Indian Journal of Clinical Anaesthesia 2019;6(4):548–552

Content available at: iponlinejournal.com

Indian Journal of Clinical Anaesthesia

Journal homepage: www.innovativepublication.com

Original Research Article

Efficacy of fentanyl versus sufentanil for labour analgesia and its comparative evaluation with intramuscular tramadol

Sudhir Pawar[1], B Naveen Naik[2], Vamsidhar Amburu[2], Tanvir Samra[2,*]

[1]*Dept. of Anaesthesiology, Maharaja Agrasen Hospital, New Delhi, India*
[2]*Dept. of Anaesthesia & Intersive Care, Post Graduate Institute of Medical Education & Research, Chandigarh, India*

ARTICLE INFO

Article history:
Received 10-04-2019
Accepted 18-09-2019
Available online 20-11-2019

Keywords:
Bupivacaine
Fentanyl
Sufentanil
Labour
Analgesia

ABSTRACT

Introduction: Knowledge about relative merits and demerits of different techniques of administration of drugs through epidural route is needed for optimum management of labour pain. Primary objective of this study is to assess the efficacy of fentanyl and sufentanil for labour analgesia in comparison with intramuscular tramadol.

Materials and Methods: This prospective randomized control study included 90 primigravida parturients who were randomly allocated to three groups of 30 each; Fentanyl group (group BF) received 50 μg of epidural fentanyl with 10 ml of 0.125% bupivacaine, Sufentanil group (group BS) received 10μg epidural sufentanil with 10 ml of 0.125% bupivacaine and Tramadol group (group T), the control group received 100mg intramuscular tramadol with 50 mg repeat dose after 4 hours.

Results: Epidural groups were comparable in their visual analogue scale (VAS) score satisfaction score, characteristics of sensory and motor blockade, mode of delivery, side effects, haemodynamic stability and neonatal outcome. Value of VAS did not exceed 3 in the epidural group during the entire study period. Onset of analgesia was early with sufentanil (10.5$\pm$2.1 mins, $p< 0.01$) and total amount of bupivacaine used was also less (44.16 mg, p =0.002). Higher VAS scores (>4), delayed onset and decreased total duration of labour was seen in tramadol group. Epidural and tramadol group were comparable in mode of delivery and neonatal outcome.

Conclusion: Quality of epidural analgesia with either fentanyl or sufentanil using intermittent bolus technique was comparable. Duration of first and second stage of labour was significantly prolonged in parturients receiving labour epidural analgesia.

1. Introduction

Techniques used to alleviate labour pain are transcutaneous electrical nerve stimulation (TENS), water bath, acupuncture, hypnosis, parenteral narcotics, inhalational agents and various neuraxial blocks.[1] Adequate pain relief alleviates maternal fear, anxiety, apprehension and prevents increase in catecholamines, cardiac output, peripheral resistance, blood pressure and oxygen consumption.[2] Neuraxial administration of a combination of low dose of local anaesthetic (bupivacaine, levobupivacaine, ropivacaine) with a lipid soluble opioid (fentanyl or sufentanil) is the most widely used technique of labour analgesia.[3–6]

The primary objective of this study was to compare quality of pain relief, progress of labour, and neonatal outcome after single bolus dose of fentanyl or sufentanil in a dose ratio of 5:1 with 0.125% bupivacaine in parturients receiving subsequent epidural labour analgesia with intermittent bolus of 0.125% bupivacaine. Patients receiving non-epidural form of pain relief in the form of intramuscular tramadol were regarded as the control group against which comparisons were made to highlight the relative merits and demerits of epidural analgesia.

