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RESEARCH ARTICLE
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A COMPARATIVE STUDY OF HAEMODYNAMIC EFFECTS OF INTRATHECAL VERSUS INTRAVENOUS FENTANYL FOR SUPPLEMENTATION OF SUBARACHNOID BLOCK IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY

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ABSTRACT

BACKGROUND: Although there are studies comparing various opioids and various dosages of fentanyl, studies comparing the two routes of administration with respect to their haemodynamic effects, especially for total abdominal hysterectomy are very few.

METHODS: Inj. fentanyl 25µg (0.25 ml) intrathecally and Inj. fentanyl 1µg/kg intravenously were compared. 15 mg of 0.5% hyperbaric Bupivacaine was used for spinal anaesthesia in both groups. Vital parameters, including heart rate, SBP, DBP, MAP, and SpO2, were measured at baseline and at intervals of 5 minutes for 30 minutes, followed by every 15 minutes till 120 minutes. Hypotension was defined as a reduction in SBP (Systolic Blood Pressure) of more than 30% below the baseline or a fall in SBP less than 90 mmHg. It was treated with increasing the rate of intravenous fluid administration and inj. mephenteramine 3mg IV in incremental doses, if required. Bradycardia was defined as a heart rate less than 30% of the baseline heart rate. It was treated by inj. atropine 0.6 mg IV.

RESULTS: The heart rate and SpO2 values at timed intervals in both groups were comparable. Between the two groups, no statistically significant variations in heart rates or SpO2 were observed. When the SBP at timed intervals was evaluated between the two groups, it was discovered that there was a statistically significant difference in the mean SBP just after the subarachnoid block and five minutes later, with the IT fentanyl group seeing a larger drop in blood pressure. IV fluids and a injection of mephenteramine 3mg were used right away to rectify it. Other time intervals showed comparable mean SBP. Clinically, the IT fentanyl group had a lower mean SBP than the IV fentanyl group. When the two groups' DBP was evaluated at timed intervals, it was discovered that there was

a statistically significant difference in the mean DBP at 30 and 45 minutes, with the IT fentanyl group seeing a larger drop in blood pressure. IV fluids and a 3mg injection of mephenteramine were used right away to rectify it. Other time periods had similar mean DBP. Clinically, the IT fentanyl group had a lower mean DBP than the IV fentanyl group. When the two groups' MAP at timed intervals were examined, it was shown that there was a statistically significant difference in mean MAP at 30 and 45 minutes, with the IT fentanyl group seeing a larger drop in blood pressure. IV fluids and a 3mg injection of mephenteramine were used right away to rectify it. At other intervals, the mean MAP was similar. Clinically, the IT fentanyl group had a lower mean MAP than the IV fentanyl group.

CONCLUSION: Although comparatively lower Systolic Blood Pressure, Diastolic Blood Pressure & Mean Arterial Pressure were observed with intrathecal administration, the incidence of hypotension (SBP<90 mmHg) was higher with intravenous fentanyl. Intrathecal administration of fentanyl provides longer duration of sensory and motor block and better postoperative analgesia when compared to intravenous fentanyl.

KEYWORDS: Intrathecal, Intravenous, Fentanyl, Subarachnoid Block.

INTRODUCTION

Subarachnoid block with Bupivacaine alone is most often used as the anaesthetic technique for gynaecological procedures like total abdominal hysterectomy. Patients, however, experience varying degrees of pain and discomfort when the procedure is prolonged.[1] Increasing the dose of Bupivacaine may increase the level of block and duration, but it also increases the risk of hypotension and bradycardia.[2] This led to the study of the use of adjuvants like opioids with subarachnoid blocks to reduce the dose of bupivacaine and to increase the effectiveness of the block.[3,4]

Low-dose fentanyl may sufficiently augment local anaesthetic mediated block to decrease nociceptive stimulation. It provides efficient intraoperative and prolonged postoperative analgesia. The incidence of perioperative adverse reactions like nausea and vomiting is also reduced.[5,6] According to research, opioids that are used in addition to spinal anaesthesia may not entirely act in the spinal cord. According to an experimental study, a sizable portion of a lipophilic opioid, like fentanyl, that is administered intrathecally is lost through diffusion into the epidural space and then into the plasma.[7] This suggests that fentanyl may cause analgesia through a systemic mechanism rather than a spinal one.

