Effect of Bupivacaine and Fentanyl v/s Bupivacaine and Butorphanol in labour analgesia by Epidural technique :A Comparative Study in a Tertiary Care Hospital,Telangana,India

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Abstract:

Background: The primary reason for epidural analgesia is labour pain. It is the only method that effectively reduces intense labour pain. It provides a labour trial for high-risk patients who have had a previous Caesarean section, anticipates a challenging intubation, and is obese **Objectives** :To compare the efficacy of Bupivacaine and Fentanyl v/s Bupivacaine and Butorphanol regarding onset of analgesia, duration of analgesia, quality of analgesia and fetal out come in epidural labour analgesia.**Methodology:** One hundred primigravida patients between the ages of 18 and 26 with ASA grades 1 and 2 were chosen at random and split into two groups of fifty each. Patients in Group 1 received 0.1% Bupivacaine and 0.0002% Fentanyl by lumbar epidural method, while patients in Group 2 received 0.1% Bupivacaine and 1 mg Butorphanol. Throughout the surgery, the mother's and foetus' hemodynamics were monitored. The onset, duration, and quality of analgesia, the length of labour, the frequency of instrumental deliveries, the frequency of side effects, and the outcome for the newborn were all noted, compared, and statistically assessed.**Results:**

Patients in group 1 receiving 0.1% bupivacaine with 0.0002% fentanyl experienced faster onsets of analgesia. In group 2, the first dose's analgesic effect lasted longer, top-up doses were not as frequently needed, and the group's analgesic quality was also higher. In neither group did the need for instrumentation or surgical intervention increase noticeably. Even with the addition of low dose butorphanol administered by epidural, the neonatal outcome was favourable and nearly equal in both groups without any signs of respiratory depression. **Conclusion:** When compared to 0.1% bupivacaine and 0.0002% fentanyl, the combination of 0.1% bupivacaine and 1mg butorphanol during epidural analgesia during labour offers great pain relief, an extended duration of action, and simultaneously reduces the need for top-ups (20mcg).

Keywords : Bupivacaine, Epidural labour analgesia, Quality of Analgesia,Fentanyl

INTRODUCTION

Labor pain is the main reason that people get epidural analgesia. It is the only method that effectively reduces intense labour pain[1]. It offers labour trials for high-risk pregnancies, prior Caesarean sections, anticipated challenging intubations, and obesity. According to Jouppila et al., epidural analgesia significantly increases intervillous blood flow in pre-eclamptic parturients. Ramos Santos et al. demonstrated utilising doppler techniques that epidural obstruction dramatically lowers uterine vascular resistance in pre-eclamptic parturients. Pre-elcampsia, pulmonary, renal, and some cardiac issues are maternal reasons for epidural analgesia. Due to their exceptional analgesia, dates cause preterm and smallness in foetuses[2]. They also boost the mother's oxygen saturation and enable a more controlled delivery thanks to calm pelvic floor muscles and a less impulse to push[4]. Moreover, epidural analgesia improves acid-base balance, reduces the incidence of intracerebral haemorrhage in premature infants, and nearly eliminates newborn depression[5].

Many medications, including xylocaine, bupivacaine, tetracaine, and others, have a place in the drug arsenal used in localised obstetric analgesic procedures. An amide amino group of local anaesthetics called bupivacaine was rated as a better option for reducing labour discomfort[6]. When administered in concentrations between 0.0625% and 0.25%, it induces effective sensory blockade with reduced motor blockade. It also acts for a long time with little tachyphylaxis. It has a low maternal ratio of 0.3 and little impact on the neurobehavioral development of newborns. These benefits made it a better option as an agent for labour epidural analgesia[7].

Moreover, a variety of opioid analgesics including morphine, pethidine, fentanyl, sufentanil, tramodol, and butorphanol are employed. Synthetic opioid analgesics like fentanyl are frequently used to treat various kinds of pain[8]. Fentanyl interacts with opioid receptors in the brain and spinal cord in a manner similar to other opioids (substantia gelatinosa). It is 76–125 times more potent than morphine. Synthetic opioid analgesic butorphanol is frequently used to treat a variety of pain conditions. Butorphanol acts on opioid receptors in the brain and spinal cord similarly to other opioids (substantia gelatinosa). It is 7 times more potent than morphine. The negative effects and problems are significantly decreased when used in combination with local anaesthesia in modest doses during labour. So, by extending the benefits and positive effects of both opioids and local anaesthetics, one can increase mother satisfaction, action duration, and block depth while also lowering dosages of each drug and preventing negative pharmacological effects[9,10].

