

Comparative Study of Subarachnoid Fentanyl and Buprenorphine Added with Bupivacaine for Postoperative Analgesia in Lower Limb and Lower Abdominal Surgeries

Amit Kocheta¹, Ritu Verma², Deepti Agrawal³, Krishan Kumar Thakur⁴

^{1,2}Assistant Professor, Department of Anaesthesiology, Mahaveer Institute of Medical Sciences and Research

^{3,4}Associate Professor, Department of Anaesthesiology, Mahaveer Institute of Medical Sciences and Research

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Corresponding Author: Dr. Krishan Kumar Thakur

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Abstract:

Objective: To compare the analgesic effects, duration of analgesia, haemodynamic parameters of fentanyl and buprenorphine, administered intrathecally with bupivacaine against the control group of bupivacaine alone.

Methods: The patients were divided into three groups according to the drugs administered for subarachnoid block.

In Group I: 3 ml of 0.5% bupivacaine (H) + 15 ug fentanyl.

In Group II: 3 ml of 0.5% bupivacaine (H) + 150 ug buprenorphine.

In Group III: 3 ml of 0.5% bupivacaine.

The patients of three groups were comparable at demographic data.

For the assessment of postoperative pain using numerical scale of one hour interval until the end of analgesia explained to all the patients to make them able to express pain in terms of scale.

Results: The duration of analgesia obtained following intrathecal fentanyl administration (10.72 ± 2.84 hours) is statistically highly significant than following bupivacaine administration (2.88 ± 0.55 hours). The duration of analgesia obtained following intrathecal buprenorphine administration (14.02 ± 2.45 hours) is statistically significantly more than fentanyl (10.72 ± 2.84 hours). The duration of analgesia obtained by intrathecal buprenorphine (14.02 ± 2.45 hours) is statistically highly significant than analgesia obtained by bupivacaine alone (2.88 ± 0.55 hours).

Conclusion: Both fentanyl & buprenorphine can be used effectively for post operative analgesia but buprenorphine is superior than the fentanyl regarding duration of analgesia. There are some side effects like nausea-vomiting, in both the groups & pruritis in buprenorphine group.

Keywords: Fentanyl, Buprenorphine, Post operative analgesia.

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Introduction

Surgical trauma is real and severe tissue damage and surgical pain is a universal phenomenon which is aggravated by associated muscle spasm and visceral distention. In recent times, the increasing use of subarachnoid narcotics for post operative analgesia promises of new venue in this field. Efficacy of this is based on demonstration of specific opiate receptors in the substantia gelatinosa of the posterior horn cells of the spinal cord. The mainstay of post operative pain relief is still the use of potent analgesics in the post operative period. It has proved difficult to find a drug which is a great improvement over narcotics.

These drugs when given parenterally in doses for effective pain relief produce unwanted side effects, because they act equally on central pain mechanism

and central respiratory mechanism, leading to unwanted side effects like nausea, vomiting, pruritis and severe respiratory depression. The use of regional anaesthesia has been confronted with the need to produce an adequate level and degree of blockade in an acceptable period with a safe dose of local anaesthetic, the nerve blockade produced needs to be complete and reproducible and must have a desired duration of action.

The major advancement in improving the success of regional anaesthesia has come from the use of adjuvant drug with spinal and epidural anaesthesia. The primary drugs used with local anaesthetic at spinal cord level are opioids. The combination has a synergistic effect because they have antinociceptive effects in spinal cord via different mechanisms.

Another benefit by giving opioids along with local anaesthetics is also justified with the fact that pain receptors are non-adapting in nature, that means the threshold for excitation of the pain fibres becomes progressively lower and lower as the pain stimulus continues, thus, allowing these receptors to become progressively more activated with time, this increase in sensitivity of pain receptors is called hyperalgesia. Superiority of intrathecal/ extradural route for administration of opioids has now been proven beyond doubt through research studies and clinical experience.

