horn of the spinal cord and inhibits the release of excitatory neuropeptides. It is preferred over morphine as it does not migrate cranially in sufficient

concentration to cause delayed respiratory depression when administered intrathecally [4].

Tramadol is a centrally acting opioid which acts by inhibition of neuronal reuptake of norepinephrine and serotonin and by inhibition of presynaptic stimulation of 5-hydroxytryptamine release. Its analgesic action is also attributed to its action on the  $\mu$ -receptor and to a lesser extent on the  $\delta$ - and  $\kappa$ -opioid receptors [5].

Our study was conducted to compare the post operative analgesic efficacy of these adjuvant drugs when combined with bupivacaine intrathecally.

### Aims and Objectives of the Study

To compare the efficacy of intrathecal Fentanyl and Tramadol as adjuvant drugs to Bupivacaine in total abdominal hysterectomy surgeries in terms of

- Onset of sensory and motor block
- Duration of analgesia
- Hemodynamic variations and complications if any

### Materials

#### Source of Data

The present study was conducted at SIMS, Shivamogga by the department of anaesthesiology in collaboration with the department of gynecology.

**Study Design:** Randomized comparative study.

**Sample size:** Total of 84 patients with 42 in each group after randomization

**Estimation of Sample Size:**  $4pq/d^2$

Prevalence of lower abdominal hysterectomies conducted at our institute per year is about 5.5% of all the surgeries. Based on the above formula,  $p$ -prevalence=5.5%;  $q=(100-p)$ ;  $d$ - is the allowable error, we would like to consider 5% error for the present study. Hence our sample size will be 83.16; we would like to recruit 84 samples, 42 in each group.

### Inclusion Criteria

Female patients aged between 18 to 70 years posted for elective abdominal hysterectomy procedure belonging to ASA 1 and ASA 2 physical status.

### Exclusion Criteria

1. History of allergy to local anesthetics.
2. ASA 3 and ASA 4
3. Emergency hysterectomies are excluded from the study.
4. Patients with known case of AV block, morbid obesity
5. Patients with contraindication for subarachnoid block are excluded from the study.

### Methodology

After obtaining the ethical clearance, 84 patients fulfilling the inclusion criteria were recruited in the study. A thorough pre-anesthetic evaluation was done a day prior to surgery. A written informed consent was taken from every patient.

All the patients were kept overnight fasting. On arrival to operation theatre, intravenous (IV) line was secured and crystalloid intravenous infusion of 6-8 ml/kg/hr was started. Routine monitors like ECG, NIBP and pulse oximetry were connected, and baseline parameters were recorded. Patients were randomized into two groups of 42 each by simple randomization using computer generated chits. Under aseptic precautions subarachnoid block was performed at L3-L4 interspace, after ensuring free flow of CSF following study drugs were injected.

**Group F:** 2.5 ml of 0.5% bupivacaine heavy + 0.5 ml (25  $\mu$ g) of fentanyl citrate

**Group T:** 2.5 ml of 0.5% bupivacaine heavy +0.5 ml (25 mg) of tramadol

Vital parameters like pulse, blood pressure, oxygen saturation, respiratory rate were monitored every minute for the first 5 min and every 5 min till 1hr and every 15min from thereafter. Sensory blockade was assessed by pin prick stimuli and motor blockade was assessed using modified Bromage scale at every 2 min interval. Intensity of the pain was assessed by visual analog scale (VAS), when the VAS score was more than 4 rescue analgesic in the form of injection paracetamol 1g slow IV was given which marks the end of our study. Time taken for first rescue analgesic drug was noted.