* *Corresponding author*.
E-mail address: drtanvirsamra@yahoo.co.in (T. Samra).

https://doi.org/10.18231/j.ijca.2019.107

2. Materials and Methods

This prospective randomized control study was commenced in a tertiary care center after approval from the Institute ethics committee. Written informed consent from parturients participating in the study was obtained. Primigravida with period of gestation >37 weeks, aged 18- 38 years with American Society of Anesthesiologists Physical Status (ASA PS) grade I/ II with single live foetus and in active labour with at least 3 cm cervical dilatation were randomly allocated into three groups of 30 each. Fentanyl group (group BF) receivede pidural analgesia with single bolus dose of 50 μg fentanyl and 10 ml of 0.125% bupivacaine followed by intermittent bolus of 10 ml of 0.125% bupivacaine till delivery. Sufentanil group (group BS) received e pidural analgesia with single bolus dose of 10μg sufentanil and 10 ml of 0.125% bupivacaine followed by intermittent bolus of 10 ml of 0.125% bupivacaine till delivery. Tramadol group (group T) received 100mg intramuscular tramadol and 50mg was repeated after 4 hours. Parturients with known hypersensitivity to any of the study drugs, bleeding diathesis, twin pregnancy, low birth weight babies, intra uterine growth retardation, anatomical deformities of the spine, psychiatric disorders, cervical dilation of more than 5 cm, preterm labour, placenta previa, pregnancy induced hypertension and any systemic illness like diabetes mellitus, cardiac and respiratory disorder were excluded from the study.

After arrival to the operation theatrea 18G intravenous cannula was placed in all the parturients in the epidural group. Patient was positioned in left lateral position. Under all aseptic precautions a 18 G Tuohy needle was inserted in the L2-L3 or L3-L4 epidural space using loss of resistance technique. Epidural test dose (3 ml of 2% lidocaine with adrenaline 5 μ/ml) was given between two uterine contractions in all patients before initiation of epidural labour analgesia with the above mentioned drug dosing regimes. Heaviness of legs or a rise in heart rate by 10 beats per minute above the maximum maternal heart rate were considered positive of either inadvertent intrathecal or intravascular placement of catheter. Parturients in group T were administered 100 mg of tramadol via intramuscular route. This was repeated at a dose of 50mg after 4 hours in parturients with visual analogue scale (VAS) >3. Tramadol was not administered to parturients who had progressed to second stage of labour.

Time of onset of sensory (assessed by loss of sensation to cold) and motor blockade, duration of analgesia and level of maternal satisfaction were recorded. Density of motor block was assessed at 5, 15, 30, 60 minutes and then one hourly using bromage score (full range of motion - 0, moves feet and knees - 1, moves feet only - 2, and unable to move feet or knees – 3).[7] Level of maternal satisfaction was rated as: 0 - worse than expected, 1- as expected, 2 - better than expected.[8] Pain relief was assessed using VAS (0= no pain, 10= worst pain imaginable) which was recorded prior to induction and then at 1, 5, 10, 20, 30, 60 minutes and hourly thereafter. Top-up doses with 10 ml of 0.125% bupivacaine were given at VAS greater than 3. Total amount of bupivacaine administered for epidural labour analgesia was recorded in both the groups. Duration of analgesia was defined as the time interval between first and second bolus administrations of drug in epidural space. Maternal pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), SPO_2 and fetal heart rate (FHR) were recorded. Episodes of hypotension (SBP $<$ 100 mm H g or fall of more than 20 % of the baseline), respiratory depression (RR$\leq$10 per min), headache, pruritus, nausea and vomiting and urinary retention were noted. Duration of first, second and third stages of labour, mode of delivery and neonatal outcome (Apgar score at 0, 1, and 5 minutes) were compared.

Data were recorded using Microsoft Excel for Windows and statistical analysis was done using SPSS version 12 for Windows. Analysis of variance (ANOVA) was used for continuous variables, student's t test for parametric data and chi-square test for non parametric data. Kruskal Wallis test, Mann Whitney test and N Par test were also used. P value $<$0.05 was considered significant.

3. Results

All the groups were comparable with respect to demographic data (Table 1).VAS was comparable between group BF and group BS, it did not exceed value of 3 during the entire study period. Significant difference in VAS was observed when groups BF and BS were compared with group T (Figure 1). The mean satisfaction scores were comparable between group BF and group BS; 1.95$\pm$0.7 and 1.97$\pm$0.6; (p$<$0.05) respectively. Majority of parturients in group T had a score of 0 (73.33%) and none had score of 2. The difference in the score between group T and the two epidural groups was clinically as well as statistically significant (p $<$0.01).