Predicted advantages of intrathecal opioids are: 1) Segmental analgesia with no motor loss. 2) No autonomic block with consequent absence of hypotension. 3) Availability of large number of drugs. 4) Existence of specific antagonist. Opioids and NSAIDs have been the mainstay of post operative pain management. The routine modes (e.g. intravenous or intramuscular injections of opioids or NSAIDs), usually provide analgesia but involve multiple painful injections to the patient. In addition to that, there are certain painfree periods with some very painful periods (e.g. preinjection period). One modern method of pain relief (e.g. patient controlled analgesia or continuous epidural block) can provide good analgesia but requires special equipments.

It was this need of a cost effective but efficient mode of analgesia which prompted us to study and compare the quality of analgesia and complications of intrathecal administration of fentanyl and buprenorphine. Fentanyl belongs to the partial agonist group of opioid drugs which provides good pain relief. The main advantage of fentanyl is lesser incidence of side effects associated with it. Buprenorphine is a very potent analgesic belonging to agonist - antagonist group of opioid drugs. Advantage of buprenorphine is the quality analgesia

obtained while the disadvantage is occurrence of side effects such as resistant respiratory depression.

Materials and Methods

The present study was carried out in the Department of Anesthesiology Mahaveer Institute of Medical Sciences and Research Bhopal. The study comprised of Ninety patients who underwent various surgical procedures:

- Lower abdominal
- Lower limb
- Urological procedures under spinal anesthesia.
- All the patients were in the ASA grade I & II of either sex.
- Age 20-45 years
- Patients with local skin infections on the back or with severe spinal deformities were excluded from the study.
- Informed consent of the patient was taken regarding participation in this study. All the patients were thoroughly examined during pre-operative checkup and investigated as shown in proforma.

History suggestive of any medical illness like jaundice, diabetes mellitus, ischemic heart disease, stroke, asthma etc. was asked for. History of surgery in the past and type of anaesthesia was asked. Routine investigations like haemoglobin and urine examination for sugar and albumin were done in all the patients. Specific investigations like blood sugar, blood urea, serum electrolytes, X-ray chest, electrocardiogram, liver function tests were done wherever necessary. The procedure was explained to each and every patient in detail.

Patients were randomly divided into three groups.

Group	No. of Patients	Inatathecal Drugs
I	30	3ml of 0.5% Bupivacaine(H) +inj. fentanyl 15 mic.gm
II	30	3ml of 0.5% Bupivacaine (H) + Buprenorphine 150 mic.gm
III	30	3ml of 0.5% Bupivacaine (H)

Procedure

Patients underwent a careful and detailed examination on the operation table and baseline data were entered in the proforma. Lumbar puncture was performed under aseptic precautions in sitting or lateral position using 23/25G lumbar puncture needle.

After the drug was injected, following observations were recorded:

1. Time of onset of sensory block
2. Time of onset of motor blockade
3. Level of sensory block
4. Degree of motor block

Grade 0 (nil) - Free movement of leg and feet

Grade I (partial) - Just able to flex knee with free movement of feet.

Grade II (almost complete) - Unable to flex knee with free movement of feet.

Grade III (complete) - Unable to move leg and feet. After the satisfactory level of analgesia was achieved, surgeons were asked to start the operation.

Monitoring and management: PR, BP and RR were recorded every 5 mins till, at 30th min and then half hourly till the completion of surgery. In post operative period they were recorded in

immediate post operative period and after 30 minutes.

Efficacy of analgesics

- Good - No extra analgesics were required throughout the surgery.
- Fair - Some discomforts were there but surgery proceeded with small dose of sedatives.
- Poor - Increase in pain was there and supplementary analgesia was given, either

high dose of pentazocine or gas: O₂ mixture via face mask.

- Failed - Converted to GA.

Analgesia -duration of analgesia was measured from the time of regression of sensory block level by two dermatomal segments, to request for first analgesic by the patient & correlated with the visual analogue scale (VAS).