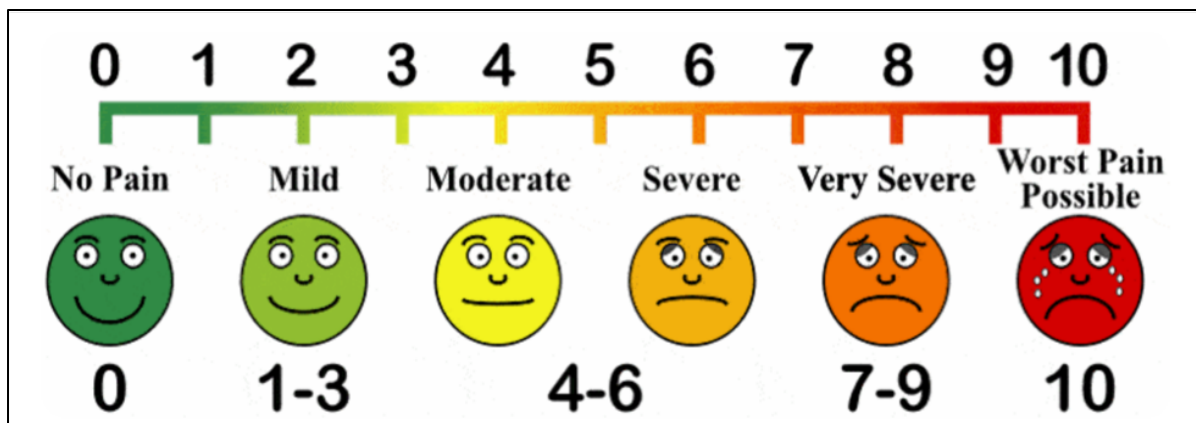


Figure 1:

**Results**

This study is a randomized comparative study, conducted on 84 patients in the age group of 18 to 70years undergoing total abdominal hysterectomies.

Table 1: Age in years –frequency distribution in two groups studied.

Figure 1: Age in years –frequency distribution in two groups studied.

Demographic profile in both the groups studied were comparable as indicated by the above table.

Table 2: ASA Grade- frequency distribution in two groups studied.

Figure 2: ASA Grade-frequency distribution in two groups studied.

ASA physical status distribution of the patients studied were similar in both the groups.

Table 3: Comparison of study variables in two groups of patients studied.

Figure 3: Time of onset of sensory block (min)

Figure 4: Time of onset of motor block (min)

Figure 5: Duration of analgesia (min)

Block characteristics like time of onset of sensory blockade and motor blockade were similar in both the groups as indicated by the p value. Duration of anal-

gesia studied in group F was 274.88± 64.41min and group T was 186.31± 16.27 min with p value <0.001, making it statistically significant.

Table 4: SPO 2%-A comparison in two groups of patients studied.

Figure 6: SPO 2%-A comparison in two groups of patients studied.

Table 5: HR per min- a comparison in two groups of patients studied.

Figure 7: HR per min- a comparison in two groups of patients studied.

Table 6: MAP (mm hg) a comparison in two groups of patients studied.

Figure 8: MAP (mm hg) a comparison in two groups of patients studied.

Hemodynamic variables like heart rate, MAP, SpO2 changes studied in both the groups were similar and not clinically significant.

Table 7: Intraop Complications- A comparison in two groups of patients studied.

Fig 9: Intraop Complications- A comparison in two groups of patients studied.

There were no significant intraoperative complications in both the groups studied.

**Table 1: Age in years –frequency distribution in two groups studied.**

Age in Years	Group F	Group T	Total
<40	5(11.9%)	3(7.1%)	8(9.5%)
40-50	24(57.1%)	20(47.6%)	44(52.4%)
51-60	13(31%)	19(45.2%)	32(38.1%)
Total	42(100%)	42(100%)	84(100%)
Mean ± SD	48.31± 6.27	50.05± 5.04	49.18± 5.72