The idea behind a few studies comparing the effectiveness of intrathecal and intravenous fentanyl administration is that if intrathecal fentanyl causes analgesia by absorption into the bloodstream instead of by spinal action, it might have the same effect when administered intravenously. Few studies, nevertheless, have examined the two pathways' haemodynamic profiles. Therefore, with a focus on the haemodynamic consequences, our study examined the effects of intrathecal versus intravenous fentanyl for supplementing subarachnoid block in patients undergoing total abdominal hysterectomy.

METHODS

This was a prospective randomized study involving 140 (70 patients in group IT (intrathecal) and 70 patients in group IV (intravenous)) patients of age group 40-60 years, belonging to ASA grade I and grade II, posted for elective total abdominal hysterectomy. Patients who belonged to the IT (intrathecal) group were given 15 mg of 0.5% hyperbaric bupivacaine and Inj. fentanyl 25µg (0.25 ml) intrathecally. Patients who belonged to the IV (intravenous) group were given 15 mg of 0.5% hyperbaric bupivacaine and 0.25 mL of distilled water intrathecally, followed by inj. fentanyl 1µg/κg intravenously. Vital parameters, including heart rate, SBP, DBP, MAP and SpO2 were measured at baseline and at intervals of 5 minutes for 30 minutes, followed by every 15 minutes till 120 minutes. Hypotension was defined as a reduction in SBP of more than 30% below the baseline

or a fall in SBP less than 90 mmHg. It was treated with increasing the rate of intravenous fluid administration and injection mephenteramine 3mg IV in incremental doses, if required. Bradycardia was defined as a heart rate less than 30% of the baseline heart rate. It was treated by inj. atropine 0.6 mg IV.

Mean± SD was used to display findings for continuous data, while number (%) was used to display results for categorical measurements. The 5% level of significance was used to evaluate significance. The significance of research parameters on a continuous scale between two groups (intergroup analysis) on metric parameters was determined using the two-tailed, independent student t-test. In order to evaluate the homogeneity of variance, Leven's test was conducted. The significance of research parameters on a categorical scale between two or more groups was determined using the chi-square/Fisher's exact test.

RESULTS

The mean age distribution of subjects in intrathecal fentanyl (IT fentanyl) group was 46.37±5.14 and that of intravenous fentanyl (IV fentanyl) 46.87±5.52. There was no significant difference in mean age as evidenced by a p-value of 0.580.

Age (in years)	**IT Fentanyl**	**IV Fentanyl**	**Total**
40-49	48 (68.6%)	47 (67.1%)	95 (67.9%)
50-59	22 (31.4%)	23 (32.9%)	45 (32.1%)
Total	70 (100%)	70 (100%)	140 (100%)
Mean ± SD	46.37±5.14	46.87±5.52	6.62±5.32
Table 1: Age Distribution			
Samples are age matched with P=0.580, Student t test			

There was no difference between the two groups with respect to height (p = 0.197) and weight (p = 0.166) and hence they were comparable.

Height (cm)	**IT Fentanyl**	**IV Fentanyl**	**Total**
<150	4 (5.7%)	3 (4.3%)	7 (5%)
150-160	38 (54.3%)	41 (58.6%)	79 (56.4%)
161-170	23 (32.9%)	25 (35.7%)	48 (34.3%)
>170	5 (7.1%)	1 (1.4%)	6 (4.3%)
Total	70 (100%)	70 (100%)	140 (100%)
Table 2: Height (cm) Distribution in Two Groups of Patients Studied			
P=0.425, Not Significant, Fisher Exact			

Weight (kg)	**IT Fentanyl**	**IV Fentanyl**	**Total**
<50	2 (2.9%)	1 (1.4%)	3 (2.1%)
50-60	16 (22.9%)	15 (21.4%)	31 (22.1%)
61-70	23 (32.9%)	30 (42.9%)	53 (37.8%)
>70	29 (41.4%)	24 (34.3%)	53 (31.2%)
Total	70 (100.0%)	70 (100.0%)	140 (100.0%)
Mean ± SD	68.00±10.75	66.67±7.22	67.34±9.15
Table 3: Weight (kg) Distribution in Two Groups of Patients Studied			
P=0.392, Not Significant, Student t test			

There were no statistically significant changes noted in heart rate between both groups at each of the study points. The heart rate values in both groups were comparable.