The goal of the current study was to assess the effectiveness of bupivacaine and fentanyl to a combination of bupivacaine and butorphanol when used in an intermittent bolus epidural method to treat labour pain.

METHODOLOGY: This study titled “Effect of Bupivacaine and Fentanyl v/s

Bupivacaine and Butorphanol in labour analgesia by Epidural technique :A Comparative Study in a Tertiary Care Hospital,Telangana,India"was carried out during the period from March 2011 to April 2012.The study was conducted on 100 selected patients[7] fulfilling the criteria. The study was conducted at Government Chanda Kanthaiah Memorial Maternity Hospital, Kakatiya MedicalCollege Warangal with an aim to compare the Effect of Bupivacaine and Fentanyl v/s Bupivacaine and Butorphanol in labour analgesia by Epidural technique

Inclusion criteria:

Healthy Gravida I patients at term (ASA I / ll)

Maternal request for epidural analgesia,

Well informed literate subjects,

Age group 18- 30 years,

Women in active labour with cervical dilatation in primi of *3-5* cms,

Vertex presentation

Exclusion criteria:

Patients unwilling for the procedure.

Parturients- multigravida.Parturients with multiple pregnancies.

Severe **anaemia** .

Cephalo-pelvic disproportion.

Breech presentation.

Previous LSCS.

History of antepartum haemorrhage

History of allergy to local anaesthetic

History of bleeding disorders

Diabetes mellitus

History of psychiatric or neurologic disease

Pregnancy induced hypertension

History of CVS/RS disorder

Ethics: This study was approved by the Institutional Ethics Committee, Government Chanda Kanthaiah Memorial Maternity Hospital, Kakatiya Medical College Warangal,Telangana,India. An informed written consent was taken from all the patients involved in the study after explaining regarding the study.

Study Procedure: All the patients were explained the procedure of the technique and written consent was obtained. The patients were thoroughly evaluated and examined. Pulse rate, blood pressure, fetal heart rate were recorded before providing epidural analgesia. An intravenous line was secured with 18G IV cannula and all the patients were preloaded with 500ml of Ringer lactate.

The patients were placed in left lateral position with hips and knees flexed fully as possible such that the back is perpendicular to the edge of the table. The coronal planes of hips and shoulders should be vertical as nearly as possible so that the median plane is horizontal. After scrubbing up as for a surgical operation with sterile gown and gloves, the patients back was cleaned over an area extending from lower thoracic region to the lower part of the sacrum and including both flanks. The back was draped with a sterile towel with a central hole.

Mid line approach was used in all cases. Either L2-3 OR L3-4 interspinous space was selected according to the convenience. After local infiltration with 1% lignocaine, 18G epidural needle was placed exactly in midline perpendicular to the skin with the bevel facing upwards. After piercing skin, subcutaneous tissue, supraspinous ligament and interspinous ligament, the stylet was removed and a 5ml syringe was attached with 2-3ml of air. The

needle was advanced step by step in millimeters at a time, with simultaneously appreciating pneumatic bounce. Once the epidural space was entered, sudden loss of resistance feel was appreciated at the plunger of the syringe. Epidural space was confirmed with gentle aspiration to ensure that no CSF or blood was aspirated. Care was taken to see that no attempt was made to advance the needle through the ligamentum flavum during active uterine contractions.

INSERTION OF THE EPIDURAL CATHETER:With the bevel of the needle directed cephalad, the catheter was threaded through the needle while the needle was held steadily. A slight resistance was felt as the catheter enters the epidural space. A further 3-4cm length of catheter was introduced. The needle was withdrawn over the catheter by maintaining pressure on the catheter during withdrawal

FIXING THE CATHETER: A gauze piece was placed around the catheter at the site of skin puncture and held in positionwith waterproof adhesive tape. Catheter was then taped along the midline of the mother's back towards the right side of the neck. It was attached to the bacterial filter and was covered with a sterile guaze piece.