Samples are age matched P=0.165, student t test

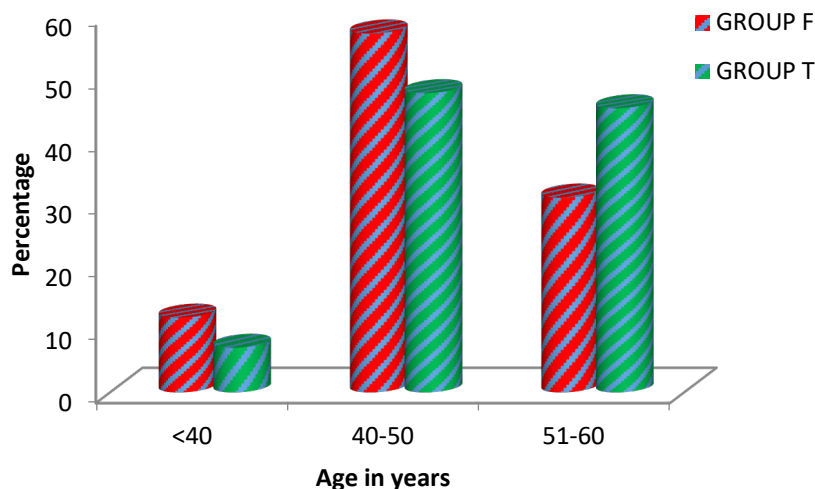


Figure 1: Age in years –frequency distribution in two groups studied

Table 2: ASA Grade- frequency distribution in two groups studied

ASA Grade	Group F	Group T	Total
1	28(66.7%)	32(76.2%)	60(71.4%)
2	14(33.3%)	10(23.8%)	24(28.6%)
Total	42(100%)	42(100%)	84(100%)

P=0.466, Not Significant, Chi-Square Test

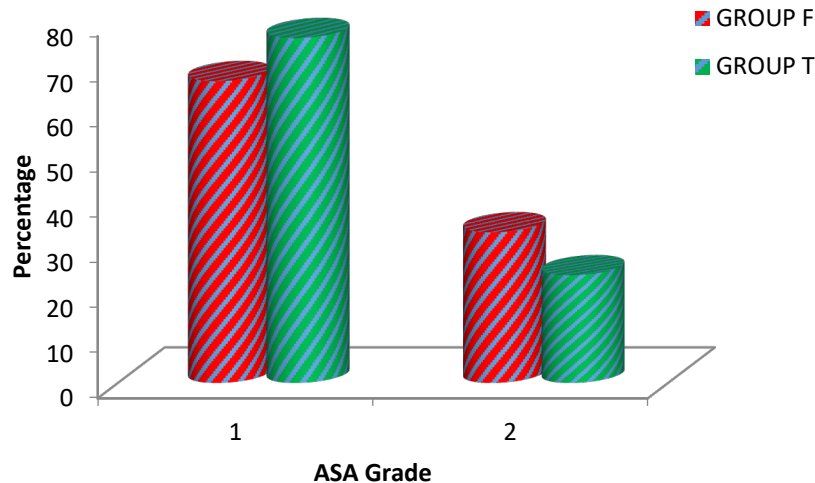


Figure 2: ASA Grade-frequency distribution in two groups studied

Table 3: Comparison of study variables in two groups of patients studied

Variables	Group F	Group T	Total	P Value
Time of onset of sensory block(min)	2.76± 1.25	2.81± 1.17	2.79± 1.2	0.857
Time of onset of motor block(min)	7.43± 1.84	6.95± 1.27	7.19± 1.59	0.170
Duration of analgesia(min)	274.88± 64.41	186.31± 16.27	230.6± 64.53	<0.001**

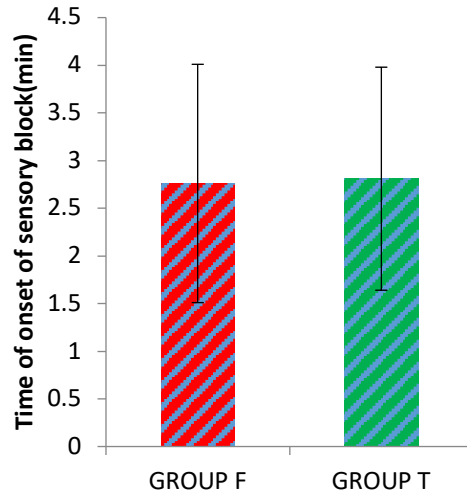


Figure 3: Time of onset of sensory block (min)

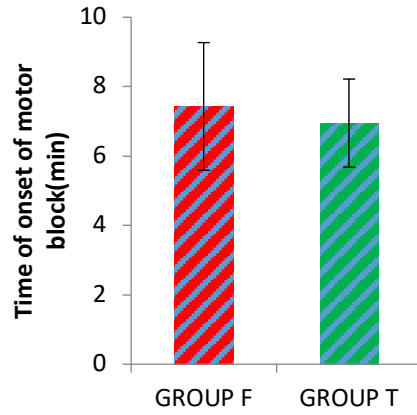


Figure 4: Time of onset of motor block (min)