Observation Chart

Table 1: Age and Sex Distribution

Age	Group-I		Group-II		Group-III	
	No.	%	No.	%	No.	%
21-25 years	11	36.33	10	33.33	9	30
26-30 years	6	20	5	16.66	6	20
31-35 years	5	16.66	5	16.66	4	13.33
36-40 years	4	13.33	4	13.33	6	20
41-45 years	4	13.33	6	20	5	16.66
Total	30	100	30	100	30	100

Table 2: Show Baseline Data in Each Group Preoperatively

Parameter	Group-I		Group-II		Group-III	
	Mean	Range	Mean	Range	Mean	Range
Pulse/min	90.35	72-110	88.0	78-108	87.5	75-105
Systolic BP	115.5	88-150	119.5	98-146	120.0	86-140
Diastolic BP	72.5	60-90	68.0	64-88	70.5	62-94
Resp. rate/min	21.0	18-23	20.5	19-21	20.0	18-22

Table 3: Duration Of Analgesia

Age	Group-I		Group-II		Group-III	
	No.	%	No.	%	No.	%
0-12 hours	20	66.66	8	26.66	30	100
12-18 hours	10	33.33	17	56.66	-	-
> 18 hours	-	-	5	16.66	-	-
Total	30	100	30	100	30	100

Mean duration of analgesia in hours

Group I = 10.72 ± 2.84

Group II = 14.02 ± 2.45

Group III = $2.88 \pm .55$

This shows that group II is statistically more significant that group I group III similarly group I statistically more significant that group III.

Table 4: Degree and Duration of Sedation in the Postoperative Period

Duration of Sedation	Group	Alert		Calm and Quiet		Deep Sedation	
		No.	%	No.	%	No.	%
0-4 hours	I	12	40	18	60	-	-
	II	6	20	24	80	-	-
	III	30	100	-	-	-	-
4-8 hours	I	15	50	15	50	-	-
	II	5	16.66	25	83.33	-	-
	III	30	100	-	-	-	-
12-16 hours	I	28	93.33	2	6.66	-	-
	II	20	66.66	10	33.33	-	-
	III	25	100	-	-	-	-
16-24 hours	I	30	100	-	-	-	-
	II	26	86.66	4	13.33	-	-
	III	30	100	-	-	-	-

Table 5: Effect of Fentanyl and Buprenorphine on Pulse Rate in the Postoperative Period in First Ten Hours

Duration in hours after intrathecal injection	Group I (Mean±SD)	Group II (Mean±SD)	Group III (Mean±SD)
0-1	86.8 ± 8.01	89.6 ± 7.5	90.7 ± 11.05
1-2	86.2 ± 8.30	90.6 ± 8.3	89.4 ± 6.50
2-3	85.1 ± 8.50	86.3 ± 6.5	89.1 ± 9.20
3-4	86.1 ± 8.50	87.2 ± 9.9	88.3 ± 10.2
4-5	86.2 ± 6.2	87.0 ± 5.5	87.4 ± 4.5
5-6	86.4 ± 6.4	87.0 ± 5.5	87.5 ± 4.3
6-7	86.5 ± 6.9	84.2 ± 6.2	86.5 ± 7.3
7-8	85.6 ± 7.3	86.5 ± 7.0	87.3 ± 7.1
8-9	86.3 ± 9.3	87.0 ± 8.5	88.7 ± 6.4
9-10	86.2 ± 8.3	89.9 ± 9.5	89.3 ± 10.9

So, there is no significant change in pulse rate among three groups.

Table 6: Effect of Fentanyl and Buprenorphine on Systolic Blood Pressure in the Postoperative Period in First Ten Hours

Duration in hours after intrathecal injection	Group I (Mean±SD)	Group II (Mean±SD)	Group III (Mean±SD)
0-1	116.4 ± 10.2	114.9 ± 9.5	117.7 ± 10.3
1-2	119.5 ± 9.50	115.4 ± 10.7	119.1 ± 7.3
2-3	117.7 ± 10.4	119.3 ± 8.5	118.5 ± 10.4
3-4	118.1 ± 7.1	117.0 ± 5.6	115.3 ± 4.8
4-5	120.4 ± 7.6	121.3 ± 8.3	118.0 ± 7.8
5-6	118.1 ± 7.1	123.3 ± 6.8	118.9 ± 6.3
6-7	118.9 ± 6.3	118.0 ± 7.5	119.5 ± 9.5
7-8	116.5 ± 10.4	123.5 ± 9.3	120.4 ± 7.8
8-9	120.4 ± 7.8	120.6 ± 7.5	116.4 ± 9.5
9-10	117.7 ± 10.4	122.5 ± 10.5	114.3 ± 38

So, there is no significant change in Systolic Blood Pressure among three groups.