Heart Rate (bpm)	IT Fentanyl	IV Fentanyl	Total	P-Value
Before SAB	88.96±13.77	91.11±15.09	90.04±14.44	0.379
After SAB	91.47±12.17	91.14±13.79	91.31±12.96	0.881
5 mins	92.87±14.68	91.11±16.35	91.99±15.51	0.505
10 mins	91.63±15.27	87.94±16.18	89.79±15.79	0.168
15 mins	88.44±13.85	87.59±18.51	88.01±16.29	0.757
20 mins	87.71±14.45	83.83±16.90	85.77±15.79	0.146
25 mins	86.71±14.36	82.97±19.10	84.84±16.94	0.192
30 mins	84.04±14.46	81.3±18.25	82.67±16.46	0.326
45 mins	82.54±14.54	82.04±16.61	82.29±15.56	0.850
60 mins	83.83±14.35	82.60±15.51	83.21±14.90	0.627
90 mins	84.66±12.38	84.71±13.41	84.69±12.86	0.979
120 mins	87.44±11.79	87.23±14.72	87.34±13.29	0.924

Table 4: Heart Rate (bpm) Comparison between Two groups of Patients

The SBP at timed intervals were compared between both groups and found that a statistically significant difference in mean SBP was found immediately after subarachnoid block and immediately 5 minutes later (p = 0.042 and 0.049, respectively), with a greater fall in BP in the IT fentanyl group. Lower SBP was observed in the IT group at the end of the observation period, i.e., 120 minutes, and the difference was statistically significant (p = 0.002). The SBP was comparable at other timed intervals.

SBP (mm Hg)	IT Fentanyl	IV Fentanyl	Total	P-Value
Before SAB	130.01±10.01	130.91±10.28	130.46±10.12	0.601
After SAB	126.77±12.88	131.33±13.33	129.05±13.26	0.042*
5 mins	119.19±13.35	123.99±15.23	121.59±14.47	0.049*
10 mins	119.54±13.76	121.76±14.5	120.65±14.13	0.356
15 mins	115.59±15.05	117.9±15.38	116.74±15.21	0.370
20 mins	116.9±15.92	117.77±15.8	117.34±15.81	0.746
25 mins	117.86±16.31	118.51±16.02	118.19±16.11	0.810
30 mins	117.20±14.57	120.43±14.27	118.81±14.46	0.188
45 mins	117.89±14.28	121.26±15.44	119.57±14.92	0.182
60 mins	118.83±11.22	120.64±12.95	119.74±12.1	0.377
90 mins	120.33±9.36	121.94±11.61	121.14±10.54	0.367
120 mins	120.56±8.64	125.66±10.26	123.11±9.79	0.002**

Table 5: SBP (mm Hg) Comparison in Two Groups of Patients

The DBP at timed intervals was compared between both groups, and it was found that a statistically significant difference in mean DBP was found at 30 and 45 minutes, with a greater fall in BP in the IT fentanyl group (p-0.013 and 0.015, respectively). Lower DBP was observed in the IT group at the end of the observation period, i.e., 120 minutes, and the difference was statistically significant (p < **0.001).** The DBP was comparable at other timed intervals.