TEST DOSE

The position of catheter in epidural space was confirmed once again with aspiration test. 3cc of 1.5% lignocaine with epinephrine [15mcg] was administered and observed for the development of any subjective symptoms including sensory and motor blockade in the lower limbs, dizziness, light headedness, palpitations and objective signs of rise in pulse rate and blood pressure to rule out either inadvertent intrathecal or intravascular injection of local anesthetic. The patients were divided into two groups randomly consisting of 50 patients ineach group.

Group-1

This group of patients received Bupivacaine with Fentanyl 0.0002% during theprocedure until the delivery of fetus. The loading dose consisted of 10ml of Bupivacaine 0.1% and Fentanyl 0.0002% [20mcg]. The top up doses were 10ml of 0.1% Bupivacaine andFentanyl 0.0002%, administered whenever the patients complained of pain. when patients enters into second stage a further 12-15ml was injected with patients in sitting position or semi-sitting position.

Group-2

This group of patients received Bupivacaine with Butorphanol 1mg. The loading dose consisted of 10ml of Bupivacaine 0.1% and 0.01% Butorphanol. The top up doses included Bupivacaine 0.1% alone in 10ml solution whenever the patients complained of pain. When patients enter into second stage, then an additional dose of 12-15ml was injected with patients in sitting position or semi-sitting position. The stages and progressof labor was monitored with the help of an obstetrician.

TIMING OF INDUCTION OF EPIDURAL ANALGESIA

Epidural analgesia for child birth is administered in two stages and depending upon the demand of the parturient. Identification of the stage of labor was done with the help of the obstetrician.

Assessment of Stage -1

1. Presenting part:	Engaged
2.Cervical effacement:	100%
3.Cervical dilatation:	3-5cm for primigravida
4.Uterine contractions:	Duration >30 seconds
	Interval: 3 uterine contractions /10 min

Segmental sensory block T10 - L1 is required in relation to stretching of uterine tissues and simultaneously dilatation of cervix and stretching of lower segment.

Assessment of Stage -2

1.Cervical effacement: 100%

.Cervical dilatation: Complete

3.Uterine contractions: Duration >30 seconds

Interval:every 3min or less

4.Clinical findings: Perineal bulging, moderate to severe bearing down pains, completed fetal flexion and internal rotation.

Segmental sensory T10-S4 is required in relation to stretching of pelvic structures and perineum added to pain of uterine contractions.

MONITORING

Maternal blood pressure, pulse rate, fetal heart rate were monitored every 1-2 min for first 10 min and then every 5-10 min for subsequent 30 min and later every half an hour.Time of onset of analgesia, level of sensory blockade and motor blockade, if any was noted. VISUAL ANALOGUE PAIN SCALE [VAPS] assessed pain at different time intervals.

Visual analogue pain scale (VAPS)

Instruct the patient to point to the position on the line between the faces to indicate how much pain they are currently feeling. The far left end indicates ‘No pain’ and the far right endindicates ‘Worst pain ever’.

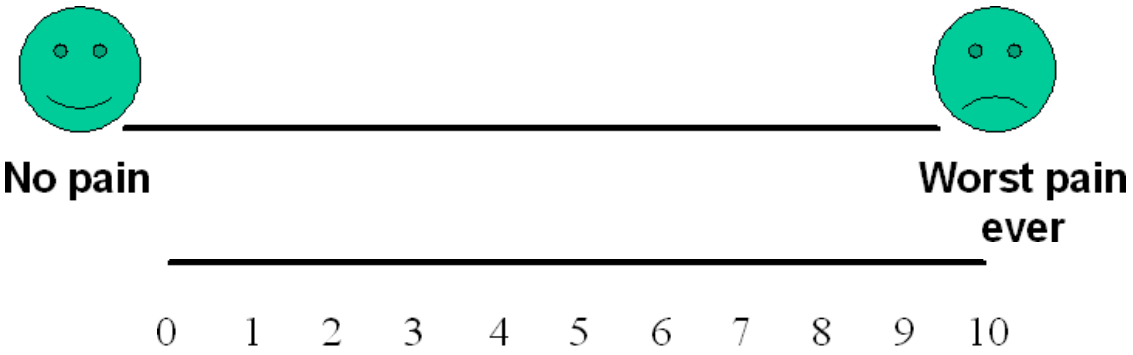

Figure 1: VISUAL ANALOGUE PAIN SCALE

The sedation was assessed by WILSON GRADING

Awake, alert	1
Alert, drowsy	2
Sedation arousable by verbal commands	3
Sedation arousable by mild physical pain	4
Not arousable by pain	5

