ORIGINAL RESEARCH

Comparative assessment of Levobupivacaine Alone versus Levobupivacaine with Ketamine in Subcutaneous Infiltration for Postoperative Analgesia

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ABSTRACT

Introduction: After a lower segment caesarean section, local anaesthetic wound infiltration is used as part of multimodal analgesia to lessen pain and opiate use (LSCS). Ketamine extends the effects of analgesia by blocking additional spinal pain pathways.

Aims: To compare the analgesic effectiveness of ketamine and levobupivacaine when injected into subcutaneous wounds.

Materials and Methods: 50 patients receiving under spinal anaesthetic, a randomisedwas done. Both Group A and Group B parturients received surgical wound infiltration with 0.5% levobupivacaine diluted with normal saline at a dose of 2 mg/kg body weight for Group A, and 0.5% levobupivacaine with ketamine at a dose of 1 mg/kg body weight for Group B. We evaluated postoperative pain scores, first rescue analgesia time (FRA), hemodynamic parameters, and overall opioid analgesic use.

Results: Group B had a 1.5-hour longer pain-free duration and shorter time to FRA, along with lower mean VAS scores. Additionally, Group B participants consumed significantly fewer opioids overall and overall pain levels (P = 0.003). 97% of parturients in Group A and just 50% of those in Group B required rescue analgesia. The patient satisfaction score in Group B was considerably higher (P = 0.009). Between the groups, there was no difference in the frequency of nausea and vomiting (P = 0.5234).

Conclusions: Adding ketamine to levobupivacaine for surgical wound infiltration increases patient satisfaction, prolongs the duration of analgesia, and reduces the need for 24-hour opioid use.

Keywords: Levobupivacaine, Ketamine, Opioid consumption, Postoperative

INTRODUCTION

Postoperative pain is one of the major concerns during and after cesarean sections. [1] Post-operative discomfort may result in a body's stress reaction and issues with the heart or the lungs [2]. Consequently, postoperative pain should be managed as soon as feasible. An essential component of the best perioperative care is postoperative analgesia. Multimodal analgesia is a well-known method for lowering postoperative pain because it combines

several medications with varying durations of action and varied routes of administration, minimising the adverse effects of individual medications. To deliver efficient and secure analgesia, various medication combinations are supplied by various routes, including oral, intramuscular (IM) intravenous (IV), rectal route, and perineural infiltration [3]. In order to effectively manage post-operative pain, wound infiltration with local anaesthetic medications is now often employed in a variety of surgical procedures [4]. A safe, efficient, and affordable technique of managing postoperative pain is wound infiltration. It offers immediate pain relief that lasts for a short while without having any negative side effects [5]. Levobupivacaine, an amino amide local anaesthetic and the pure S (-) enantiomer of bupivacaine, has strongly emerged as a safer option to conventional local anaesthetic agents for regional anaesthesia with reduced cardiotoxicity and neurotoxicity. It is one of the most often used local anaesthetic agents. [6]

As a supplement to local anaesthetic, the anaesthetic drug ketamine has generated some interest. Pharmacologically, ketamine and the hallucinogen phencyclidine are related.[7] It also called as dissociative anaesthetic which provide marked analgesia without inducing respiratory depression.[8]

Such increased usage mandates documentation of evidence-based literature with regards to risk and safety concerns as well as clinical issues related to levobupivacaine. [9]The aim of the present study was to compare levobupivacaine alone versus levobupivacaine with ketamine in subcutaneous infiltration for postoperative analgesia.

MATERIAL AND METHODS

An institutional ethics committee authorised the study protocol, which was carried out in a tertiary care hospital. Prior to the procedure, all the parturients provided written informed consent.

The study comprised 50 adult patients who underwent caesarean sections while under spinal anaesthesia and had no obstetrical or medical conditions. They all had Physical Status II or III according to the American society of anesthesiologists (ASA).

The study excluded participants who were unwilling or uncooperative, had a history of anaphylaxis to local anaesthetics, opioids, or other drugs to be used, were currently abusing drugs or had a history of abusing drugs in the past, had a psychiatric illness, weighed more than 100 kg, or were unable to understand the Visual Analog Scale (VAS).