DBP (mm Hg)	IT Fentanyl	IV Fentanyl	Total	P-Value
Before SAB	85.20±7.36	86.43±7.92	85.81±7.64	0.343
After SAB	81.53±9.34	83.43±9.82	82.48±9.59	0.243
5 mins	75.77±10.47	78.30±12.17	77.04±11.38	0.190
10 mins	73.99±9.94	77.00±11.16	75.49±10.64	0.094+
15 mins	71.30±10.95	74.16±10.80	72.73±10.93	0.122

20 mins	73.21±11.28	75.23±12.07	74.22±11.69	0.310
25 mins	73.30±10.56	75.64±12.69	74.47±11.69	0.237
30 mins	73.16±11.01	78.14±12.29	75.65±11.89	0.013*
45 mins	73.41±10.89	78.43±13.17	75.92±12.3	0.015*
60 mins	76.49±8.83	78.96±10.9	77.72±9.96	0.143
90 mins	77.59±8.00	79.77±8.12	78.68±8.10	0.111
120 mins	77.86±7.71	83.09±7.81	80.47±8.17	<0.001**

Table 6: DBP (mm Hg) Comparison in Two Groups of Patients

The MAP at timed intervals was compared between both groups and found that a statistically significant difference in mean MAP was found at 30 and 45 minutes (p-0.034 and 0.035, respectively), with a greater fall in BP in the IT fentanyl group. Lower MAP was observed in the IT group at the end of the observation period, i.e., 120 minutes, and the difference was statistically significant (p **< 0.001**). The mean MAP was comparable at other timed intervals.

MAP (mm Hg)	IT Fentanyl	IV Fentanyl	Total	P-Value
Before SAB	99.16±7.01	100.21±7.14	99.69±7.07	0.378
After SAB	95.64±9.63	98.41±10.07	97.03±9.91	0.098+
5 mins	89.30±9.98	92.54±11.99	90.92±11.11	0.084+
10 mins	88.20±10.55	90.96±11.00	89.58±10.83	0.132
15 mins	85.21±11.49	87.87±11.27	86.54±11.42	0.169
20 mins	86.93±11.92	88.53±12.24	87.73±12.06	0.435
25 mins	87.33±11.63	89.03±13.00	88.18±12.32	0.416
30 mins	86.94±11.54	91.26±12.31	89.1±12.08	0.034*
45 mins	87.33±11.17	91.8±13.29	89.56±12.43	0.033*
60 mins	89.66±8.71	91.9±10.62	90.78±9.74	0.174
90 mins	90.83±7.82	92.81±8.64	91.82±8.27	0.156
120 mins	91.11±7.38	96.27±8.06	93.69±8.12	<0.001**

Table 7: MAP (mm Hg) Comparison in Two Groups of Patients

There were no statistically significant changes noted in SpO2 between both groups at each of the study points. The SpO2 values in both groups were comparable.

In addition to the above findings, intrathecal fentanyl 25µg when supplemented with 0.5% hyperbaric bupivacaine for subarachnoid block was observed to provide longer duration of sensory and motor block and better postoperative analgesia when compared to intravenous fentanyl 1µg/kg.

About 4% of patients had nausea and vomiting, and about 13% had hypotension in the IT fentanyl group. Whereas the IV fentanyl group had about 14% of patients with nausea and vomiting, 16% with hypotension, and 4% with pruritis. Hypotension was immediately corrected with IV fluids and Inj. mephenteramine 3mg. The p-value of 0.020 suggested statistical significance. With a p-value of 0.020, there are statistically significant findings that patients in the IV fentanyl group had more adverse effects, such as bradycardia and hypotension, than the patients in the IT fentanyl group.

DISCUSSION

Spinal anaesthesia with local anaesthetic agents, especially bupivacaine, has side effects such as hypotension, respiratory depression, vomiting, and shivering in a dose-dependent fashion.[3] So co-administration of small doses of intrathecal or intravenous opioids with bupivacaine for spinal anaesthesia is advisable and advantageous in order to decrease the intensity as well as severity of spinal complications associated with spinal anaesthesia.[8]