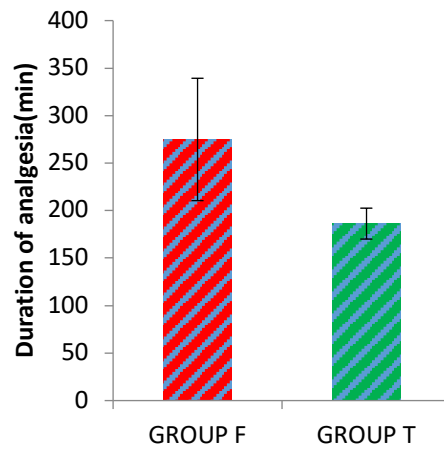
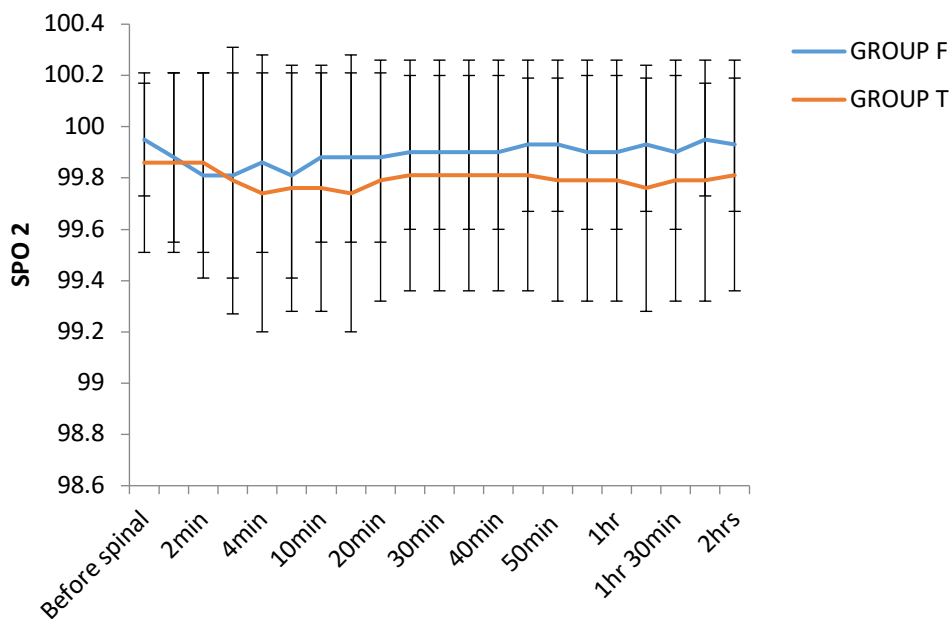


Figure 5: Duration of analgesia (min)

**Table 4: SPO 2%-A comparison in two groups of patients studied**

SPO 2	Group F	Group T	Total	P Value
Before spinal	99.95± 0.22	99.86± 0.35	99.9± 0.3	0.140
1min	99.88± 0.33	99.86± 0.35	99.87± 0.34	0.750
2min	99.81± 0.4	99.86± 0.35	99.83± 0.37	0.564
3min	99.81± 0.4	99.79± 0.52	99.8± 0.46	0.814
4min	99.86± 0.35	99.74± 0.54	99.8± 0.46	0.238
5min	99.81± 0.4	99.76± 0.48	99.79± 0.44	0.624
10min	99.88± 0.33	99.76± 0.48	99.82± 0.42	0.191
15min	99.88± 0.33	99.74± 0.54	99.81± 0.45	0.149
20min	99.88± 0.33	99.79± 0.47	99.83± 0.41	0.285
25mn	99.9± 0.3	99.81± 0.45	99.86± 0.38	0.259
30min	99.9± 0.3	99.81± 0.45	99.86± 0.38	0.259
35min	99.9± 0.3	99.81± 0.45	99.86± 0.38	0.259
40min	99.9± 0.3	99.81± 0.45	99.86± 0.38	0.259
45min	99.93± 0.26	99.81± 0.45	99.87± 0.37	0.145
50min	99.93± 0.26	99.79± 0.47	99.86± 0.38	0.089+
55min	99.9± 0.3	99.79± 0.47	99.85± 0.4	0.169
1hr	99.9± 0.3	99.79± 0.47	99.85± 0.4	0.169
1hr 15min	99.93± 0.26	99.76± 0.48	99.85± 0.4	0.053+
1hr 30min	99.9± 0.3	99.79± 0.47	99.85± 0.4	0.169
1hr 45min	99.95± 0.22	99.79± 0.47	99.87± 0.37	0.040*
2hrs	99.93± 0.26	99.81± 0.45	99.87± 0.37	0.145