Onset of analgesia in group BF, group BS and group T were, 13.4$\pm$2.7, 10.5$\pm$2.1 and 18$\pm$4.9 minutes respectively and the difference was statistically significant (P $<$ 0.01). There was statistically significant difference in the amount of bupivacaine used in group BF (55.83 mg) and group BS (44.16 mg), (p =0.002). Difference in the mean duration of analgesia in group BF (95.67 minutes), group BS (101.67 minutes) and group T (97.60 minutes) was not significant. Median sensory levels were comparable in both the groups during entire study period and ranged between T10 - T12. Bromage score of 1 was obtained in 3 parturients in group BF and 4 in group BS. All remaining parturients had full range of leg motion during the first 60 minutes.

Duration of first stage and second stage was significantly prolonged in the epidural group (Table 2). Mode of delivery was comparable in all three groups. Percentage

of parturients with normal vaginal deli very was 53%, 50% and 50% in groups BF, BS and T respectively. Maximum number of caesare an sections were encountered in control group T; 30% as compared to 20% in epidural group. Percentage of assisted deliveries was higher in epidural group, 26% and 30% in group BF and BS respectively but the difference was not statistically significant when compared with tramadol group (20%).

There was no statistically significant difference between the APGAR scores and fetal birth weight in all the three groups (Table 3). N o significant change in mean fetal heart rate was noted in any group. None of the parturients developed fetal bradycardia during the study period. Frequency of side effects was very low and was similar in the three groups (Figure 2). Haemodynamic stability was maintained in all the three groups. Maximum percentage fall in mean SBP was recorded at 30 minutes in group BF and BS and at 60 minutes in group T. The fall in SBP was comparable in group BF and BS but less severe in group T. Two parturients in group BF and BS experienced hypotension (BP <20% of the baseline) and were treated with intravenous fluids and ephedrine. There was no episode of hypotension in group T. Group BF and BS showed significantly greater fall in pulse rate at 30-60 minutes when compared to group T. However, none of the parturient in any groups had symptomatic bradycardia requi ring administration of vagolytics.

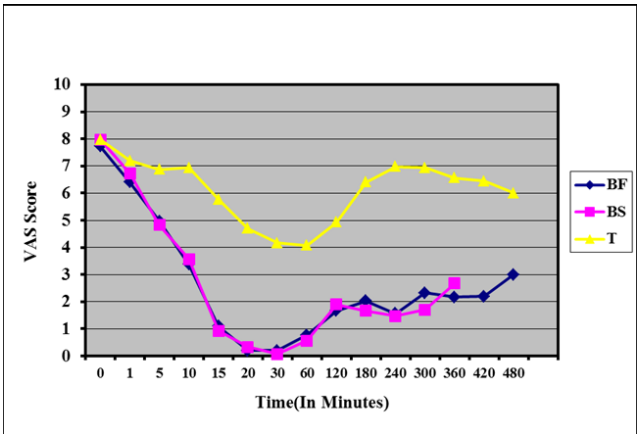

Fig. 1: Graph comparing mean VAS scores of fentanyl, sufentanil and tramadol group.

4. Discussion

In our study the VAS score, satisfaction score, dermatome level of sensory block, intensity of motor block, modes of delivery, side effects and neonatal outcome were comparable for those administered either fentanyl or sufentanyl in a dose ratio of 5:1. We reported early onset of analgesia with epidural administration of sufentanil (10.5±2.1 minutes) in comparison to fentanyl (13.4±2.7