Literature on the topic is very sparse. Although there are studies comparing various opioids and also various dosages of fentanyl, studies comparing the two routes of administration, especially for total

abdominal hysterectomy, are very few. Although the few studies available have mentioned the incidence of hypotension as a side effect, none have delved into the haemodynamic changes that occur after the administration of the drugs. The following discussion is based on available literature.
We found that haemodynamic parameters were comparable in both groups in terms of heart rate, SpO2, systolic blood pressure, diastolic blood pressure, and mean arterial pressures. Though both groups of patients were hemodynamically stable, clinically, patients receiving fentanyl intrathecally had lower blood pressures than those receiving fentanyl intravenously. Hypotension was immediately corrected with IV fluids and inj. mephenteramine 3mg.
M.D. Larson et al.,[9] investigated the autonomic effects of fentanyl administered intravenously and epidurally and discovered that both methods reduced arterial pressure and heart rate. In terms of inhibiting these autonomic reactions, neither injection technique was superior. During anaesthesia, heart rate and arterial pressure might not be an accurate indicator of nociception. In particular, one study by Guinard JP et al.,[10] that employed haemodynamic reflexes as a nociception measure came to the conclusion that administering an epidural had no advantages over intravenous fentanyl.
In the Kararmaz et al. study,[11] sixty patients were divided into three groups at random. Spinal anaesthesia was administered using 10 mg of plain bupivacaine + 20 µg of fentanyl in Groups I and II, and 10 mg of plain bupivacaine in Group III. The first peak sensory block level was noted. Additionally, after the sensory blockage reached the greatest dermatomal level, Group I received saline, whereas Groups II and III received fentanyl 50µg intravenously. Systolic and diastolic blood pressures drastically dropped in all groups following spinal anaesthesia, however they remained unchanged after intravenous fentanyl treatment. The scientists came to the conclusion that fentanyl could be given intravenously as well as intrathecal to increase the distribution of bupivacaine-induced spinal analgesia. Concurrent administration of fentanyl via the spinal and supraspinal routes, however, results in a longer duration of anaesthesia and a larger distribution of spinal analgesia without causing additional side effects.
In the study conducted by Siddik-Sayyid et al.,[12] forty-eight healthy participants scheduled for elective cesarean delivery were randomly allocated to receive intrathecally either 12 mg of hyperbaric bupivacaine plus 12.5µg of fentanyl (n 23) or bupivacaine alone (n 25). Following spinal anaesthesia, 12.5µg of fentanyl was given intravenously to the latter group. Compared to the IT Fentanyl group, the IV Fentanyl group experienced a significantly higher incidence of ephedrine needs and severe hypotension, which was defined as SBP <90 mm Hg ($p = 0.01$). The scientists came to the conclusion that severe hypotension, nausea, and vomiting were less common in the IT fentanyl group.
In a study conducted by Irshad Yousuf et al., patients were divided into two groups of 30 at random.[13] Patients in the intrathecal fentanyl group were given 0.25 ml of normal saline intravenously, 10 mg (2 ml) of bupivacaine, and 12.5µg (0.25 ml) of fentanyl. Patients in the intravenous fentanyl group were given 0.25 ml of normal saline intrathecally, 10 mg of bupivacaine (2 ml), and 0.25 ml of fentanyl (12.5µg microgram) intravenously. Similar to Dhumal PR et al.[14] and Shashikala TK et al., they found no statistically significant differences in mean arterial blood pressure and mean heart rate at different time intervals in either group.[15]
In contrast, a study conducted in Nepal revealed that there was no discernible variation in the incidence of bradycardia, which was 5.7% in the control group and 2.8% in the BF group. Bradycardia occurred in 3 patients in the treatment group and 4 patients in the control group, according to a comparable trial conducted in Texas, although the differences were not statistically significant.[16] There were no bradycardia cases among the participants in Irshad Yousuf et al.[13] compared to the two studies mentioned previously. In contrast to the intrathecal group, the authors found that the intravenous fentanyl group experienced a higher incidence of severe hypotension, which was defined as blood pressure below 90 mmHg and the need for mephentermine.

CONCLUSION

Although comparatively lower Systolic Blood Pressure, Diastolic Blood Pressure & Mean Arterial Pressure were observed with intrathecal administration, the incidence of hypotension (SBP<90 mmHg) was higher with intravenous fentanyl. Intrathecal administration of fentanyl provides longer duration of sensory and motor block and better postoperative analgesia when compared to intravenous fentanyl. Since the literature comparing intrathecal and intravenous fentanyl is limited, further research into the findings is required.

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