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A COMPARATIVE STUDY OF INTRATHECAL FENTANYL 25µg AND BUTORPHANOL 25 µg AS ADJUVANTS TO 0.5% HYPERBARIC BUPIVACAINE FOR INFRA UMBILICAL SURGERIES

Anesthesiology

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ABSTRACT

Introduction:-Spinal anesthesia-Regional anesthesia, is the most commonly used technique which provides a fast and effective onset of sensory and motor block, excellent muscle relaxation, and prolonged postoperative analgesia. In an attempt to further minimize the effects of local anesthetics and prolong the duration of intraoperative and postoperative analgesia, various adjuvants have been used. Short acting opioids like fentanyl and sufentanyl have been used intrathecally in elderly patients to provide pain relief but for adult patients needs long acting opioids for more post operative analgesia. Butorphanol is a lipophilic opioid agonist-antagonist analgesic with a greater affinity for opioid receptors, When used interathecally in combination with bupivacaine it has known to improve the quality and duration of postoperative analgesia compared to bupivacaine alone. Therefore, the present study is being undertaken to evaluate and compare the effects of Butorphanol and fentanyl as intrathecal adjuvants to bupivacaine heavy (hyperbaric) in patients undergoing infra umbilical surgeries **Material and methods:-** The study was conducted in Department of Anesthesiology, Jhalawar Medical College, Jhalawar, Rajasthan, from dec.2019 to june2020. Due permission from institutional ethical committee was obtained. This is Hospital based prospective observational study. This study included 90 Cases of either sex admitted for infra umbilical surgeries. The patients were randomly divided into 3 groups of 30 each.
Group BF- 2.5ml of 0.5% hyperbaric bupivacaine + 25µg(0.5ml) Fentanyl
Group BB- 2.5ml of 0.5% hyperbaric bupivacaine + 25µg(0.5ml) Butorphanol
Group BS- 2.5ml of 0.5% hyperbaric bupivacaine + 0.5ml Normal Saline
All data were collected and analysed with the help of suitable statistical parameters.
Results:- The mean duration of sensory block in group-BF was 166.13 + 17.78min and in group-BB was 187.17 + 23.83min and in group-BS was 146.33+ 14.39. With a statistically significant difference. The mean duration of motor block in group-BF was 128.80 + 9.18min and in group- BB was 130.92 + 13.327 min and in group BS was 126.32 + 4.52. With a statistically insignificant difference. Whereas the duration of analgesia was longest (348.33 + 11.55) in group BB (Butorphanol) and highly significant ($p<0.001$) difference when compared to fentanyl and control group. Sedation score was higher in group BB as compare with group BF and group BS.

KEYWORDS

Spinal Anesthesia , Fentanyl, Butorphanol, Infra Umbilical Surgeries

INTRODUCTION:

The management of pain is a major aspect of anaesthesia. Today's anesthesiologist is not only involved in the preoperative and intraoperative care of the patients but is also responsible for the postoperative pain relief.[1] Spinal anesthesia is the most commonly used technique which provides a fast and effective onset of sensory and motor block, excellent muscle relaxation, and prolonged postoperative analgesia.[3] Levobupivacaine is a preferred local anaesthetic due to its longer sensory block, lower cardiac and central nervous system toxicity and shorter motor block.

In an attempt to further minimize the effects of local anesthetics and prolong the duration of intraoperative and postoperative analgesia, various adjuvants such as vasoconstrictors, alpha-2 agonists, and opioids have been used. [4]

Almost all opioids have been used as adjuvants intrathecally. Most commonly used opioid in regional anesthesia is fentanyl citrate which is a µ1 - and µ2 -receptor agonist. It is a highly potent drug because of its high lipophilicity with minimal cephalad spread making it the least likely of all the intrathecal opioids to cause delayed respiratory depression [5]. Furthermore, it is reported that a single administration of an opioid may also induce a long lasting increase of threshold pain sensitivity, leading to delayed hyperalgesia [3]. However, pruritus, nausea, vomiting, **respiratory depression**, and urinary retention are other common side effects for which search for ideal nonopioid adjuvants goes on.[2]

Short acting opioids like fentanyl and sufentanyl have been used intrathecally in elderly patients to provide pain relief but for adult patients needs long acting opioids for more post operative analgesia.