Table 7: Effect of Fentanyl and Buprenorphine on Respiratory Rate in the Postoperative Period in First Ten Hours

Duration in hours after intrathecal injection	Group I (Mean±SD)	Group II (Mean±SD)	Group III (Mean±SD)
0-2	18.2 ± 2.17	20.3 ± 2.1	19.2 ± 1.7
2-4	19.0 ± 2.1	20.1 ± 1.6	18.3 ± 2.3
4-6	19.4 ± 2.13	20.0 ± 1.4	20.3 ± 1.9
6-8	19.6 ± 3.9	16.6 ± 4.6	20.0 ± 3.2
8-10	19.5 ± 1.6	17.6 ± 4.3	18.6 ± 2.5
10-12	20.6 ± 1.9	17.4 ± 3.9	20.25 ± 3.7
12-14	19.8 ± 1.3	19.5 ± 8.2	20.9 ± 2.7
14-16	17.4 ± 2.4	19.7 ± 4.4	17.8 ± 3.4
16-18	20.4 ± 1.6	19.7 ± 4.4	17.8 ± 3.4
18-20	19.7 ± 3.2	20.1 ± 10.6	20.3 ± 2.3
20-22	17.6 ± 4.4	19.8 ± 3.2	16.8 ± 3.7
22-24	16.6 ± 1.9	20.4 ± 1.9	18.3 ± 1.8

So, there is no significant change in respiratory rate among three groups.

Table 8: Side Effects of Intrathecal Fentanyl and Buprenorphine

Side Effects	Upto 8 hours						8-16 hours						16-24 hours					
	I		II		III		I		II		III		I		II		III	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Nausea	12	40	9	30	0	-	4	13.33	-	-	-	-	-	-	-	-	-	-
Vomiting	8	26.66	6	20	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Itching	-	-	3	10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Headache	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urinary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Retention	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Respiratory Depression	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypotension	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Results

1. The duration of analgesia obtained following intrathecal fentanyl administration (10.72 ± 2.84 hours) is statistically highly significant than following bupivacaine administration (2.88 ± 0.55 hours).
2. The duration of analgesia obtained following intrathecal buprenorphine administration (14.02 ± 2.45 hours) is statistically significantly more than fentanyl (10.72 ± 2.84 hours).
3. The duration of analgesia obtained by intrathecal buprenorphine (14.02 ± 2.45 hours) is statistically highly significant than analgesia obtained by bupivacaine alone (2.88 ± 0.55 hours).
4. Nausea and vomiting was seen in both groups. But more often in fentanyl group (40%) than buprenorphine group (30%) within 8 hours which then gradually decreased. Nausea and vomiting was not seen with bupivacaine alone.
5. No significant hemodynamic changes were seen in all the groups.
6. No significant cardiorespiratory effects were seen in all the groups.
7. Urinary retention and headache was not seen in any of the patients.

Statistical Analysis:

The collected data was summarized by using frequency, percentage, mean & S.D. To compare the qualitative outcome measures Chi-square test or Fisher's exact test was used. To compare the quantitative outcome measures independent t test was used. If data was not following normal distribution, Mann Whitney U test was used. SPSS version 22 software was used to analyse the collected data. p value of <0.05 was statistically significant.

Discussion

A randomised controlled trial to evaluate the effectiveness of intrathecal bupivacaine combined with different adjuvants (fentanyl, clonidine and dexmedetomidine) in caesarean section was done by

Li Z et al. The purpose of this study was to evaluate comparatively 3 different adjuvants (fentanyl, clonidine, and dexmedetomidine) on quality of blockade and maternal and neonatal repercussions. Hemodynamic parameters evaluated were the onset and level of sensory block, perioperative analgesia, degree and recovery time of motor block, duration of analgesia, sedation, and maternal-foetal repercussions. It was concluded that addition of dexmedetomidine and clonidine as adjuvants to hyperbaric bupivacaine provided adequate anesthesia and postoperative analgesia compared to fentanyl adjuvant without causing any significant side effects.

