Post-Caesarean Section Analgesia: A Comparison of Epidural Morphine and Nalbuphine

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ABSTRACT

BACKGROUND

Epidural opioids can be used for postoperative pain management. The aim of this study is to compare the clinical profile of epidural morphine and nalbuphine following intra operative intrathecal bupivacaine, for post-operative analgesia in elective lower segment caesarean section.

METHODS

The study was conducted in 50 female patients who underwent elective lower segment caesarean section under spinal anaesthesia. Patients were randomly divided into two groups: Group M and Group N. All the patients in each group received 0.5% Bupivacaine 2 ml intrathecally. After which Group M received Morphine 2 mg diluted in 10 ml of 0.2% ropivacaine epidurally and Group N received Nalbuphine 2 mg diluted in 10 ml of 0.2% ropivacaine epidurally. Onset time and duration of first dose of epidural analgesia were recorded. Total amount of epidural morphine / nalbuphine, the total amount of rescue analgesia given during the post-operative period of first 24 hours along with side effect if any were noted.

RESULTS

The onset time of first dose of epidural analgesia was 11.72 ± 3.0 minute for Group M as compared to 7.48 ± 2.4 minute for Group N ($p<0.001$). Duration of first dose of epidural analgesia for Group M was 935.40 ± 204.61 minute as compared to 380.40 ± 60.48 minute for Group N ($p<0.001$). All the cases in Group N required three epidural doses whereas in Group M, only two cases required three doses ($p<0.001$). In Group M, rescue analgesia was given only once in 96% of cases but in Group N, all cases needed two doses of rescue analgesia ($p<0.001$). There was no side effect except nausea which was seen 20.5% in Group M and 8.0% in Group N ($p>0.05$) during the first 6 hours and 12 hours respectively following the first dose of epidural analgesia.

CONCLUSIONS

Epidural morphine when given for post-operative analgesia provides longer duration of analgesia and requires less rescue analgesia as compared to that of epidural nalbuphine.

KEYWORDS

Epidural, Morphine, Nalbuphine, Postoperative Analgesia

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BACKGROUND

An optimal pain management can avoid many unwanted effects and can enhance early mobilisation and postoperative discharge.[1] besides, pain control after caesarean delivery presents unique demands compared to other surgeries, because women require a rapid recovery to ambulate and care for the baby. Pain relief must be rapid and effective, with minimal adverse effects for both the mother and the new born. Neuraxial opioids give superior post-operative analgesia compared to intravenous analgesia.[2] Epidural analgesia also reduces the incidence of deep vein thrombosis by attenuating the hypercoagulable response of surgery and facilitating the early mobility by effective analgesia during post-operative period.[3]

Among the available drugs, morphine is a μ receptor opioid agonist which produces profound postoperative analgesia however, is associated with undesirable side effects like respiratory depression, pruritus, nausea, vomiting and urinary retention.[4,5] Similarly, nalbuphine is an agonist-antagonist synthetic opioid analgesic which has a ceiling effect on respiratory depression. Analgesic and sleep producing effects of nalbuphine are through agonism at kappa-opioid receptors and it also has the potential to attenuate the μ opioid receptor-related adverse effects.[6] Both morphine and nalbuphine are reported to have 1:1 equivalent doses.[7] In our study we are comparing epidural morphine and nalbuphine, with doses of 2 mg each, for postoperative analgesia following elective lower segment caesarean section.

METHODS

After obtaining Research Ethics Board approval and written informed consents, fifty female adult patients aged 18-40 years, American Society of Anaesthesiology (ASA) physical status II,[8] undergoing elective lower segment caesarean section were recruited in this randomized double blind prospective study conducted in the department of Anaesthesiology of a tertiary hospital at Imphal over a period of two years. The sample size was calculated based on a previous study assuming mean duration of action of morphine and nalbuphine to be 700 and 600 minute respectively with a common standard deviation of 120 minute for α value of 5% and the power of 80%. It came out to be 23 in each group but considering drop out cases, 25 patients were enrolled in each group. Study drugs were prepared by a colleague not directly involved in the study. Using computer generated randomization; the patients were allotted into two groups:

Group M: Morphine 2 mg diluted in 10 ml of 0.2% ropivacaine epidurally.

Group N: Nalbuphine 2 mg diluted in 10 ml 0.2% ropivacaine epidurally.

Patients with bleeding tendency, sepsis, hypotension, spinal deformity, local site infection, uncooperative patient, patient with cardio-respiratory, renal, hepatic or neurological disorders and hypersensitivity to the study drugs were excluded from the study.