Butorphanol is a lipophilic opioid agonist-antagonist analgesic with a greater affinity for opioid receptors in vitro of 1:4:25 (µ: δ:κ) which can also be administered safely in subarachnoid space [6] When used interathecally in combination with bupivacaine it has known to improve the quality and duration of postoperative analgesia compared to bupivacaine alone.

Therefore, the present study is being undertaken to evaluate and compare the effects of Butorphanol and fentanyl as intrathecal adjuvants to bupivacaine heavy (hyperbaric) in patients undergoing infra umbilical surgeries

MATERIAL AND METHOD:

Study Area: The study was conducted in Department of Anesthesiology, Jhalawar Medical College, Jhalawar, From December 2019 to June 2020. With Due permission from institutional ethical committee was obtained.

Study Design : Hospital based prospective study observational study.

Study Universe: patients of Surgery and Orthopedic department of Jhalawar Medical College and SRG Hospital, Jhalawar Rajasthan.

Study Groups : The study was conducted in following three groups of patients. Each group consist of 30 patients (n =30/group). Ninety (90) patients aged between 20 to 60 years of physical status ASA grade I and II of either sex, undergoing elective infra umbilical surgeries were included in the study after ethical clearance.

Group BF	2.5ml of 0.5% hyperbaric bupivacaine + 25µg(0.5ml) Fentanyl
Group BB	2.5ml of 0.5% hyperbaric bupivacaine + 25µg(0.5ml) Butorphanol
Group BS	2.5ml of 0.5% hyperbaric bupivacaine + 0.5ml Normal Saline

Pre-anaesthetic assessment:

- Standard protocol was followed for Pre-anaesthetic assessment of patients.

Inclusion criteria:-
- All the patients who are posted for elective lower abdominal surgeries
- Age group- 20- 60 years.
- ASA I and II.
- Either gender male and female
- Height 150-180 cm.

Exclusion criteria:-
- Parturient refusal.
- Diabetes, pre-eclampsia or eclampsia.
- Parturient with cardiac, respiratory, renal, hepatic or neurologic disease.
- Bleeding or coagulation disorders, thrombocytopenia.
- Local or systemic sepsis.
- Hypersensitivity to study drugs.
- History of drug abuse.

Procedure:
Informed written consent was obtained after complete explanation about the study protocol and the procedure. Spinal anesthesia was performed at L3-L4 interspace with the standard protocol.

Observations:
Intraoperatively, vital parameters like heart rate, noninvasive blood pressure, SpO2, Respiratory Rate were recorded every 5 minutes for first 15 minutes , every 15 min up to 60 min & then every 60 min until end of surgery.

Alteration in the hemodynamic parameters such as hypotension and bradycardia were treated with injection mephentermine 6mg/ml and Atropine 0.6 mg i.v. bolus.

Any adverse events like nausea, vomiting, pruritis, urinary retention etc were noted and treated accordingly.

Assessment of sensory blockade and duration – Tested by pin prick test using hypodermic needle with Hollmen scale and the time of onset, highest level of sensory blockade, duration of sensory block were noted.

Postoperatively patient was assessed every hour till S_1 regression (Great toe sensation) to measure the duration of sensory block.

Hollmen Scale :-
1. Ability to appreciate a pinprick as sharp;
2. Ability to appreciate a pinprick as less sharp;
3. Inability to appreciate a pinprick as sharp (analgesia).
4. Inability to appreciate a pin touching (anaesthesia).

Assessment motor blockade and duration - is assessed by Bromage scale. Postoperatively patient was assessed every hour till Bromage 1to measure duration of motor blockade.

