Patient-Controlled Epidural Analgesia After Hysterectomy With Bupivacaine 0.125%: Comparison Of Different Concentrations Of Sufentanil And Fentanyl

T Chand, P Bundela, K Joshi, A Agarwal, A Dupargude,

Citation

T Chand, P Bundela, K Joshi, A Agarwal, A Dupargude,. *Patient-Controlled Epidural Analgesia After Hysterectomy With Bupivacaine 0.125%: Comparison Of Different Concentrations Of Sufentanil And Fentanyl*. The Internet Journal of Anesthesiology. 2012 Volume 30 Number 3.

Abstract

Aims: The aim of the study was to compare the analgesic efficacy and the safety profile of different concentrations of sufentanil and fentanyl as an adjuvant to bupivacaine for postoperative lumbar epidural analgesia.Settings and Design: Prospective double blind, randomized controlled ,single centre study.Material and Methods: 80 patients of ASA-I-II aged 40-55 years who underwent vaginal hysterectomy were randomly allocated in four groups. The PCEA pump was programmed to deliver a 2 ml bolus with a lockout interval of 12 min and background infusion of 4 ml/h. 0.125% bupivacaine with sufentanil 0.5 µg/mL ,0.75 µg /mL and 1 µg /mL was administered and compared with fentanyl 4µg/ml. Patients were observed for analgesic profile and side effects. Statistical analysis : Statistical analyses were performed by using SPSS 14. p< 0.05 was considered significant.Results: The quality of postoperative analgesia of all combinations of bupivacaine-sufentanil were equivalent to bupivacaine-fentanyl . Pruritus was significantly less with bupivacaine – sufentanil 0.5µg/ml (P < 0.05). Conclusion: Sufentanil 0.5 µg/ml is the recommended dose for PCEA

INTRODUCTION

Adjuvants when co-administered with local anesthetics improve the speed of onset, duration of analgesia and reduce the dose thereby eliminating quite a few side effects associated with larger doses of local anaesthetics [1] .Sufentanil produces analgesia via both spinal and supraspinal effects[2,3,4]. Studies comparing postoperative analgesia with IV or epidural sufentanil have shown that both the quality of analgesia and plasma levels are similar after either route of administration. However, the incidence of respiratory depression and sedation appears to be greater in the IV group[5].These properties can be of special value in postoperative epidural analgesia.

Patient Controlled Epidural analgesia (PCEA) allows, patient titration to the desired level of pain and a considerable placebo effect by pressing the PCEA button. It is associated with less local anaesthetic consumption. Continuous infusion techniques ,with demand boluses ,take advantage of sufentanil's rapid onset and short duration of action and may reduce respiratory risks associated with intermittent administration of large boluses[6].

Since sufentanil blocks µ-receptor more selectively than fentanyl[7], it has been suggested that sufentanil has increased analgesic effects and fewer side effects than fentanyl.

Based on previous studies[7.8,9],we administered 0.125% bupivacaine with sufentanil 0.5 µg/mL ,0.75 µg /mL and 1 µg /mL by PCEA and compared it with fentanyl 4µg/ml.

To eliminate possible confounding factors, such as type of incision or operation that could affect the incidence of pain and side effects, we chose to restrict the study only to patients undergoing a vaginal hysterectomy , in whom a lumbar epidural catheter was placed for postoperative analgesia.

Our prospective, double-blinded, randomized study was thus aimed to compare the effectiveness on pain and the incidence of side effects of sufentanil-bupivacaine or fentanyl bupivacaine through PCEA. Secondly, we evaluated the optimal dose of epidural sufentanil .

METHOD

After approval from institutional review board and informed

written consent 80 women of ASA I & II status aged 40 -55 years requiring elective vaginal hysterectomy were recruited .Exclusion criteria were those with hypertension, bleeding or coagulation test abnormalities, psychiatric diseases, diabetes, history of drug abuse and allergy to local anesthetics of the amide type or any contraindication to epidural administration.