Parturients (25 in each group) were randomly assigned to one of the two groups using computer-generated numbers stored in separate, sealed, and numbered envelopes. The maximum safe dose of 0.5% levobupivacaine was administered to Group A parturients as a subcutaneous surgical wound infiltration at a rate of 2 mg/kg body weight (rounded to nearest multiple of 10) up to a maximum of 150 mg in a total volume of 32 ml of sterile saline. Group B parturients received subcutaneous surgical wound infiltration with a solution of 0.5% levobupivacaine 2 mg/kg body weight (rounded to nearest multiple of 10) to a maximum of 150 mg plus ketamine 1 mg/kg body weight diluted with normal saline to a total volume of 32 ml. The study drugs were prepared by an anaesthetist who was not engaged in the administration of anaesthesia or postoperative care and gave them to the surgeon for subcutaneous infiltration before skin closure while taking all necessary aseptic measures. Before the surgery, a full preanesthetic check-up was carried out that included a thorough review of the patient's medical history, a general physical examination, and a systemic examination. Prior to surgery, routine tests were performed, including complete hemograms, coagulation profiles, random blood sugar tests, and other tests as needed. Prior to surgery, the VAS was demonstrated and the scoring system was described. The pregnant women were advised before surgery that they could withdraw from the trial at any moment and ask for an analgesic if they felt pain following the procedure.

Prior to subarachnoid block, the parturients were moved to the operating room and placed in the left lateral position. The following measurements were made: electrocardiogram (ECG), noninvasive blood pressure (NIBP), respiratory rate (R.R.), oxygen saturation (SpO2), and pulse rate (P.R). All during the process, these variables were tracked and recorded every ten minutes. Preloading with 10 ml/kg of body weight of a balanced salt solution was performed after gaining intravenous access. Subarachnoid block was then administered while the patient was seated and under strict aseptic conditions. At the L3 4/L4 5 vertebral level, a 26 gauge Quincke's needle was inserted into the subarachnoid space. After ensuring that CSF was starting to flow, 2.0 ml of 0.5% heavy bupivacaine was injected through the spinal needle with the opening facing cephalad. The spinal needle was then removed, and the parturient was then turned supine. After achieving sensory block up to level T4 and motor block up to level 3 on the modified Bromage scale, the procedure was approved. The parturient was removed from the trial if spinal anaesthesia was only partially successful or failed. After the procedure, the surgeon administered the study drug subcutaneously to the parturients in a blinded way based on random group allocation.

The heart rate, blood pressure, respiratory rate, and oxygen saturation of parturients were continually recorded. After entering the postoperative recovery room, hemodynamic parameters, postoperative pain scores, and analgesic needs were immediately recorded at 0 minutes, 30 minutes, 1, 2, 4, 6, 8, 12, 16, 20, and 24 hours, respectively. As part of a multimodal postoperative analgesic regimen, all parturients received a slow infusion of 75 mg of diclofenac sodium in 100 ml of saline at 0 min and then every 8 hours after that. A 50 mg intravenous injection of tramadol, a rescue analgesic, was given to every pregnant woman who had a VAS of four or higher or who had ever expressed pain. It was noted when the first rescue analgesic (FRA) request occurred. After receiving tramadol for an hour, if the parturient still reported a VAS of 4, comparable doses were repeated up to a maximum of 100 mg in consecutive 4 hours or 400 mg in 24 hours. The total amount of rescue analgesics consumed in the 24 hours following surgery was noted.