**Figure 6: SPO 2%-A comparison in two groups of patients studied**

**Table 5: HR per min- A comparison in two groups of patients studied**

HR	Group F	Group T	Total	P Value
Before spinal	80.64± 10.43	82.38± 9.04	81.51± 9.74	0.417
1min	79.48± 10.97	86.95± 9.47	83.21± 10.86	<0.001**
2min	76.05± 10.26	79.81± 6.77	77.93± 8.84	0.051+
3min	74.52± 8.96	75.38± 5.57	74.95± 7.43	0.600
4min	75.24± 9.57	74.98± 4.96	75.11± 7.57	0.875

5min	75.67± 10.5	74.9± 6.21	75.29± 8.58	0.687
10min	75.76± 10.51	76.1± 5.34	75.93± 8.29	0.855
15min	73.43± 9.28	77.05± 5.42	75.24± 7.77	0.032*
20min	73.17± 10.2	79.6± 6.5	76.38± 9.1	<0.001**
25mn	73.14± 10.16	77.45± 5.77	75.3± 8.49	0.019*
30min	71.33± 8.11	76.43± 7.29	73.88± 8.08	0.003**
35min	74.57± 9.52	78.52± 6.01	76.55± 8.16	0.025*
40min	72.79± 7.77	77.57± 6.15	75.18± 7.37	0.002**
45min	74.33± 9.75	77.12± 5.82	75.73± 8.11	0.116
50min	74.4± 14.81	75.67± 6.69	75.04± 11.44	0.616
55min	77.52± 8.21	78.24± 6.35	77.88± 7.3	0.657
1hr	77.62± 8.63	75.93± 6.98	76.77± 7.85	0.327
1hr 15min	78.05± 8.22	78.95± 7.28	78.5± 7.73	0.595
1hr 30min	78.19± 8.4	79.31± 5.74	78.75± 7.17	0.478
1hr 45min	76.21± 6.89	78.4± 5.84	77.31± 6.44	0.120
2hrs	78.02± 8.13	78.19± 6.82	78.11± 7.46	0.919