BROMAGE SCALE assessed the motor blockade

No motor block, full flexion of knee and foot	0
Inability to raise extended leg, just able to move knees	1
Inability to flex knee but able to move foot only	2
Inability to flex ankle joint, unable to move foot or knee	3

Progress of labor and site effects if any were noted in the epidural record sheet. During the procedure the supine position was avoided as far as possible. Care was taken to ensure that urinary bladder does not become over distended. Administration through the intravenous cannula was continued throughout the procedurewith either ringer lactate or normal saline depending on the blood pressure of the mother.After delivery an additional dose of the

respective drug was given before removal of the epidural catheter for further analgesia. Catheter was checked for any damage and ensured thatno portion of the epidural catheter was retained. The puncture site at the skin was cleaned with antiseptic and covered with adhesive tape over a sterile gauze pieces.

All the newborns in both the groups were assessed for the effect of the drug by determining the APGAR scores immediately after delivery at 1min and 5min.

STATISTICAL ANALYSIS: Data was expressed as mean + or - standard deviation where appropriate, statistical analysis for parametric data which included age, height, weight, cervical dilatation, onset of analgesia, duration of analgesia, number of top up doses. Probability values < 0.005 were considered as statistically significant

Results :

AGE: All patients were between the ages of 18-26 years.Statistical analysis reveals the following data in years.

Table :1 Age Distribution

	Group 1	Group 2
Mean	23.38	22.48
Median	23	22
Mode	22	22
Standard deviation	2.47345	2.20611

Unpaired student *t* test results

P value and statistical significance:

The two-tailed P value equals 0.0577

By conventional criteria, this difference is considered to be not quite statistically significant.

HEIGHT:

All patients were between heights of 150 -160 cms.

Statistical analysis reveals the following data in cms

Table :2 Height Distribution

	Group 1	Group 2
Mean	160.07	160.18
Median	160.75	160
Mode	161	164
Standard deviation	4.95182	4.82422

Unpaired Student *t* test results

P value and statistical significance:The two-tailed P value equals 0.9106

By conventional criteria, this difference is considered to be not statistically significant.

WEIGHT:

All patients were weighing between 55-65kgs

Statistical analysis reveals the following data in kgs

Table :3 Weight Distribution

	Group 1	Group 2
Mean	60.48	60.02
Median	60	60
Mode	63	58
Standard deviation	2.48251	2.02777

Unpaired *t* test results

P value and statistical significance:The two-tailed P value equals 0.3127

By conventional criteria, this difference is considered to be not statistically significant.

INITIATION OF EPIDURAL ANALGESIA
The epidural analgesia was initiated to patientss with cervical dilatation as depicted below:

Table :4 Initiation of Epidural Analgesia

	3cm	4cm	5cm
Group-1	43[86%]	5[10%]	2[4%]
Group-2	42[84%]	6[12%]	2[4%]

	Group 1	Group 2
Mean	3.18	3.2
Median	3	3
Mode	3	3
Standard deviation	0.48192	0.49487

Unpaired *t* test results

P value and statistical significance:The two-tailed P value equals 0.8382

By conventional criteria, this difference is considered to be not statistically significant.

Table No : 5 DEMOGRAPHIC DATA

S.No	Parameter	Group-1	Group-2	P value
1	Primigravida	50 (100%)	50 (100%)	-
2	Age (years)	23.38 ± 2.47	22.48 ± 2.20	Not significant

3	Height (cms)	160.07 ± 4.95	160.18 ± 4.82	Not significant
4	Weight (kgs)	60.48 ± 2.48	60.02 ± 2.02	Not significant
5	Cervical dilatation (cms)	3.06 ± 0.37	3.08 ± 0.39	Not significant
6	Oxytocics used	35 (70%)	36 (72%)	Not significant

No differences were noted in demographic characteristics of each group

COMPARISION OF ONSET OF ANALGESIA:

The onset of analgesia was taken as the time from injection of the drug and the time atwhich parturient appreciated pain relief (in minutes).