To maintain the double-blind nature of the study, the observer (anaesthesia resident deployed in the postanesthesia care unit) who recorded the postoperative vitals and analgesic use was blinded to the group allocation of the parturients. The results of the parturients were assessed in terms of the degree of pain reduction (as determined by the VAS score), the timing of FRA administration, the number of times rescue analgesic was administered, and the overall amount of analgesic consumed within 24 hours after surgery. The potential for negative impacts on parturients was also assessed. The VAS scale and the total amount of analgesics consumed during the first 24 hours after surgery were used to measure the primary outcome, which was postoperative pain alleviation. Patient satisfaction score (PSS), the secondary outcome, was evaluated 24 hours after surgery and was rated as follows: Excellent (4), Good (3), Moderate (2), and Poor (1)

Data were presented as percentages and numbers. We computed the mean and standard deviation. Using the Student t test, quantitative variables were compared. Depending on the situation, the Chi square (2) or exact test was used to compare categorical data. For statistical significance, a probability value (P value) of less than 0.05 was used. All statistical calculations were performed using SPSS version 25.0.

RESULTS

In terms of demographic statistics, we saw that both groups were comparable. Groups A and B had comparable baseline zero hour mean heart rates (P = 0.942). With the exception of the 4th and 6th hours following surgery, the mean heart rate of group A was greater than that of group B, a difference that was statistically insignificant at most time periods. When the mean

heart rates of the two groups were compared, both groups' values gradually dropped with time, but group B's decline was more pronounced. [Table 1].

Table 1: Mean Heart Rate in postoperative

HR	Group A	Group B	p-value
	Mean ± SD	Mean ± SD	
0 h	91.52 ± 15.23	91.41± 13.67	0.942
30 min	92.25 ± 14.52	91.25 ± 14.54	0.821
1 h	94.43 ± 15.67	90.51 ± 14.89	0.504
2 h	93.51 ± 14.45	89.32 ± 11.43	0.189
4 h	93.07 ± 14.32	87.73 ± 11.23	0.132
6h	94.32 ± 13.68	86.63 ± 9.49	0.114
8 h	90.26 ± 12.75	8616 ± 9.54	0.421
12 h	85.42 ± 11.17	85.34 ± 8.78	0.735
16 h	84.31 ± 11.70	83.62 ± 7.75	0.952
20 h	83.22 ± 11.29	83.54 ± 8.43	0.968
24 h	83.55 ± 10.56	82.43 ± 8.54	0.456

The mean time to FRA for group A was 3.35 ± 2.21 hours (194 minutes), whereas it was 4.97 ± 2.36 hours for group B. (286 mins). P=0.043 indicates that this difference was statistically significant. As a result, parturients in Group B reported experiencing pain 1.5 hours after those in Group A [Table 2]. Only 45% of parturients in group B who got ketamine in addition to levobupivacaine required rescue analgesia, compared to approximately 95% in group A who received levobupivacaine alone. [Table 3] In comparison to group B, parturients in group A consumed a mean total opioid dose of 98.25 ± 35.32 mg in 24 hours. As a result, group A consumed more opioids than group B on a statistically significant basis (P = 0.002, Table 4). Only 7% of parturients in Group A had excellent-quality PSS, compared to 24% of parturients in Group B, while 25% of Parturient in Group A and 45% of Parturient in Group B had good-quality PSS. As a result, there was a statistically significant difference between the two groups' patient satisfaction scores. (P = 0.007, Table 5).

Table 2: Mean time to First Rescue Analgesia

	Group A	Group B	p-value
	Mean ± SD	Mean ± SD	
Time to First Rescue Analgesic consumption (h)	3.65 ± 3.51	4.50 ± 2.52	0.045

Table 3: Total Opioids analgesic consumption in 24 hours

	Group A	Group B	p-value
	Mean ±SD	Mean ±SD	
Total opoids analgesic consumptions in 24hr (mg)	98.25 ± 35.32	63.20 ± 21.45	0.002

Table 4: Parturients (%) requiring rescue analgesic in both groups

	Group A	Group B
Yes	47	22
No	3	28

Table 5: Patients satisfaction score among two groups if parturients (%)

Score	Group A	Group B
1	5	0
2	29	16

3	12	22
4	4	12

DISCUSSION

Local anaesthetic infusion into subcutaneous wounds is efficient, risk-free, affordable, and does not require special training. The analgesic effectiveness of various local anaesthetic wound infiltration strategies for postoperative analgesia following caesarean section was supported by a systemic review and meta analysis.[10] With local anaesthetic wound infiltration, they noticed a statistically significant decrease in postoperative pain scores and overall opioid use in 24 hours [11]. For local wound infiltration following caesarean section, we employed levobupivacaine alone and levobupivacaine with ketamine due to their analgesic and anti-inflammatory characteristics as well as a lower cardiotoxic profile.