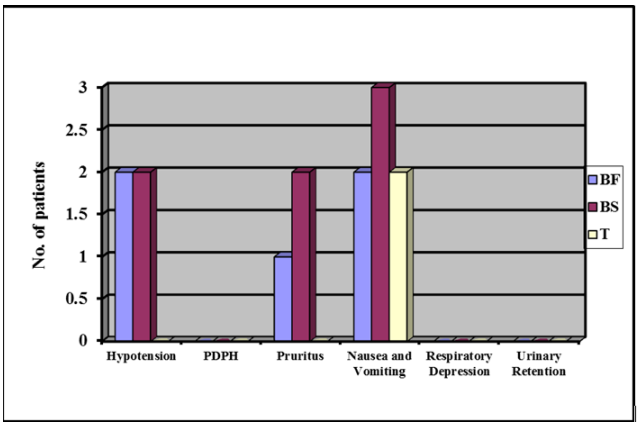

Fig. 2: Graph depicting side effect profile of all the three groups.

min) which is due to greater lipid solubility of sufentanil ($p < 0.01$). Duration of first stage and second stage of labour was significantly prolonged in the epidural group.

Significantly greater amount of bupivacaine was administered in the fentanyl group for pain relief (55.8±11.2mg vs 44.2±15.6mg; $p = 0.002$). This is due to shorter mean duration of analgesia with fentanyl (95.67 min) in comparison to sufentanil (101.67 min). Longer duration of labour analgesia has been documented with sufentanil in previous studies also.[9,10] But difference of only 3 minutes in onset time and 11 mg of bupivacaine has been reported in our study.

Low values of VAS and high maternal satisfaction was reported with single epidural bolus of fentanyl or sufentanil (dose ratio of 5:1) followed by subsequent intermittent bolus of 0.125% bupivacaine. Mean satisfaction score approached value of 2 and value of VAS did not exceed 3 at any time during the entire study period. Haemodynamic stability was maintained and no adverse maternal or fetal outcome occurred.

Intermittent epidural bolus dosing was also chosen as a method of labour analgesia by *Lim et al*[10] and compared with technique of continuous epidural infusion. Higher maternal satisfaction and lower incidence of breakthrough pain was reported with automated regular bolus delivery. In our study we have successfully managed labour pain with intermittent epidural bolus of bupivacaine and a lipid soluble opioid (fentanyl or sufentanil). The technique of epidural analgesia is however different from that described by *Lim et al.*[11] They used combined spinal epidural (CSE) and administered 25μg of fentanyl in subarachnoid space prior to initiation of labour analgesia with intermittent epidural bolus dosing. Drug combination administered in each epidural bolus was also different; 0.1% of levobupivacaine with 2 μg/ml of fentanyl.

Ropivacaine (0.1%) with fentanyl (2 μg/ml) has been administered as demand only patient controlled epidural analgesia (PCEA) and as PCEA with background infusion

Table 1: Demographic characteristics of parturients of fentanyl, sufentanil and tramadol group. [Values are mean±SD, * P < 0.05 (significant).]

	Group BF	Group BS	Group T	P value
Age (years)	27.4±3.8	26.1±3.2	27.2±3.5	0.28
Height (cm)	156.9±4.6	154.7±7.4	154.8±4.9	0.25
Weight (kg)	65.6±5.7	65.3±5.2	63.5±4.9	0.26
Haemoglobin (gm%)	11.4±0.9	10.9±0.9	11.2±0.9	0.16
Cervical dilation (cm)	3.35±0.42	3.37±0.41	3.35±0.37	0.98
Neonatal weight (kg)	2.93±0.31	2.91±0.29	2.96±0.29	0.77

Table 2: Duration of different stages of labour and intergroup comparision. [Values are mean±SD, * P < 0.05 (significant)]

Groups	1 st stage	2 nd stage	3 rd stage
BF vs BS	651.2±62.4; 655.8±44.2 (0.74)	77.1±5.1; 76.1±4.7(0.42)	6.3±0.9; 6.8±1.7 (0.16)
BS vs T	655.8±44.2; 619.8±49.8 (<0.004)*	76.1±4.7;73.2±3 (< 0.006)*	6.8±1.7; 6.2±0.8 (0.08)
BF vs T	651.2±62.4; 619.8±49.8 (<0.03)*	77.1±5.1 ; 73.2±3 (< 0.0006)*	6.3±0.9; 6.2±0.8 (0.65)