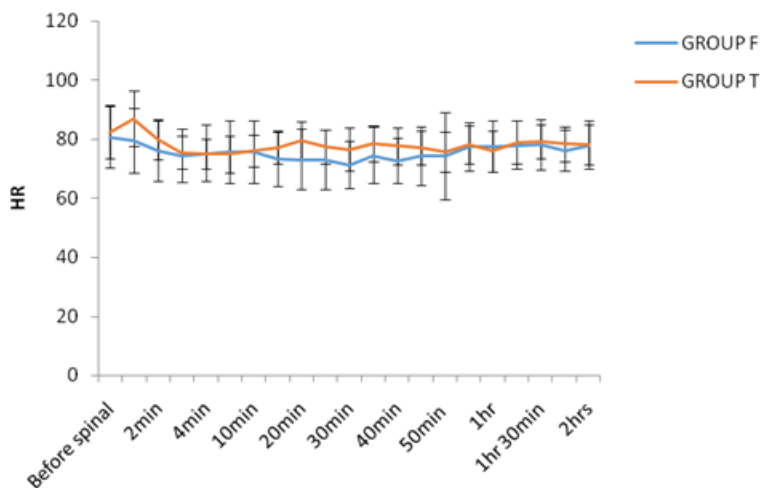


Figure 7: HR per min- A comparison in two groups of patients studied

Table 6: MAP(mm hg)- A comparison in two groups of patients studied

MAP(mm hg)	Group F	Group T	Total	P Value
Before spinal	89.95± 10.82	90.33± 7.85	90.14± 9.4	0.854
1min	86.36± 11.1	85.9± 10.16	86.13± 10.58	0.846
2min	83.14± 10.27	85.86± 12.03	84.5± 11.2	0.269
3min	80.86± 9.45	83.6± 10.78	82.23± 10.17	0.219
4min	79.45± 9.79	81.98± 10.64	80.71± 10.24	0.261
5min	78.24± 10.02	81.83± 10.97	80.04± 10.6	0.121
10min	76.64± 9.76	80.48± 10.59	78.56± 10.3	0.088+
15min	77.02± 9.8	80± 10.65	78.51± 10.28	0.186
20min	77.24± 9.58	79.43± 9.41	78.33± 9.5	0.294
25mn	76.43± 10.45	78.36± 10.49	77.39± 10.45	0.401
30min	76.07± 10.75	78.4± 11.17	77.24± 10.96	0.332
35min	76.1± 10.63	77.74± 9.96	76.92± 10.27	0.467
40min	75.74± 10.55	78.24± 10.13	76.99± 10.36	0.271
45min	75.88± 10.13	76.57± 7.97	76.23± 9.07	0.729
50min	76.64± 10.24	78.1± 9.69	77.37± 9.94	0.506
55min	77.1± 9.57	78.67± 10.04	77.88± 9.78	0.465

1hr	77.31± 9.76	77.95± 11.72	77.63± 10.73	0.785
1hr 15min	77.1± 10.33	79.19± 10.77	78.14± 10.54	0.366
1hr 30min	78.26± 10.77	78.98± 10.26	78.62± 10.46	0.756
1hr 45min	78.55± 12.06	79.9± 8.91	79.23± 10.56	0.559
2hrs	77.98± 11.35	78.43± 11.73	78.2± 11.47	0.858

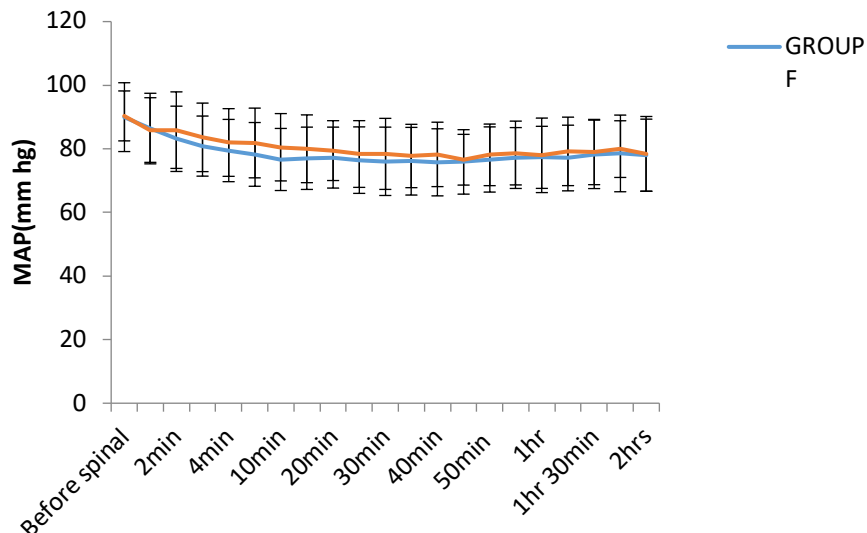


Figure 8: MAP (mm hg)- A comparison in two groups of patients studied

Table 7: Intraop Complications- A Comparison In Two Groups Of Patients Studied

Intraop Complications	Group F	Group T	Total
No	35(83.3%)	39(92.9%)	74(88.1%)
Yes	7(16.7%)	6(14.3%)	13(15.5%)
• Hypotension	1(2.4%)	0(0%)	1(1.2%)
• Nausea and vomiting	2(4.8%)	3(7.1%)	5(6%)
• Pruritis	4(9.5%)	0(0%)	4(4.8%)
Total	42(100%)	42(100%)	84(100%)