Neither of the 50 parturients in our study were eliminated, and both groups' age, weight, and ASA grade were statistically comparable. Patients in group B (L+K) reported having no postoperative pain for up to 286 minutes, but those in group A (L) required rescue analgesia at 194 minutes. This shows that local wound infiltration offers sufficient analgesia and that adding ketamine to levobupivacaine considerably lengthens the period of painlessness (P = 0.043). The mean VAS score at FRA in both groups was comparable (4.85 1.26 in group A and 4.67 0.59 in group B), although the statistically significant longer delays to FRA that we observed. This suggests that while ketamine was helpful in extending the time needed for FRA, levobupivacaine still had a significant analgesic effect in both groups. In 48 patients having abdominal hysterectomy, Abdallah et al. assessed the analgesic efficacy of preincisional infiltration with ketamine or levobupivacaine.[12] With ketamine and levobupivacaine, they noticed an extended period of analgesia lasting up to 158 minutes (P = 0.001). The use of less volume and concentration of levobupivacaine solution for infiltration, i.e., 20 ml and just 0.25% levobupivacaine in their study group, can be explained by the shorter time to FRA in their study group compared to our study group A. [13].

In our investigation, group A had higher overall VAS ratings with statistically significant higher values at 1, 4, 6, and 12 hours. This has been connected with a substantial rise in heart rate in the same group at 4 and 6 hours. This means that while the groups receiving ketamine as an adjunct to levobupivacaine for infiltration experienced less pain during the same period, the groups receiving levobupivacaine alone experienced relatively initial peaks of higher pain scores reflected by higher heart rates at the same time of observations. Levobupivacaine is therefore made more effective in terms of providing deep, long-lasting postoperative analgesia by the inclusion of ketamine as an adjunct.

In group B, only 45% of the patients required rescue analgesia, whereas 95% in group A required further tramadol supplementation. Accordingly, the mean amount of tramadol used as a rescue analgesic in group B was 63 mg, compared to 96 mg in group A, with a statistically significant difference (P = 0.002). These results support ketamine's ability to reduce opioid-related adverse effects like nausea, vomiting, pruritus, and drowsiness when administered in conjunction with levobupivacaine.

Demiraran et al. studied 90 patients undergoing general anaesthesia for caesarean sections, with the wound being infiltrated with 20 ml of 0.25% levobupivacaine at the conclusion of the procedure. In the trial group, a total of 483 mg of tramadol was consumed, compared to 560 mg in the placebo group (P = 0.07). The utilisation of lower concentration and volume of levobupivacaine in their study can be linked to the study group's generally higher tramadol consumption than group A. Furthermore, we employed multimodal analgesia by administering an intravenous injection of diclofenac 75mg eight times a day to all the expectant mothers, which was not a component of their trial [14].

In comparison to placebo, parturients who underwent wound infiltration after caesarean section under regional anaesthesia experienced a statistically significant reduction in morphine use at 24 hours, according to a Cochrane review of 20 papers on the subject. Though the catheter was positioned above the fascia that affected the dissemination of the drug, this investigation found no additional benefit in terms of patient satisfaction score when ketamine was added to continuous wound infiltration with 0.125% bupivacaine [15]. Contrarily, we found that group B's patient satisfaction scores were statistically and clinically significantly higher than those of group A (P = 0.02), which can be attributed to the use of a greater concentration of ketamine and levobupivacaine (0.5%).

CONCLUSION

For local wound infiltration, ketamine is an effective adjunct modality to levobupivacaine due to its improved pain relief, decreased requirement for rescue opioid analgesia, and lack of significant side effects.

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