Table 3: Neonatal outcome in all the three groups. [Values are mean ± SD]

	Group BF	Group BS	Group T	P Value
APGAR score				
0 minute	7.7±0.8	7.8±0.7	7.8±.8	0.88
1 minute	8.4±0.7	8.7±0.6	8.6±0.5	0.09
5 minute	9.1±0.4	9.2±0.5	9.1±0.3	0.91
Birth weight	2.9±0.3	2.9±0.3	2.9±0.2	0.78

in nulliparous parturients.[5] The authors however initially used combined spinal epidural technique to initiate labour analgesia. Drugs administered in subarachnoid space were 2 mg of ropivacaine and 15 μg of fentanyl. Increased incidence of breakthrough pain, higher pain scores, shorter duration of analgesia, and lower maternal satisfaction have been reported with demand-only PCEA.[5] Contrary to these results, use of demand-only PCEA by Boselli et al[12] has been reported to be associated with decreased consumption of local anaesthetic, reduced cost of analgesia and good pain relief. The contrasting results of the above mentioned studies emphasize the need for further research on this subject.

We have reported a shorter onset of analgesia and decreased bupivacaine consumption with sufentanil. This is in accordance with a previous study in which use of sufentanil (1μg/ml) led to superior quality of pain relief and fewer bupivacaine rescue doses when compared with fentanyl (2 μg/ ml) in combination with very low dose bupivacaine (0.015%) and epinephrine (2 μg/ml).[13] Contrary to this equal efficacy of fentanyl and sufentanil for labour analgesia has been demonstrated in clinical studies administering the drugs in a dose ratio varying from 10: 1[6,14,15] to 3.5:1.[16]

In our study we used fentanyl or sufentanil in a dose ratio of 5:1. Analgesic dose-response relationships for epidural fentanyl and sufentanil with bupivacaine 0.125% in labo u ring patients have reported ED95 value of 8 micrograms and 50 micrograms for sufentanil and fentanyl respectively.[17]

VAS sco re was >4 at all time periods in tramadol group and 73.3% of parturients described pain worse than expected in tramadol group in our study. *Viegas et a* Incidence of caesarean section was comparable in all the three groups in our study also.

One of the limitation of previous studies was the inclusion of both primiparous and multiparous parturients.[15,18] In our study we included only primigravida. One of the limitations of our study is the absence of blinding of the obstetric staff which is nearly impossible in experimental trials on labour analgesia. Thus, probability of a research bias affecting the results of the study cannot be ruled out. We had included a control (nonepi dural) group and used tramadol in this group as it is unethical to deny labour analgesia to a parturient. In our study opioids were administered in combination with bupivacaine only once. Addition of opioids is known to have a synergistic action with local anaesthetics but minimal dosing avoids side effects like pruritus, nausea and vomiting, urinary retention, respiratory depression and poor neonatal outcome.[19]

5. Conclusion

Epidural analgesia in the form of a single bolus dose of either fentanyl (50μg) or sufentanil (10μg) followed by subsequent intermittent bolus dosing using 0.125%

bupivacaine provides excellent analgesia and high patient satisfaction. Both the opioids are equally efficacious and safe in terms of maternal and neonatal outcome. Early onset of analgesia and decreased bupivacaine consumption seen with sufentanil is not clinically relevant. Duration of first and second stage of labour was significantly prolonged in parturients receiving labour epidural analgesia.

6. Source of Funding

None.

7. Conflicts of interest

None.