Table :6 Comparision of onset of Analgesia

	Group 1	Group 2
Mean	8.18	12.68
Median	8	13
Mode	9	13
Standard deviation	1.68656	0.95704

Unpaired *t* test results

P value and statistical significance:The two-tailed P value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.

It indicates that the onset of analgesia is faster in group-1 patients compared to group-2 patients.

COMPARISION OF DURATION OF ANALGESIA WITH FIRST DOSE:

The duration of analgesia with the first (loading) dose was taken as a time for complete pain relief to the time when the patients first complained of pain (in minutes).

Table :7 Comparision of Duration of Analgesia with first dose

	Group 1	Group 2
Mean	68.68	92.16
Median	68.5	90.5
Mode	75	76,109
Standard deviation	9.19059	14.24188

Unpaired *t* test results

P value and statistical significance: The two-tailed P value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.

It indicates that duration of analgesia is more in group-2 patients compared to group-1 patients.

COMPARISON OF TOTAL NUMBER OF DOSES REQUIRED

The statistical analysis of total number of doses required by parturients in the studygroup is as follows:

Table No :8 Comparision of Duration of Analgesia with first dose

	Group 1	Group 2
Mean	4.58	2.82
Median	4	3
Mode	4	3

Standard deviation	0.7848	0.71969

Unpaired *t* test results

P value and statistical significance:

The two-tailed P value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statisticallysignificant.

It indicates the group-1patients required more number of doses than group-2 patients.

COMPARISON OF DURATION OF LABOUR

The duration of labour was calculated from the initiation of epidural analgesia to thetime of delivery of fetus in minutes.

Table No:9 Comparison of Duration of Labour

	Group 1	Group 2
Mean	302.9	290.18
Median	309	292.5
Mode	310	321
Standard deviation	42.92673	47.49423

Unpaired *t* test results

P value and statistical significance:The two-tailed P value equals 0.1632

By conventional criteria, this difference is considered to be not statistically significant.

COMPARISON OF APGAR SCORES

The neonatal outcome was assessed by APGAR scoring system at 1min and 5min.The comparison statistical data is tabulated as follows

Table No:10 Comparision of APGAR Scores

APGAR	1 minutes		5 minutes	
GROUP	Group-1	Group-2	Group-1	Group-2
MEAN	7.36	7.6	9.36	9.6
MEDIAN	8	8	10	10
MODE	8	8	10	10
Standard deviation	1.10213	0.98974	1.10213	0.98974

Unpaired student *t* test results found to be same for both 1min and 5min

P value and statistical significance:The two-tailed P value equals 0.2547

By conventional criteria, this difference is considered to be not statistically significant.

COMPARISON OF QUALITY OF ANALGESIA (Visual Analogue Pain Scale)

Table No :11 COMPARISON OF QUALITY OF ANALGESIA

	Group 1	Group 2
Mean	1.42	0.34
Median	0.5	0
Mode	0	0
Standard deviation	1.90692	1.50658

Unpaired *t* test results

P value and statistical significance:

The two-tailed P value equals 0.0022

By conventional criteria, this difference is considered to be very statistically significant.

COMPARISON OF MODE OF DELIVERY Mode of delivery was recorded as normal spontaneous vaginal deliveries, vaginal deliveries, vaginal deliveries with instrumental intervention and caesarean section are tabulated as follows

Table No:12 Comparison of Mode of Delivery

	Spontaneous Vaginal deliveries	Instrumental deliveries	Caesarean deliveries
Group-1	40 (80%)	8 (16%)	2 (4%)
Group-2	43 (86%)	5 (10%)	2 (4%)

The instrumental deliveries were found to be less in group-2 patients compared togroup-1 patients.

Discussion :

As emotional and sensory experience, labour pain is subjective. As a safe and efficient method of pain treatment during childbirth, epidural analgesia employing newer opioids and low concentrations of local anaesthetic has acquired widespread acceptance..