Bromage scale[7]:

Grade	Criteria	Degree of block
0	Free movement of legs & feet	Nil (0%)
I	Just able to flex knees with free movement of feet	Partial (33%)
II	Unable to flex knees with free movement of feet	Almost complete (66%)
III	Unable to move or flex legs or feet	Complete (100%)

Sedation-will be assessed with Observer's assessment of alertness sedation scale[OAASS]

Observer's assessment of alertness sedation scale[8][OAASS]

Response	Score
Agitated	6
Responds readily to name spoken in normal tone (alert)	5
Lethargic response to name spoken in normal tone	4
Responds only after name is called loudly and/or repeatedly	3
Responds only after mild prodding or shaking	2
Does not respond to mild prodding or shaking	1
Does not respond to deep stimulus	0

ANALGESIA: Postoperatively patient was assessed every hour till 24 hours to measure the duration of analgesia.

Visual analogue score – postoperatively, the pain was assessed by using visual analog pain scale (VAS) between 0 and 10 (0= no pain, 10= worst possible pain). It was assessed at every 30 min. If VAS was noted more than 4 scale then inj. Diclofenac 75 mg intramuscular was given as a rescue analgesia.

Data entry and Statistical analysis
Collected data was coded and entered in Microsoft Excel 10. The data was subjected to statistical analysis using Statistical Package for the Social Sciences (SPSS trial version 16.0). Normally distributed continuous variables in three groups were compared using one/way ANOVA test and multiple comparisons were done with post-hoc analysis using Bonferroni test. Appropriate tables and figures were generated. Data is expressed as mean with standard deviation and P values < 0.05 are considered as statistical significant.

RESULTS:

Table: 1 Duration Of Sensory Block

Groups	BF	BB	BS	P value		
				BF&BB	BF&BS	BB&BS
TIME (Min.) Mean ± SD	166.13 ± 17.78	187.17 ± 23.83	146.33± 14.39	<0.05	<0.001	<0.001

This table shows the comparison of duration of sensory block & there is statistically significant difference between all the three groups. Duration of sensory block was longest in group BB (Butorphanol) and statistically highly significant ($p<0.001$) also when compared control group (BS) and also significant ($p<0.05$) when compared to fentanyl group (BF).

Table: 2 Duration Of Motor Block

Groups	BF	BB	BS	P value		
				BF&BB	BF&BS	BB&BS
TIME (Min.) mean ± SD	128.80 ± 9.18	130.92 ± 13.327	126.32 ± 4.52	0.108	0.082	0.087

This table shows the duration of motor block (Time to reach grade I Bromage Score in mintes) in the three groups & there is statistically no significant difference between the groups. Duration of motor block was longest in Group BB (Butorphanol) but the comparative results are not significant with fentanyl & control group.

Table: 3 Duration Of Analgesia

Groups	BF	BB	BS	P value		
				BF&BB	BF&BS	BB&BS
TIME (minutes) Mean ± SD	297.33 ± 12.91	348.33 ± 11.55	209.50 ± 9.77	<0.001	<0.001	<0.001

This table shows the comparison of duration of analgesia (time from injecting drug intrathecally to the time when VAS >5) among the groups & there is statistically significant difference between the groups. The duration of analgesia was longest in group BB (Butorphanol) and highly significant ($p<0.001$) difference when compared to fentanyl and control group.

Table: 4 Sedation Score (OAASS)

OAAS Score	BF		BB		BS		P VALUE		
	MEAN	SD	MEAN	SD	MEAN	SD	BF&BB	BF&BS	BB&BS
2 HR	4.6	0.5	4.9	0.3	4	0.4	.006	<.001	<.001
3 HR	4.5	0.5	4.9	0.3	3.9	0.4	.002	<.001	<.001
4 HR	4.6	0.5	5	0.2	4	0.4	<.001	<.001	<.001
5 HR	4.5	0.5	4.9	0.3	4	0.4	.003	<.001	<.001
6 HR	4.6	0.5	4.9	0.2	4.2	0.4	.001	<.001	<.001
9 HR	4.5	0.5	4.9	0.3	4.1	0.6	.027	.006	<.001
12 HR	4.27	0.44	4.73	0.44	3.83	0.45	<.001	.001	<.001
24 HR	4.33	0.47	4.9	0.3	4.13	0.49	<.001	.245	<.001

This table shows comparison of three groups in regard to mean change in sedation score ± from baseline value at various time intervals. There is statistically significant difference ($p<0.05$) between all the three groups. Sedation score was higher in group BB as compare with group BF and group BS.

