

A Comparative Analgesic Efficacy of Buprenorphine or Clonidine with Bupivacaine in the Caesarean Delivery.

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ABSTRACT

Background: Many drug combinations and techniques have been used to give more effective and safer analgesia, especially in caesarean deliveries. Aims and Objectives: To evaluate the analgesic efficacy and side effects of buprenorphine or clonidine with bupivacaine in the caesarean deliveries. **Methods:** A prospective, randomized and triple-blinded study was carried out in 100 patients. The patients were divided into 3 groups, Bupivacaine (0.125%) at 3 hour intervals and buprenorphine (0.075 mg) at 12-hour intervals, Bupivacaine (0.125%) and clonidine (37.5 micrograms) at three-hour intervals and Bupivacaine (0.125%) alone at three-hour intervals. The onset and the duration of analgesia was noted along with side effects like nausea and vomiting, shivering, pruritus, respiratory depression (respiratory rate less than 12 / minute), and sedation and hypotension were recorded up to 24 hours after administration of drug. The obtained data was analyzed using the Statistical Package for Social Science (version 10.0 for Windows, SPSS). Analysis of variance / Chi square test was used to compare the variables between groups. A P value of < 0.05 was considered significant. **Results:** The mean duration of analgesia was significantly longer in group one patients receiving buprenorphine plus bupivacaine in comparison to group two patients receiving bupivacaine plus clonidine and it was the least in group three patients receiving bupivacaine alone. **Conclusion:** Epidural buprenorphine with bupivacaine produced a significantly rapid onset, better quality and longer duration of analgesia than bupivacaine combined with clonidine or bupivacaine alone with minimum side effects in lower segment caesarean section patients.

Keywords: Analgesia, Bupivacaine, Buprenorphine, Caesarean Section, Clonidine.

INTRODUCTION

Post operative pain management is main criteria after any surgery. Caesarean delivery is distinct from other surgeries, as mothers need an early ambulation to take care of their babies. Most of doctors concentrate on this aspect by using several drug combinations and techniques to give more effective and safer analgesia. Buprenorphine has given an encouraging result in analgesic potential.^[1,2]

Buprenorphine has a high affinity at both Mu (μ) and kappa (κ) opiate receptors and is an effectual analgesic, like morphine, in about all-clinical conditions. It can be given intrathecally, as it is compatible with the cerebrospinal fluid (CSF), without any adverse reactions. But it has some side effects like being potentially catastrophic, delayed respiratory depression. Hence, studies are carried out to develop non-opioid analgesics, with less annoying side effects, one such analgesic being intrathecal clonidine which is a potent analgesic without some opioid-related side effects. It may be used either

alone or in combination with opioids and local anaesthetics in surgeries.^[3,4]

The aim of our prospective, triple-blind, randomised controlled study was to evaluate the analgesic efficacy and side effects of buprenorphine or clonidine with bupivacaine in the caesarean deliveries

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MATERIALS AND METHODS

This prospective, randomized and triple-blinded study was carried out in 100 patients from June 2015 to May 2016, after obtaining institutional ethical committee approval. Consent was obtained from all the patients. Initially 107 patients were enrolled in the study. 7 patients were excluded as they did not

meet the inclusion criteria. The patients were divided into 3 groups.

Inclusion Criteria

1. Patients at term (ASA-I and ASA-II), planned for lower segment caesarean section under epidural anaesthesia.

Exclusion Criteria

1. Patients with complicated pregnancy,
2. Patients with Acute foetal distress and
3. Patients with history of hypersensitivity to opioids / local anaesthetics.

All the patients were explained about the study and were made familiar with visual analogue scales (VAS: 0 means ‘no pain’ and 10 ‘worst pain imaginable’) and vital signs were recorded all through the perioperative period. Epidural anaesthesia was used for surgery and later epidural route was used for postoperative analgesia also. We scored postoperative pain intensity during the first 24 hours at hourly intervals.

The patients were divided in to 3 groups

1. Bupivacaine (0.125%) at 3 hour intervals and buprenorphine (0.075 mg) at 12-hour intervals or when the pain score was 4 or more, or if the patient requested analgesia (whichever occurred earlier).
2. Bupivacaine (0.125%) and clonidine (37.5 micrograms) at three-hour intervals or when the pain score was 4 or more, or if the patient requested analgesia (whichever occurred earlier).
3. Bupivacaine (0.125%) alone at three-hour intervals or when the pain score was 4 or more, or if the patient requested analgesia (whichever occurred earlier).