The current clinical investigation compares the effectiveness of buprenorphine plus fentanyl to buprenorphine and butorphanol in treating pain and its impact on newborn outcomes. A total of 100 primigravidae, all of which belonged to ASA1-2, were chosen and randomly split into two groups of 50 each. Group 1 has n = 50. This group received an initial dosage of 0.1% Bupivacaine 10ml plus 0.0002% Fentanyl and further doses of 0.1% Bupivacaine 10ml plus 0.0002% Fentanyl. n=50 for group 2. This group was given an initial dosage of 0.1% bupivacaine in 10ml combined with 1mg of butorphanol, then further doses of 0.1% bupivacaine in 10ml. The onset of analgesia, duration of analgesia with loading dosage, total number of doses needed throughout labour, APGAR scores at 1 and 5 minutes, and parturients' expressions of relief from pain were the variables that were observed and statistically assessed. The level of sensory block, level of motor block, pulse rate, blood pressure, respiration rate, temperature, SpO2, foetal heart rate, and any adverse effects are also noted. The visual analogue pain scale, which has the worst pain at both ends and a range

of 0 to 10 cm, was used to measure the degree of pain reduction. The main drawback of the butorphanol group is the onset of analgesia; in our investigation, group 1 experienced sensory blockade faster than group 2, and when this data was statistically examined using a students 't' test, the p value was 0.0001 (i.e., significant). Because fentanyl is more lipid-soluble than butorphanol in Group 2, it may have a quicker onset of effect in Group 1. Groups 1 and 2 are comparable to writers like Reynold et al and Chestnet et al in terms of when analgesia starts to kick in.

The main benefit of the butorphanol group is duration of analgesia with first dose, as the mean duration of analgesia with first dose in group -2 [92.16 14.24] is longer than that observed in group -1 [68.68 9.19]. The p value for the "t" test, which was statistically analysed by the students, is 0.0001, which is statistically significant. The prolonged duration in group 2 may be related to butorphanol's lower systemic absorption and lower lipid solubility. Similar to authors Reynold et al. and Price et al., group -1's analgesia lasted for a similar amount of time. Results from Group 2 resembled those of investigations carried out by Hunt et al. in 1989[3] and Rodriguez et al[5]. in 1990.

When assessed by students' 't' test, the P value is 0.0001, which is significant. The necessity of top-up doses is also much lower in group 2 when compared to group 1. In other words, butorphanol decreased the amount of doses necessary for the complete dose of bupivacaine. In our investigation, the total time from drug injection to delivery was Group-1 [302.9 42.92] and Group-2 [290.18 47.49]. The p value is > 0.5, which is not statistically significant, according to the statistical analysis.

According to the visual analogue scale, group-2's quality of analgesia is higher than group-1's, which may be because butorphanol in group-2 also acts on Mu1, Mu2, and K receptors. The student t test results in a statistically significant p value of 0.0022, indicating that group

2 had better analgesia than group 1. All of these findings are consistent with earlier research by David H. Chestnut [11,12,13,14], Hunt et al[3]., 1989, Tank TK, Ann. Acad. Med. Singapore, 1998, and (American Family Physician Nov. 15, 1998).When the delivery methods in the two groups were examined, instrumental delivery and caesarian sections were practically equally necessary in both. By using the student 't' test to examine these results, the P value was found to be >0.5, which was not statistically significant. The chord around the neck, cord prolapse, and foetal distress were the reasons for Caesarean section in the pregnant women under study. APGAR grading was used to determine the neonatal outcome at 1 and 5 minutes. With the exception of one neonate in Group 2 who had foetal distress because the cord was wrapped around his neck during birth, the majority of them achieved APGAR scores at 1 minute between 7 and 8 in both groups.

Nonetheless, the APGAR ratings at 5 minutes were between 9, indicating that newborns did not have clinically significant respiratory depression or decreased neurobehavioral ratings. The addition of butorphanol caused patients to become drowsy but awake, with improved analgesia that helped them accept the procedure better than those in Group -1. The addition of butorphanol had no impact on uterine contractions, and the quantity of caesarian sections and instrumentation did not rise. Moreover, the motor blockage did not differ much from Group-1. All of the data show that adding a minor dose of opioid, such as butorphanol 1 mg to 0.1% bupivacaine, boosted the quality and duration of analgesia and significantly decreased the need for top-up doses. As indicated by APGAR score, there was no appreciable incidence of infant asphyxia, which is particularly favourable in increasing obstetric analgesia.