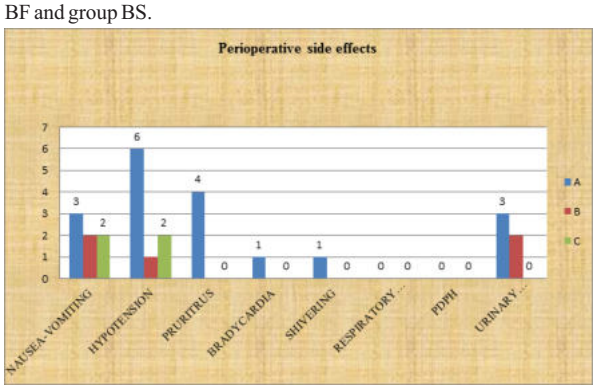

Fig. 1 Perioperative side effects
(A for group BF, B for group BB, C for group BS)

DISCUSSION:

Lower abdominal surgeries may be performed under general anaesthesia (GA) or regional anaesthesia (RA). Due to availability of newer anaesthesia equipments and medications, GA and RA management has become more refine. RA technique like central and peripheral neuroaxial block can provide adequate anaesthesia and decrease postoperative analgesic requirements for lower abdominal surgeries. Opioids as spinal adjuvants to local anaesthetics improve the quality of the block and provide a dose – sparing effect. We chose to investigate **Fentanyl**, a μ receptor agonist and **Butorphanol**, a strong kappa-receptor agonist and a partial μ receptor agonist- antagonist administered along with **hyperbaric Bupivacaine** for intraoperative and post – operative analgesia.

In our study we compared efficacy of Butorphanol & Fentanyl when administered as adjuvants to Bupivacaine in sub-arachnoid block for lower abdominal surgeries. 90 patients were randomly divided into three groups. We injected 2.5 ml of 0.5 % Hyperbaric bupivacaine (12.5 mg) with 25 μg fentanyl (group BF), 25 μg butorphanol (group BB) and 0.5ml normal saline (group BS) used in accordance with past studies **Singh V et al. (2006)**[9] and **Kumar B et al. (2011)**[10] who had used similar amounts and volumes of drugs for lower limb orthopedic surgeries. We undertook this study for infraumbilical surgeries to see whether we will obtain similar or different results from their studies.

The observations and results were recorded and compared in all the three groups both intraoperatively & postoperatively.

Duration of sensory block :

Duration of sensory block in our study was 166.13 ± 17.78 min in fentanyl (group BF), 187.17 ± 23.83 minutes in butorphanol (group BB) and 146.3314.39 min in bupivacaine (control (BS) group) which was similar with study done by **Kaur M et al. (2011)**[11] who found equal prolongation in duration of sensory block with fentanyl and butorphanol groups(156.8323.83 min in bupivacaine alone group, 170.87 ± 22.21 min in bupivacaine-fentanyl group and 171.17 ± 23.99 min in bupivacaine-butorphanol group).

The results from our study prove that quality of the sensory block is significantly improved with the addition of both the opioids to Bupivacaine. Majority of the patients in group BF (Fentanyl) and group BB (Butorphanol) had good quality of analgesia. No patient required any supplemental analgesic during the surgery. In the duration of sensory block, there was significant statistical difference among all the groups (p value < 0.05).

Duration of Motor Block :

Duration of motor block in our study was 128.80 ± 9.18 minutes in fentanyl (group BF), 130.9213.32 minutes in butrphanol (group BB) and 126.32 ± 4.52 minutes (group BS). which are not significant and same in all the three groups.

Similar duration of motor block was there in study by **Singh V et al. (2006)**[9], **Kumar B et al. (2011)**[10] and **Kumar M et al. (2011)**[11]

Post-Operative Visual Analogue Scale :

The pain scores as assessed on the VAS were low and remained low for a significant time in the post operative period with the addition of Fentanyl or Butorphanol to Bupivacaine. VAS score were higher in group BS as compared to group BF and BB. If VAS was noted more than 4 scale then inj. Diclofenac 75 mg intramuscular was given as a rescue analgesia and at 150 min in group BS (control group), 180 min in group BF (fentanyl) and 210 min in group BB (butorphanol). There was highly significant difference in the VAS scores between group BB & BS, group BF & BS ($P<0.001$) throughout the study period. **Kumar B et al (2011)**[9] and **Kaur M et al (2011)**[10] observed similar time to rescue analgesia.