References

1. ACOG practice bulletin: clinical management guidelines for obstetricians gynaecologists number. *Obstet Gynecol*. 2002;36:177–191. : obstetric analgesia and anesthesia.
2. ACOG committee opinion #295: pain relief during labor. *Obstet Gynecol*. 2004;104:213–213.
3. Miro M, Guasch E, Gilsanz F. Comparison of epidural analgesia with combined spinal-epidural analgesia for labor: a retrospective study of 6497 cases. *Int J Obstet Anesth*. 2008;17:15–19.
4. Vyver MVD, Halpern S, Joseph G. Patient-controlled epidural analgesia versus continuous infusion for labour analgesia: a meta-analysis. *Br J Anaesth*. 2002;89:459–465.
5. Lim Y, Ocampo CE, Supandji M, Teoh WHL, Sia AT. A randomized controlled trial of three patient-controlled epidural analgesia regimens for labor. *Anesth Analg*. 2008;107:1968–1972.
6. Karla S, Saraswat N, Agnihotri GS. Comparision of efficacy of bupivacaine and fentanyl with bupivacaine and sufentanil for epidural labor analgesia. *Saudi J Anaesth*. 2010;4:178–181.
7. Lim Y, Ocampo CE, Supandji M, Teoh WH, Sia AT. A randomized controlled trial of three patient-controlled epidural analgesia regimens for labor. *Anesth Analg*. 2008;107:1968–1972.
8. Thomas T, Robinson C, Champion D, Mckell M, Pell M. Prediction and assessment of the severity of post-operative pain and of satisfaction with management. *Pain*. 1998;75:177–185.
9. Akkamahadevi P, Srinivas H, Siddesh A, Kadli N. Comparision of efficacy of sufentanil and fentanyl with low-concentration bupivacaine for combined spinal epidural labour analgesia. *Indian J Anaesth*. 2012;56:365–369.
10. Lilker S, Rofaeel A, Balki M, Carvalho JC. Comparison of fentanyl and sufentanil as adjuncts to bupivacaine for labor epidural analgesia. *J Clin Anesth*. 2009;21:108–112.
11. Lim Y, Sia AT, Ocampo C. Automated regular boluses for epidural analgesia: A comparison with continuous infusion. *Int J Obstet Anesth*. 2005;14:305–309.
12. Boselli E, Debon R, Cimino Y, Rimmele, Allaouchiche B, Chassard D. Background infusion is not beneficial during labor parturient controlled analgesia with ropivacaine 0.1% plus 0.5g/mL sufentanil. *Anesthesiol*. 2004;100:968–972.
13. Cohen S, Amar D, Pantuck CB, Pantuck EJ, Goodman EJ, Leung DH. Epidural analgesia for labour and delivery: fentanyl or sufentanil? *Can J Anaesth*. 1996;43:341–346.
14. Russell R, Reynolds F. Epidural infusions for nulliparous women in labour. A randomised double-blind comparison of fentanyl/bupivacaine and sufentanil/bupivacaine. *Anaesth*. 1993;48:856–861.
15. Russell R, Reynolds F. Epidural infusion of low-dose bupivacaine and opioid in labour. Does reducing motor block increase the spontaneous delivery rate? *Anaesth*. 1996;51:266–273.
16. Rolfseng OK, Skogvoll E, Borchgrevink PC. Epidural bupivacaine with sufentanil or fentanyl during labour: a randomized, double-blind study. *Eur J Anaesthesiol*. 2002;19:812–818.
17. Herman NL, Sheu KL, Decar TKV, Rubin JD, Gadalla F, Koff HD. Determination of the analgesic dose-response relationship for epidural fentanyl and sufentanil with bupivacaine 0.125% in laboring patients. *J Clin Anesth*. 1998;10:670–677.
18. Wong CA, Mccarthy RJ, Sullivan JT, Scavone BM, Gerber SE, et al. Early compared with late neuraxial analgesia in nulliparous labor induction: a randomized controlled trial. *Obstet Gynecol*. 2009;113:1066–1074.
19. Chaney MA. Side effects of intrathecal and epidural opioids. *Can J Anaesth*. 1995;42:891–903.

Author biography

Sudhir Pawar Junior Consultant

B Naveen Naik Assistant Professor

Vamsidhar Amburu Senior Resident

Tanvir Samra Assistant Professor

Cite this article: Pawar S, Naik BN, Amburu V, Samra T. Efficacy of fentanyl versus sufentanil for labour analgesia and its comparative evaluation with intramuscular tramadol. *Indian J Clin Anaesth* 2019;6(4):548-552.