Conclusion:

The findings suggest that when compared to 0.1% bupivacaine and 0.0002% fentanyl, the combination of 0.1% bupivacaine and 1mg butorphanol during epidural analgesia during labour delivers excellent pain relief, a prolonged duration of action, and minimises the need for top-ups (20mcg)

References :

1.Swathi N, Ashwini N, Shukla MI. Comparative study of epidural bupivacaine with butorphanol and bupivacaine with tramadol for postoperative pain relief in abdominal surgeries. Anesth Essays Res. 2016 Sep-Dec;10(3):462-467. doi: 10.4103/0259-1162.177522. PMID: 27746533; PMCID: PMC5062192.

2.Malik P, Manchanda C, Malhotra N. Comparative evaluation of epidural fentanyl and butorphanol for postoperative analgesia. *J Anaesthesiol Clin Pharmacol.* 2006;22:377–82.

3. Hunt CO, Naulty JS, Malinow AM, Datta S, Ostheimer GW. Epidural butorphanol-bupivacaine for analgesia during labor and delivery. Anesth Analg. 1989 Mar;68(3):323-7. PMID: 2919772.

4. Shrestha CK, Sharma KR, Shrestha RR. Comparative study of epidural administration of 10 ml of 0.1% bupivacaine with 2 mg butorphanol and 10 ml of 0.25% plain bupivacaine for analgesia during labor. JNMA J Nepal Med Assoc. 2007 Jan-Mar;46(165):1-6. PMID: 17721555.

5. Rodriguez J, Abboud TK, Reyes A, Payne M, Zhu J, Steffens Z, Afrasiabi A. Continuous infusion epidural anesthesia during labor: a randomized, double-blind comparison of 0.0625% bupivacaine/0.002% butorphanol and 0.125% bupivacaine. Reg Anesth. 1990 Nov-Dec;15(6):300-3. PMID: 2291885.

6. Bruyère M, Mercier FJ. Alternatives à l'analgésie péridurale au cours du travail [Alternative techniques to labour epidural analgesia]. Ann Fr Anesth Reanim. 2005 Nov-Dec;24(11-12):1375-82. French. doi: 10.1016/j.annfar.2005.07.072. Epub 2005 Aug 22. PMID: 16115746.

7. NagarjunaReddy, K, S SachidanandR, B srinivasrao, Praveen Kumar Devulapalli, T. Nagender and M V Srinath. "A COMPARATIVE STUDY OF BUPIVACAINE AND FENTANYL V/s BUPIVACAINE AND BUTORPHANOL IN LABOUR ANALGESIA BY EPIDURAL TECHNIQUE." *Journal of Evolution of medical and Dental Sciences* 2015:4; 13799-13813.

8. Guo S, Li B, Gao C, Tian Y. Epidural Analgesia With Bupivacaine and Fentanyl Versus Ropivacaine and Fentanyl for Pain Relief in Labor: A Meta-Analysis. Medicine (Baltimore). 2015 Jun;94(23):e880. doi: 10.1097/MD.0000000000000880. PMID: 26061307; PMCID: PMC4616487.

9. Hitzeman N, Chin S. Epidural analgesia for labor pain. Am Fam Physician. 2012 Aug 1;86(3):241-2. PMID: 22962986.

10. Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med. 2010 Apr 22;362(16):1503-10. doi: 10.1056/NEJMct0909254. PMID: 20410515.

11. Koppel BS, Chiechi M. Epidural analgesia for labor and delivery. N Engl J Med. 2010 Jul 22;363(4):394-5. doi: 10.1056/NEJMc1005898. Erratum in: N Engl J Med. 2010 Nov 25;363(22):2178. PMID: 20660410.

12. Halpern S, Leighton B. Epidural labor analgesia and cesarean delivery. Birth. 2000 Mar;27(1):74-5. PMID: 10865565.

13. Young P, Emery NC, Reisin R. Epidural analgesia for labor and delivery. N Engl J Med. 2010 Jul 22;363(4):395. PMID: 20677364.

14. Chestnut DH, Owen CL, Bates JN, Ostman LG, Choi WW, Geiger MW. Continuous infusion epidural analgesia during labor: a randomized, double-blind comparison of 0.0625% bupivacaine/0.0002% fentanyl versus 0.125% bupivacaine. Anesthesiology. 1988 May;68(5):754-9. PMID: 3285732.