Preoperative assessment of each was done a day before the surgery. Monitoring of heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SpO_2) and electrocardiogram (ECG) were started on arrival at the operation theatre. All the patients were preloaded with ringer's lactate solution 10 ml per kg within 30 minutes of sub arachnoid block. Patient was put in left lateral position and skin over the desired site was infiltrated with 1 ml of 2% lignocaine after aseptic and anti-septic precaution. Inter vertebral space L_2-L_3 was located. Using 18G Tuohy needle, midline approach and loss of resistance technique, an epidural catheter 20G was placed in the epidural space allowing 3-4 cms of the catheter tip inside. Epidural space was confirmed by negative aspiration of blood and CSF and uniform dull resistance to 3 ml of normal saline injection. While the patient remains in the lateral position, Dural puncture was performed in L_3 - L_4 interspace under sterile conditions through 25G Quincke needle. Spinal anaesthesia was performed with 2 ml of 0.5% hyperbaric bupivacaine.

First dose of epidural morphine 2 mg or nalbuphine 2 mg diluted in 10 ml 0.2% ropivacaine was given when the patient first complained of moderate pain that is when VAS ≥ 4 (Visual Analogue Score; [9] 0=no pain, 1-3= mild pain, 4-7= moderate pain, 8-10= severe pain) in the post anaesthetic care unit (PACU). Second and third doses were planned at night (7 to 8 pm) and next morning (7 to 8 am) respectively. Rescue analgesia with IM diclofenac 75 mg were given if the patient complained of pain in between the scheduled time of second and third epidural analgesic doses. Second dose of epidural analgesia was kept optional if the patient didn't require any analgesia. Total dose of epidural opioids and rescue analgesia with IM injection diclofenac in 24 hours were be recorded.

Intravenous mephentermine were administered in 3 mg intravenous increments when Systolic BP felled to more than 20% of baseline BP or less than 100 mm Hg. Vasopressor treatment were repeated if hypotension persists. An additional rapid infusion of ringer lactate was also administered at the time of hypotension in aliquots of 100 ml.

Duration of analgesia was recorded as the time interval from the time of first dose of epidural analgesia to time when the patient first complained of pain i.e. first demand of rescue analgesia. Onset time of first epidural analgesic dose was also recorded. Total amount of epidural morphine or nalbuphine given were noted. Also the total amount of rescue analgesia given in the form of injection diclofenac 75 mg given during the post-operative period of first 24 hours was noted. The adequacy of analgesia/effectiveness of pain relief was assessed by VAS.[9] Rescue analgesia was provided by IM injection of diclofenac 75 mg when patient complains of pain or VAS ≥4. Ramsay Sedation Scale[10] was recorded just before and after the administration of first epidural

dose, one hourly for next 6 hours. Details of any other adverse effects like pruritus, anxiety, nausea, vomiting or respiratory depression (respiratory rate less than 10/minute) due to the study drugs were recorded. The data collected were analysed using windows based Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) Windows based version 21 and compared using Student t test for continuous data and Chi square test for categorical data. P<0.05 was considered statistically significant.

RESULTS

The demographic profile was comparable in both the two groups (p>0.05). The onset time of first epidural analgesia in group M (11.72 ± 3.0 minutes) was longer than that of Group N (7.48 ± 2.4 minutes) and this finding was found to be statistically significant (p<0.001). Also the duration of first dose of epidural analgesia in case of Group M was 935.40 ± 204.61 minutes which was longer than Group N (380.40 ± 60.48 minutes) and this finding was found to be statistically significant (p<0.001). All the cases in Group N required three doses of epidural analgesia but in case of Group M only 2 cases required three doses, which was found to be statistically significant (p<0.001). In Group M, rescue analgesia was required only once in 96% of cases but in case of Group N, all cases required two doses (p<0.001).

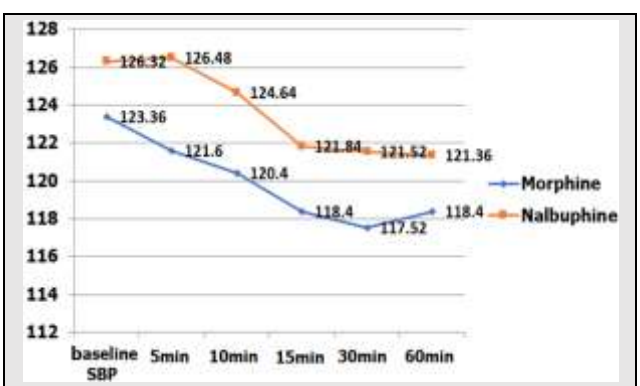

Figure 1. Mean Systolic Blood Pressure (SBP) at Different Time Points after First Epidural Dose between the Two Groups