The observer was kept blinded regarding the epidural medication and the groups to avoid bias in analysis and results. An injection of diclofenac sodium 75 mg intramuscularly was given, if the VAS score did not reduced by the one, even after 30 minutes of epidural injection. The total analgesics required for a 24-hour period was noted. The time from injection of drug till reduction in pain intensity by at least 1 in VAS was considered as onset of analgesia. Whereas the duration of analgesia was considered as the time period between the onset of analgesia and either a return to baseline VAS or the time when pain medication was requested, whichever happened earlier. Side effects like nausea and vomiting, shivering, pruritus, respiratory depression (respiratory rate less than 12 / minute), and sedation and hypotension were recorded up to 24 hours after administration of drug.

The obtained data was analyzed using the Statistical Package for Social Science (version 10.0 for Windows, SPSS). Analysis of variance / Chi square test was used to compare the variables between groups. A P value of < 0.05 was considered significant.

RESULTS

A total of 100 patients were studied. Group one and two consisted of 35 patients in each group, while group three consisted of 30 patients. The demographic details of the three groups were recorded [Table 1, Figure 1] and the differences among the groups were not statistically significant.

Table 1: Demographic details of patients

Characteristics	Group 1 (N = 35) Mean±SD	Group 2 (N = 35) Mean±SD	Group 3 (N = 30) Mean±SD	P Value
Age in years	25.13 ± 3.72	24.18 ± 4.0	26.81 ± 3.7	>0.5 (NS)
Weight in KG	65.14 ± 12.12	63.89 ± 10.23	60.72 ± 11.47	>0.5 (NS)
Height in cm	150 ± 1.2	163.5 ± 1.4	156.6 ± 1.8	>0.5 (NS)

NS=Not Significant

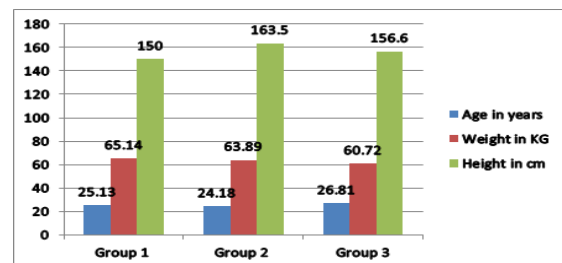


Figure 1: Demographic details of patients

The comparison of post-operative analgesia in the three groups of patients was tabulated [Table 2, Figure 2, 3]. We found that the mean duration of analgesia was significantly longer in group one patients receiving buprenorphine plus bupivacaine in comparison to group two patients receiving bupivacaine plus clonidine and it was the least in group three patients receiving bupivacaine alone.

Table 2: Comparison of post-operative analgesia in the three groups.

Effect	Group 1 (N = 35) Mean±SD	Group 2 (N = 35) Mean±SD	Group 3 (N = 30) Mean±SD	P Value
Duration of analgesia (minutes)	675 ± 25	550 ± 40	150 ± 31	<0.05 (Sig.)
Highest pain score on VAS scale (0 – 10)	3.1 ± 0.5	4.2 ± 0.6	6.3 ± 0.8	<0.05 (Sig.)
Percentage of patients requiring continuation of epidural analgesia after 15 hours	31	50	72	<0.05 (Sig.)
Percentage of patients requiring diclofenac injections	15.12	23.96	71.25	<0.05 (Sig.)

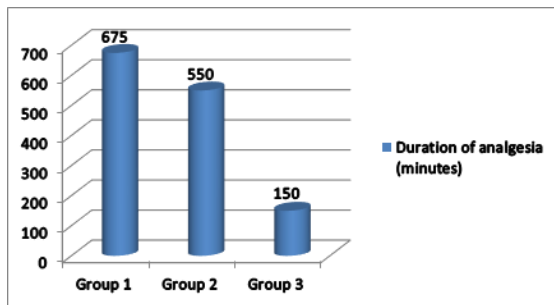


Figure 2: Duration of Analgesia (Minutes).

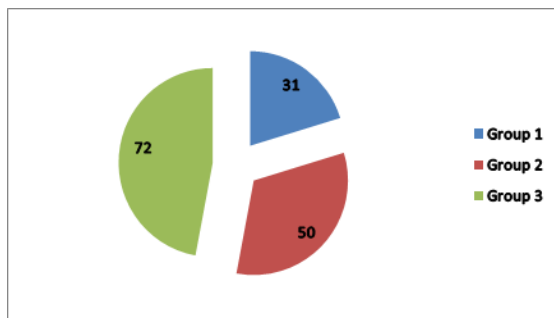


Figure 3: Percentage of patients requiring continuation of epidural analgesia after 15 hours.

The comparison of the side effects of drugs in three groups of patients is shown in [Table 3 and Figure 4]. Itching and pruritus were significantly higher in group three patients and it was the least in group one patients. However the incidence of nausea and vomiting was the highest in group three patients and least in group two patients, but the differences were not significant. We did not find any patient with Incidence of respiratory depression, sedation and hypotension.