P=0.887, Not Significant, Chi-Square Test

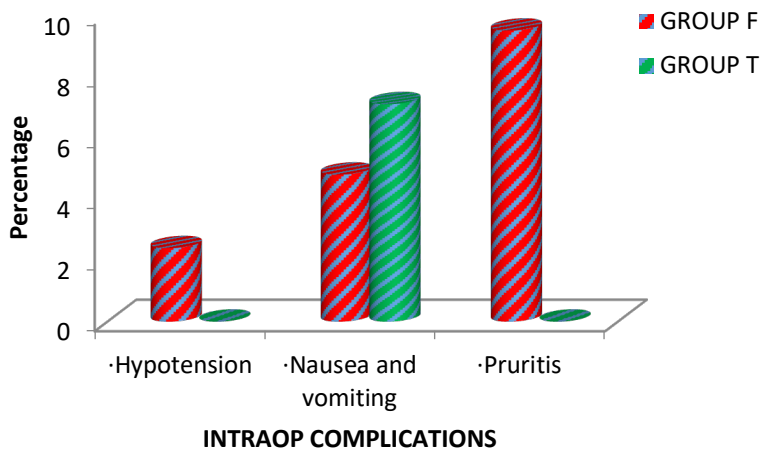


Figure 9: Intraop Complications- A comparison in two groups of patients studied



## Discussion

In our study we compared the post operative analgesic efficacy of intrathecal tramadol and fentanyl with 0.5 % hyperbaric bupivacaine in patients undergoing total abdominal hysterectomies. Doses of tramadol and fentanyl added to 2.5ml of 0.5 % hyperbaric bupivacaine – was 25 mg and 25 mcg respectively, similar to studies conducted by Afolayan JM et al.6 and Rani H.L.B et al.[7].

In terms of block characteristics time of onset of sensory blockade was defined as the time taken from the injection of the study drug till the loss of pin prick sensation at L1 sensory level, and it was found to be  $2.76 \pm 1.25$  min in group F and  $2.81 \pm 1.17$  min in group T, with no significant difference in onset time as indicated by the p value.

Time of onset of motor blockade was defined as the time taken from the injection of the study drug till modified Bromage 3 was achieved, it was found to be  $7.43 \pm 1.84$  min in group F and  $6.95 \pm 1.27$  min in group T, with no significant difference in onset time as indicated by the p value. This was similar to study conducted by Dalvi NP et al. [8].

Duration of analgesia which was defined as time taken from the injection of the study drug till the first dose of rescue analgesia as requested by the patient (VAS  $\geq$  4). It was found to be  $274.88 \pm 64.41$  min in group F and  $186.31 \pm 16.27$  min in group T which was statistically significant with p value of  $<0.001$ . This result was similar to study conducted by Afolayan JM et al. in which mean time of analgesia for fentanyl group was  $304.73 \pm 67.91$  min and tramadol group was  $238.39 \pm 61.28$  min [6].

Hemodynamic variations in terms of changes in heart rate, SpO2 and MAP studied in both the groups were not clinically significant. This was similar to study conducted by Supriya S K et al.[9]

Incidence of side effects like nausea vomiting, pruritis, bradycardia, urinary retention etc studied in both fentanyl and tramadol groups were not clinically significant. Similar side effect profile of both the study drugs were observed in the study conducted by Ragi Jain et al [10]. Study conducted by M Santhi Sree et al [11] was similar to our study where they found that fentanyl and tramadol both had similar onset time of motor and sensory blockade, hemodynamic variations and side effect profile. Mean duration of analgesia in their study showed 193.87 min in fentanyl group and 188.61 min tramadol group with no statistically significant difference, but our study showed longer duration of analgesia in fentanyl group compared to tramadol group which was significant as indicated by p value of  $<0.001^{**}$ .

Hence we concluded that postoperative analgesic efficacy of fentanyl is better than tramadol with longer duration of analgesia. Both tramadol and fentanyl produce minimal hemodynamic changes and are known to have lesser incidence of side effects making them both safe adjuvants to be added with bupivacaine.

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