In the preoperative period, all the patients were instructed about visual analogue pain scores (VAPS, 0–100 mm scale: 0 = no pain, 100 = worst pain ever).

All the patients received oral alprazolam 0.25mg the night before surgery. In the operating room a thorough quick clinical examination was done and baseline hemodynamic parameters recorded. An intravenous access was secured and 500ml of lactated ringer's solution infused. All emergency drugs and equipments were kept ready. An epidural catheter was placed in the L2–L4 intervertebral space in lateral decubitus or sitting position by using 18-gauge Tuohy`s needle with loss of resistance technique. Epidural catheter was secured 3-5 cm into the epidural space. After negative aspiration for cerebrospinal fluid and blood, correct placement of the catheter was confirmed by injecting 3 ml of 2% lignocaine HCl solution containing adrenaline 1:2, 00,000. All patients were given epidural anaesthesia - diluted solution of 0.5% bupivacaine plain in 5ml incremental boluses (according to body weight, with no adjuvant). Hemodynamic parameters, which included heart rate, Electrocardiogram, mean arterial pressure (MAP), oxygen saturation using pulse oximetry (SpO_2) and respiratory rate, were monitored continuously. All patients were given intravenous fluids depending on their body weight and operative loss.

After the surgery, patients were shifted to post anaesthesia care unit (PACU).The patients were randomly allocated to one of the four groups of 20 each according to a computer generated randomized table.

As previous studies calculated the sample size based on 20% to 33% decrease in pain score[9,10,11,12], we calculated that a mean difference in VAPS between groups of 30%, with reduced pain scores in the sufentanil group, would permit a type 1 error rate of one-tailed = 0.05 and a type 2 error of = 0.20.This analysis indicated that a sample size of 17 patients per group was essential. Considering a 15% drop out, 20 patients per group were allotted. Eight patients were not included in this study for the following reasons; patient refusal 5 and error of PCEA pump in 3 patients.

Through the PCEA pump (Fresenius vial SA, Le Grand Chemin, 38590 Brezins France), all groups received 0.125% bupivacaine and each group received either fentanyl (group F: fentanyl 4 µg/ml) or sufentanil (group S1: sufentanil 0.5 µg/ml, group S2: sufentanil 0.75 µg/ml, and group S3: sufentanil 1.0 µg/ml). The PCEA pump was programmed to deliver a 2 ml bolus with a lockout interval of 12 min and background infusion of 4 ml/h.

The randomization code was maintained in sequentially numbered opaque envelopes until just before use. The medications were supplied by hospital pharmacy.

Epidural analgesia began after the patient was shifted to PACU .The patient's pain intensity was assessed at arrival , marked as VAPS score at 0 hrs. When the patient was asleep VAPS was noted as 0. Rescue analgesia was informed to be given epidurally (if there was no relief in pain even after 30 minutes of demand bolus) comprising of 5ml of plain 0.125% bupivacaine.

The vital hemodynamic parameters were recorded at 15 min interval for the first hour and then hourly for 24 hrs. The level of sedation was also recorded according to Ramsay sedation scale (awake levels were: 1, anxious agitated or restless; 2,co-operative,oriented and tranquil; 3, responds to command; asleep levels were dependent on patients response to a light glabellar tap or loud auditory stimulus; 4, brisk response; 5, a sluggish response; and 6, no response). Patients with sedation score of ≥ 4 were considered sedated. Motor blockade was recorded by modified Bromage score. The occurrence of other side effects like nausea, vomiting, headache, pruritus and respiratory depression (defined as respiratory rate < 10/minute or SpO2 < 90% without oxygen), bradycardia and hypotension were also recorded on each time of assessment.

It was planned that postoperative hypotension (systolic BP <100 mmHg or a reduction in mean arterial pressure of more than 20% from baseline) would be treated with injection mephentermine 6 mg in bolus doses, bradycardia (heart rate<60 beats/min) would be treated with 0.3 mg of inj. atropine nausea / vomiting would be treated with 4 mg of intravenous ondansetron i.v. and pruritis with Inj. chlorpheniramine 10mg IV.