Table 3: Comparison of side effects in three groups of patients

Side Effect	Group 1 (N = 35)	Group 2 (N = 35)	Group 3 (N = 30)	P Value
Nausea	6	4	15	>0.05 (NS)
Vomiting	4	3	10	>0.05 (NS)
Itching	3	4	18	<0.05 (Sig.)
Pruritis	2	4	14	<0.05 (Sig.)

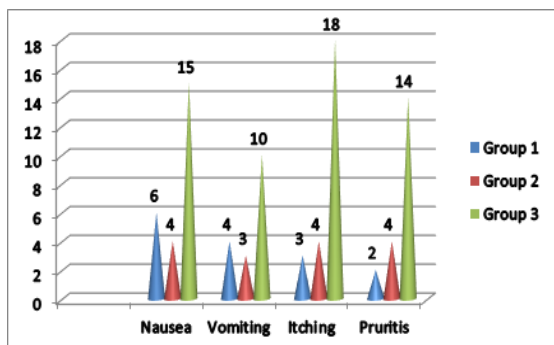


Figure 4: Comparison of side effects in three groups of patients

DISCUSSION

Post caesarean section analgesia improves breastfeeding and satisfaction of mother. Insufficient analgesia results in elevated plasma catecholamine concentrations, leading to adverse effects on all organ systems. In our study we found that lower doses of buprenorphine combined with bupivacaine, patients gave lower pain score with prolonged duration of analgesia and lesser need of diclonfenac injections postoperatively. Thus confirming the fact that a combination of an opioid and an anaesthetic augments the onset and prolongs the duration of analgesia when compared to opioid or anaesthetic alone.^[1,5]

Abboud et al used higher doses of buprenorphine (1 to 4 mg) alone, epidurally, found complete pain relief in 22 ± 2.4 minutes, and prolonged duration of post-operative analgesia than our combination group.^[6]

Studies have shown varying durations of analgesia (2.5 to 9 hours) after administration buprenorphine (1 to 4 mg) alone epidurally. We found the duration of analgesia to be in lower range of reported studies at 150 minutes. This is in accordance with that of Agarwal et al (170 minutes).^[1,7]

We found that buprenorphine showed a improved quality of analgesia regarding VAS scale. This is in accordance with that of Agarwal et al. Abboud et al also found a significantly improved quality of analgesia in patients who recieved epidural bupivacaine with buprenorphine than with bupivacaine alone.^[1,6]

Shrestha et al showed that 2 mg of epidural buprenorphine added to a lower concentration of bupivacaine (0.1%) gave an improved quality of labour analgesia in terms of incidence of motor blockade than 0.25% bupivacaine alone.^[8]

Nelson et al demonstrated that analgesia provided by buprenorphine has a significant correlation with the affective domain, with greater reduction in affective magnitude than in pain intensity.^[9]

We did not find any patient complaining of sedation in all the three groups. This is similar to the findings of Agarwal et al and dissimilar to Palacios et al, who found a very high incidence of sedation with higher doses of epidural buprenorphine in post-caesarean patients.^[10]

We did not find the complaints of itching, pruritus, or respiratory depression in any of the included patients. This is in accordance with that of Agarwal et al, Lawhorn et al and Wittels et al, who also reported, with either a total lack or a very low incidence of such side effects. Hence, the prophylactic administration of buprenorphine may be recommended to prevent the occurrence of such side effects produced after using opioids like morphine, and also may be used effectively to treat intractable pruritus associated with dermatological conditions.^[1,11,12]

We found a lower incidence of nausea and vomiting in the buprenorphine group when compared to the bupivacaine group, which was statistically insignificant. This is in accordance with that of Agarwal et al. This might be due to the use of lower doses of buprenorphine than used in other studies^[1] Few studies showed that the onset and duration of sensory and motor block gets significantly improved after addition of intrathecal clonidine to bupivacaine (even in very small doses). We also found similar finding that the addition of clonidine to bupivacaine improved the onset and duration of analgesia when compared to bupivacaine alone. But we found that the duration of analgesia was significantly lower when compared to buprenorphine combined with bupivacaine. This is in accordance with that of Agarwal et al. According to them the rapid onset and short duration of analgesia and lack of side effects with lower doses of epidural buprenorphine combined with bupivacaine, might be taken as advantage and used in situations that require rapid onset of analgesia, without much side effects.^[1,13-15]

CONCLUSION

Epidural buprenorphine in lower doses when combined with bupivacaine produced a significantly rapid onset, better quality and longer duration of analgesia than bupivacaine combined with clonidine or bupivacaine alone, and is rather safe with minimum side effects in lower segment caesarean section patients for post-operative analgesia.

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