Similar results were obtained in study done by **Yesuf et al (2017)**[12] who observed VAS score were higher in group BS (control group) compared to group BF (fentanyl group).

VAS score reduced at 4hr, 5hr and 6hr in BF group.
Analgesia request time in BF (301.00 ± 46.55) vs (200.20 ± 44.19) in minutes in BS group, $P=0.001$ also longer.

Similar results were obtained in study done by **Reddy IR et al (2018)**[13]. Who noticed VAS score were higher in group BB .

First rescue analgesia request was longer duration 245 ± 40.9 min in group BF (fentanyl) vs 290 ± 47.6 min in group BB (butorphanol).

Duration of Analgesia:

The duration of analgesia was significantly prolonged with the addition of narcotics to LA. We observed duration of analgesia with 2.5 ml 0.5% hyperbaric Bupivacaine alone (group BS) was (209.50 ± 9.77 minutes).

The duration of analgesia was prolonged (297.33 ± 12.91 minutes) with the addition of 25 μg Fentanyl to Bupivacaine in group BF. The duration of analgesia was longest (348.33 ± 11.55min) with Bupivacaine plus Butorphanol in group BB for post-operative analgesia in our study. Similar results were obtained in study done by **Kumar B et al (2011)**[10] average time of first rescue analgesia were 308 ± 14.9 minutes vs 365.9 ± 12.3 minutes in group A (fentanyl) and B (butorphanol) respectively ($p=0.0254$).

Both fentanyl and butorphanol along with bupivacaine provided adequate anaesthesia and analgesia but significantly lesser analgesic requirement was in butorphanol group. **Singh V et al. (2006)**[9] have reported lesser number of patients receiving intrathecal butorphanol requested rescue analgesia compared to those receiving intrathecal fentanyl.

We studied 25 μg dose of intrathecal fentanyl and butorphanol and results of our study were consistent with experimental evidence of synergistic interaction between spinal opioids and local anaesthetics which is characterized by enhanced somatic analgesia without effect on degree of local anaesthetic induced sympathetic or motor blockade. Similar results were obtained in study done by **Yesuf et al (2017)**[12] who found total duration of analgesia was longer in BF group (275.10 ± 42.43) than BS group (156.10 ± 34.45) in minutes, $p= 0.001$.

The synergism between intrathecal opioids in addition to local anaesthetics may be due to separate mechanism of action of local anaesthetics which acts by blockade of Na^+ channel while opioids acts on voltage gated Ca^{++} channels which allows reduction in doses of local anaesthetics and less risk of side effects. Results of **Wang C et al. (1993)**[14] also supported same findings.

Complications And Side Effects :

Narcotic analgesics are well-known for the potential side effects such as pruritus, nausea, vomiting, urinary retention and respiratory depression. Delayed respiratory depression is the most troublesome of these side effects and appears to be largely responsible for the reluctance of anesthesiologist to use intrathecal narcotics. This phenomenon is thought to be due to transport of drug in cerebrospinal fluid from the lumbar region to the fourth ventricle, with consequent depression of the medullary respiratory centers. The incidence of delayed respiratory depression appears to be greatest with poorly lipid-soluble narcotic drugs, like morphine.

Respiratory depression:- The patients in all the three groups were

continuously observed for respiratory depression with SpO2< 90% and respiratory rate< 10/min. We observed no respiratory depression in any of the groups both intra-operatively and post-operatively, which was consistent with study done by **Varrassi G et al. (1992)**[15] who noticed no significant differences in minute ventilation and respiratory drive with fentanyl 50µg with intrathecal bupivacaine. **Singh V et al. (2006)**[9]**, Kumar B et al. (2011)**[10] and **Kaur M et al. (2011)**[11] observed no respiratory depression with 25 µg fentanyl and 25 µg butorphanol intrathecally.