Data was collected and analyzed using SPSS v 14.0k .All variables are presented as means ± the standard deviation

(SD). Continuous variables were analyzed using one way ANOVA after the Komogorov-Smirnov or Kruskal-Wallis test. Categorical values were analyzed with the chi-square test or Fisher's exact test.

P value < 0.05 was considered significant.

RESULTS

All groups of patients were similar with respect to demographic data and duration of surgery (Table 1). Pain control was successful in every group. Also, there was no significant difference of VAPS in each group (Table 2).Analgesic requirements were also nearly similar (Table 3).Postoperative hemodynamic parameters were stable and comparable(Table 4). Nausea and vomiting were the most common side effects (n = 21) and pruritus (n = 18), headache (n = 10) and sedation (n = 4) also occurred, but no respiratory depression, hypotension or motor blockade was observed. The incidence of pruritus was significantly lower in group S1 than in group S2 (P = 0.0455), and lower in group S1 than in group S3 (P = 0.0440) (Table 5).

Figure 1

Table 1: Patient Demographics (Values are mean ± SD)

Variable	Group F (n=20)	Group S1 (n=20)	Group S2 (n=20)	Group S3 (n=20)	F and Pvalue
Age(years)	50.2±2.61	51.5±4.17	49.4±2.7	50.2±4.93	F=1.129,p =0.345
Weight(kg)	51.0±5.32	50.5±3.79	50.2±2.61	51.5±4.17	F=0.3906,,p =0.760
Height(cms)	152±2.13	152±2.04	152±1.70	151±2.16	F=2.174,p =0.098
Duration of surgery(min)	121±17.2	122±15.7	120±14.6	119±13.2	F=0.1031,p=0.958

Figure 2

Table 2: Visual Analogue Pain Scores (Values are mean ± SD)

Time(hrs)	Group F	Group S1	Group S2	Group S3	F and p value
o	23.1±1.70	23.4 ±1.96	22.4 ±1.82	22.4±1.93	F=1.448,p=0.235
3	22.7±1.69	24.09±1.92	22.2±1.74	22.2±1.71	F=1.581,p=0.201
6	22.6±1.79	23.1±2.01	22.1±1.69	22.0±1.65	F=1.372,p=0.258
12	22.9±1.94	23.2±1.89	22.3±1.81	22.2±1.73	F=1.271,p=0.291
24	22.9±1.87	23.1±1.79	22.1±1.60	22.4±1.76	F=1.358,p=0.262

Figure 3

Table 3: Analgesic requirements

	Group F	Group S1	Group S2	Group S3	
Bupivacaine consumption (mg)	27.2±5.35	26.8±5.81	26.6±3.78	25.8±6.11	F=0.243,p=0.86
Sufentanil consumption (microgram)	-	69.8±8.03	69.5±8.05	71.5±7.17	F=0.408,p=0.67
Fentanyl consumption (microgram)	305±20.23				
Number of Rescue analgesia doses given	2	3	3	1	On comparing group S1and S3;groupS2 and S3:p>0.05(not significant)

Figure 4

Table 4: Postoperative Hemodynamic parameters

Variable	Group F	Group S1	Group S2	Group S3	
Mean arterial Blood pressure(MAP) mm Hg	83.3±4.78	80.2±5.02	80.5±4.58	81.0±4.81	F=1.709, p=0.172
Heart Rate(beats per minute)	77.8±7.02	77.2±5.25	78.0±6.09	77.0±5.56	F=0.1164, P=0.950
Oxygen saturation(SPO2)	95.2±4.74	93±7.75	96±2.87	93.2±6.66	F=1.341, P=0.267

Figure 5

Table 5: The Incidence of Recorded Side Effects

Side effects	Group F	Group S1	GroupS2	Group S3
Nausea/vomiting	6	4	5	6
Pruritus	2	0	7*	9**
Headache	2	3	2	3
Sedation	0	0	1	1
Hypotension	0	0	0	1
Bromage score >0	0	0	0	0
Respiratory depression	0	0	0	0

*p value=0.0455(p<0.05 ,significant)

**p value=0.0440(p<0.05, significant)

DISCUSSION

The results of the present study demonstrate that the analgesic effects of the combination bupivacaine-fentanyl are equivalent and effective to those of the different combinations of bupivacaine-sufentanil. But the side effects profile was different.