The analgesic effect of the centrally acting opioid, fentanyl, is well-known. It has been shown in clinical studies that using fentanyl epidurally can provide longer duration of analgesia, without the common side effects of opioids. Chakraborty et al undertook a study to evaluate the duration of analgesia and/or pain free period produced by intrathecal fentanyl added to bupivacaine in patients undergoing major gynecological surgery in a randomized double blind placebo controlled protocol. Duration of analgesia or pain free period was estimated from the time of completion of spinal injection to administration of rescue analgesic or when the VAS score was greater than 40 mm. In Group B patients, the VAS score was significantly lower, as compared to Group A patients. The duration of analgesia was 210 ± 10.12 min in Group A; whereas, in Group B, it was 380 ± 11.82 min, which was found to be significant.

Afolayan JM et al did a prospective randomized study with the aim to evaluate the effectiveness of intra-operative analgesia produced by intrathecal fentanyl and fentanyl during bupivacaine spinal anesthesia for open appendectomy. this study showed that intrathecal fentanyl (25 mg) can safely replace intrathecal fentanyl (15 microgm) in the management of visceral pain and discomfort during subarachnoid block for appendectomy. similar study was done by Alhashemi ja et al on effect of intrathecal fentanyl. in this double-blind, placebo-controlled study, the effect of intrathecal fentanyl

administration on pain control after transurethral resection of the prostate (TURP) was studied. Postoperative morphine requirements, visual analogue scale for pain at rest (VAS) and sedation scores, times to first analgesic and hospital lengths of stay were recorded by a blinded observer. Intrathecal fentanyl was not different from saline in its effect on postoperative morphine requirements after TURP.

Prasad RB et al did a randomized placebo-controlled study on effectiveness of addition of intrathecal fentanyl with hyperbaric bupivacaine in prevention of shivering in parturients undergoing cesarean section under spinal anesthesia. The study was conducted as a single-blind study in a 350-bedded teaching hospital. The analgesic effect of the block lasted for a mean duration of 232 min in Group T and 176 min in Group NS while nausea and vomiting were increased in group T versus NS. Fentanyl (10 mg), along with bupivacaine given intrathecally plays a significant role in reducing the incidence of anesthesia-induced shivering in parturients while prolonging both the sensory and motor components of the subarachnoid block.

Zahid F et al used intrathecal fentanyl as an adjuvant in subarachnoid block to prolong the duration of analgesia. Subedi A et al studied analgesic effects of intrathecal fentanyl in patients undergoing caesarean section in a randomised, double-blind study. The present study evaluated the effect of intrathecal fentanyl on spinal block characteristics and neonatal outcome after elective caesarean section compared to intrathecal fentanyl 10 µg, fentanyl 10 mg, as an adjunct to bupivacaine for subarachnoid block for caesarean section, showed a longer duration of analgesia with a reduced incidence of shivering.

Capogna G et al did study on intrathecal buprenorphine for postoperative analgesia in the elderly patient. Prolonged postoperative analgesia, minimal disturbance of consciousness and comfortable breathing were common to the groups that received buprenorphine. The higher concentration of buprenorphine improved the quality and duration of analgesia. The only side effects found in the buprenorphine groups were nausea and vomiting in 11 and 14 patients, respectively, in groups B and C. Our study shows that buprenorphine is an effective analgesic, suitable for the management of postoperative pain in elderly patients.

Gupta M et al did study was to evaluate and compare the characteristics of subarachnoid blockade, hemodynamic stability and adverse effects of intrathecal buprenorphine and intrathecal dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine for lower abdominal surgeries. There was no significant difference between groups regarding demographic characteristics and type of surgery. The motor, sensory blockade and time of rescue analgesia were

significantly prolonged in Group D compared to Group B. The sedation level was higher in Group D compared to Group B. There was no significant difference in haemodynamic variables although Group B had lower Heart Rate (HR) than Group D. So, it was concluded that intrathecal dexmedetomidine when compared to intrathecal buprenorphine causes prolonged anaesthesia and analgesia with reduced need for sedation and rescue analgesics.