CONCLUSION:

We conclude that both 25 µg fentanyl and 25 µg butorphanol given intrathecally with 12.5 mg of hyperbaric bupivacaine are equally efficacious in patients undergoing infra-umbilical surgeries instead of bupivacaine alone.

Since butorphanol provided longer duration of analgesia and excellent sedation in postoperative period with lesser incidence of complication, so butorphanol appear as a better alternative as an adjuvant to bupivacaine.

CONFLICT OF INTEREST: there is no conflict of interest between authors.

ABBREVIATION:

ASA American Society of Anaesthesiologists
VAS Visual Analog Pain Scale
OAASS Observer's Assessment Of Alertness Sedation Scale

REFERENCES:

1. AP, Jarewal V, Kumar R, Kashyap A. Comparison of levobupivacaine and levobupivacaine with dexmedetomidine in infraumbilical surgeries under spinal anesthesia. Anesth Essays Res. 2018;12:251-5.
2. Macario A, Weinger M, Carney S, Kim A. Which clinical anaesthesiaoutcomes are important to avoid? The perspective ofpatients. Anesth Analg 1999 Sep; 89(3): 652–8
3. Attri JP, Kaur G, Kaur S, Kaur R, Mohan B, Kashyap K. Comparison of levobupivacaine and levobupivacaine with fentanyl in infraumbilical surgeries under spinal anaesthesia. Anesth Essays Res. 2015 May-Aug;9(2):178-84.
4. Helgeson LE. Sedation during regional anaesthesia: Inhalation versus intravenous. Curr Opin Anaesthesiol. 2005 Oct;18(5):534-9.
5. Casey WF. Spinal Anaesthesia - a Practical Guide. Update in Anaesthesia. 2000; 12(8): 21-34.
6. Commiskey S, Fan LW, Ho IK, Rockhold RW. Butorphanol: Effects of a prototypical agonist-antagonist analgesic on kappa-opioid receptors. J. Pharma. Sci. 2005; 98: 109–16.
7. Bromage PR. " The price of intraspinal narcotic analgesics: Basic constraints" (editorial) Anaesth. Analg 1989; 68: 323-37.
8. Chernik DA, Gillings D, Laine H, Hendler J and Silver J. Validity & reliability of observer's assessment of alertness/ sedation scale. J. Clin. Psychopharmacology. 1990 Aug; 10 (4): 244-51.
9. Singh V, Gupta LK, Singh GP. Comparison among intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries. J Anesth Clin Pharmacol 2006;22:371-5.
10. Kumar B, Williams A, Lidddle D, VergheseM. Comapison of intrathecal bupivacaine –fentanyl And bupivacaine - butorphanol mixtures for lower limb orthopedic procedures Anesthesia: Essay and Researches 2011; 5(2)190-19
11. Kaur M, Katyal S, Kathuria S, Singh P. Comperative evalution of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgeries. Saudi J. Anaesth. 2011; 5 (2) 202-207.
12. Yesuf KA, Gebremedhn EG, Melkie TB Analgesic Effect of Intrathecal Fentanyl as an Adjuvant to Spinal Anaesthesia in Comparison with Spinal Anaesthesia with Bupivacaine Only for Mothers Delivered by Emergency Cesarean Section. J Anesth Crit Care Open Access (2017) 7(5): 00278.
13. Reddy IR, Aasim SA, Komravelli KK. A Comparative study of anaesthesia and analgesia between intrathecal fentanyl and butorphanol with 0.5% bupivacaine heavy for lower limb orthopedic surgery. Int. J. Res. Health Sci. 2018; 6 (2) : 1-8.
14. Wang C, Chakrabarti MK, Whitwam JG. Specific enhancement by fentanyl of the effects of intrathecal bupivacaine or nociceptive afferent but not on sympathetic efferent pathway in dogs. Anesthesiology 1993; 79: 766-73.
15. Varrassi G, Celleno D, Capogna G, Costantino P, Emanuelli M, Sebastiani M, A F Pesce, D Niv. Ventilatory effects of subarachnoid fentanyl in the elderly. Anaesthesia 1992;47:558-62.