Brodner et al[10] and Vertommen et al.[8] have shown that epidural bolus doses of a combination of 0.75 µg/mL

sufentanil and bupivacaine 0.125% produced excellent analgesia superior to adding 0.5 µg/mL sufentanil and equal to adding 1 µg/mL sufentanil to the local anesthetic. But findings of Jeon H R [11]was similar to our study.

We found the average amount of sufentanil used by our study patients smaller (70 µg in 24 hours) compared to other similar studies by Geller et al [2] (149 µg) and Hansdottir et al [12] (120 µg). The Asians may require less analgesia because they are more likely to experience the adverse effects of opioids. Some Asians are likely to demand for less analgesia due to a stoical attitude towards coping with pain[13].But it was higher than Poopalalingam R et al [14] possibly because , they used the demand only PCEA programme, which minimised the amount of sufentanil consumed.

Other studies [15,16,17] observed no difference in total dose of bupivacaine required between fentanyl and sufentanil group like ours. In contrast, Cohen et al.[16] reported that patients receiving sufentanil required less total dose of bupivacaine than those receiving fentanyl.

The number of additional supplementary bupivacaine top ups was comparable in all the groups. This finding was in contrast to some studies[16,18].But similar to some other studies[19].

Nausea/vomiting was the most common side effect observed. Statistical analyses revealed no meaningful differences between sufentanil groups but the incidences increased when the dose of sufentanil was raised. The findings are similar to those observed by Jeon H R et al[11]. The extradural opioids are well known for their emetic effect. Several studies have been conducted in adults to examine patients' preferences for outcomes in the postoperative period. Investigators have found that avoiding vomiting is the major priority for adults [20].

Sedation due to epidural sufentanil is postulated due to rostra1 spread via CSF, and perhaps by direct transit in epidural veins, may be more important than spread resulting from systemic absorption[21,22,23]. In our study, sedation was found in one patient each in group S2 and S3 but it was statistically insignificant. None of the two patients had oxygen saturation <90% nor was their discharge from recovery room affected. Our findings were similar to other studies[10].

The absence of hypotension in our study is most likely due to the low concentration of bupivacaine used and similar to other studies[24].

Pruritus occurred commonly .Incidence increased with the dosage .Only in two patients in group S3 it was severe enough to require treatment. There was a correlation between pruritus and sufentanil dosage similar to other studies[11].However,Cohen et al [25] observed that the severity but not the incidence increased with higher dosage of sufentanil.

A limitation of our study was the small sample size of each group.

CONCLUSION

Using different doses of the sufentanil group, similar analgesic effects were observed. Therefore, sufentanil like fentanyl for PCEA can be used effectively and sufentanil 0.5 µg/ml is enough for postoperative pain control and side effects. Consequently, we think sufentanil 0.5 µg/ml is the recommended dose for PCEA.

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Author Information

Trilok Chand, M D
Professor & Head, Dept of Anaesthesia and Critical Care, S. N. Medical College

Pankaj Bundela, M D
Senior resident, Dept of Anaesthesia and Critical Care, S. N. Medical College

Komal Joshi
Postgraduate student, Dept of Anaesthesia and Critical Care, S. N. Medical College

Archana Agarwal, M D
Lecturer, Dept of Anaesthesia and Critical Care, S. N. Medical College

Abhishyand Duparguде,,
postgraduate student, Dept of Anaesthesia and Critical Care, S. N. Medical College