Rabiee SM et al did double blind randomized clinical trial study in patients for cesarean section under spinal anesthesia. The patients were randomly divided into case and control groups. Hemodynamic changes and neonatal APGAR scores (Appearance, Pulse, Grimace, Activity, Respiration) were recorded. Pain score was recorded according to the visual analog scale. Systolic blood pressure was not significantly different until the 45th minute but diastolic blood pressure showed a significant difference at the 15th and the 60th minutes ($P < 0.001$). Heart rate changes were significantly different between cases and controls at the initial 5th, 15th and after 60th minutes ($P < 0.001$). Pain-free period was significantly different between two groups (1.25 h versus 18.73 h) ($P < 0.001$). The results show that prescription of intrathecal buprenorphine prolongs the duration of analgesia without any significant considerable side effects.

The augmentation of local anesthetics with various adjuvants to enhance the quality and efficacy of subarachnoid block is clinically in practice since long. Jejani AS et al studied intrathecal buprenorphine for postoperative analgesia after cesarean section. Siddiq S et al did comparative study of the effect of intrathecal fentanyl and buprenorphine used as adjuvants to hyperbaric bupivacaine for postoperative analgesia in infraumbilical surgeries. It was concluded that both fentanyl and buprenorphine, prolong the duration of postop analgesia without adding any adverse effects, but duration with fentanyl is longer; it significantly reduces VAS and the dose of analgesic requirement in 24 h postoperatively.

Pöpping DM et al did a meta-analysis of randomized trials. They systematically searched databases and bibliographies for full reports of randomized comparisons of any opioid added to any intrathecal local anesthetic with the local anesthetic alone. Duration of postoperative analgesia was prolonged with and fentanyl. Morphine decreased the number of patients needing opioid analgesia after surgery and decreased pain intensity to the 12th postoperative hour. Morphine increased the risk of nausea vomiting, urinary retention, and pruritus. Fentanyl increased the risk of pruritus. With morphine 0.05 to 0.5 mg, the NNH for respiratory depression varied between 38 and 59 depending on the definition of respiratory depression chosen. With fentanyl 10 to 40 µg, the risk of respiratory depression was not significantly increased. For none

of these effects, beneficial or harmful, was there evidence of dose-responsiveness. Consequently, minimal effective doses of intrathecal morphine and fentanyl should be sought. For intrathecal buprenorphine, diamorphine, hydromorphone, meperidine, methadone, pentazocine, sufentanil, and fentanyl, there were not enough data to allow for meaningful conclusions.

Spinal anesthesia is a safe and reliable technique for surgeries on the lower abdomen and lower limbs. Some of its characteristics like delayed ambulation and pain after block regression may limit its use, especially for short duration surgeries. Siddaiah J et al did a comparative study on the effect of addition of intrathecal buprenorphine to 2-chloroprocaine spinal anesthesia in short duration surgeries. This study aims to compare the effect of adding intrathecal buprenorphine to 2-chloroprocaine with regard to spinal anesthesia characteristics. The time of onset of sensory and motor blocks, peak sensory block, readiness for surgery, and complete regression of both sensory and motor blocks were comparable between the groups. Group B showed significantly prolonged duration of postoperative analgesia. 91.1% patients were able to ambulate within 100 minutes in our study. It was concluded that addition of buprenorphine to 2-chloroprocaine has a significant synergistic effect on prolonging postoperative analgesia.

Conclusion

We conclude that both fentanyl & buprenorphine can be used effectively for post operative analgesia but buprenorphine is superior than the fentanyl regarding duration of analgesia. There are some side effects like nausea -vomiting, in both the groups & pruritis in buprenorphine group. which can be easily controlled with medications.

Declarations:

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Consent for publication: Consent taken

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