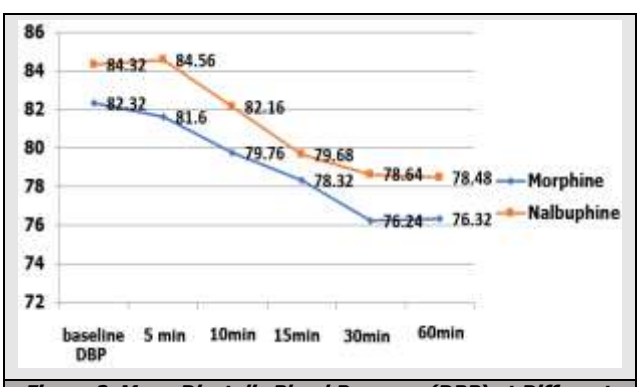

Figure 2. Mean Diastolic Blood Pressure (DBP) at Different Time Points after First Epidural Dose between the Two Groups

Baseline Characteristics	Morphine Mean ± SD	Nalbuphine Mean ± SD	t-Test
Age (years)	30.48 ± 5.68	30.92 ± 5.36	Value=-0.282 df-48 p-0.779
Bodyweight in Kg	66.68 ± 8.25	66.72 ± 6.97	Value=0.907 df-48 p-0.369
Height in cm	156.44 ± 5.32	158.73 ± 4.99	Value=1.569 df-48 p-0.123

Table 1. Demographic Profile of the Two Study Groups

Response Variables	Group M (Morphine) Mean ± SD	Group N (Nalbuphine) Mean ± SD	t-Test
Onset time of first dose of epidural analgesia (in minutes)	11.72 ± 3.0	7.48 ± 2.4	Value=5.479 df-48 p-0.000
Duration of first dose of epidural analgesia (in minutes)	935.40 ± 204.61	380.40 ± 60.48	Value=13.00 df-48 p-0.000

Table 2. Distribution of the Respondents, by Response Variable Stratified by Study Groups

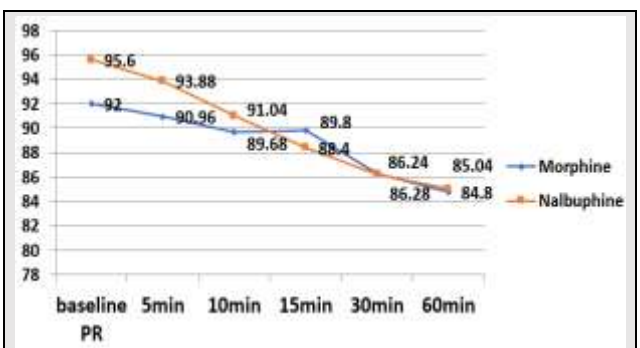

Figure 3. The Mean Pulse Rate (PR) Blood Pressure at Different Time Points After First Epidural Dose Between the Two Groups

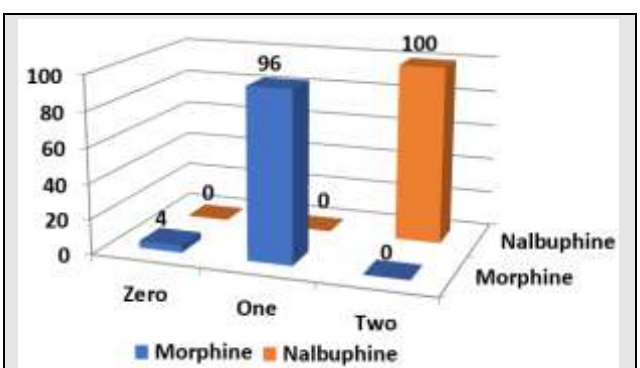

Figure 4. Distribution Respondents by Rescue Analgesia Stratified by Study Groups

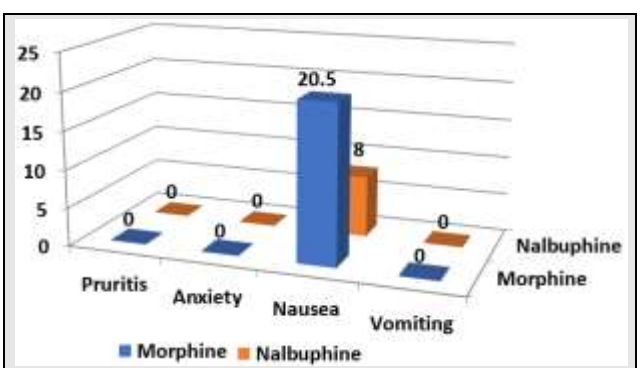

Figure 5. Bar Diagram Showing Distribution of Respondents by Side Effects Stratified by Study Group

Systolic BP, diastolic BP and pulse rate were found to decrease within physiological range in both the groups following 1st epidural dose. The median sedation scores were similar in both the groups at various time periods. There was no case of respiratory depression (which was indicated by the respiratory rate less than 10/ min) in both the Group M and Group N during the first 12 hours of the postoperative period. Nausea was seen in 20.5% of Group M and 8.0% of Group N which was not statistically significant (p>0.05). Whereas, there was no case of pruritus, vomiting and anxiety occurred in both groups.

DISCUSSION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[11] Autonomic nervous system is stimulated by pain leading to various stress responses which are deleterious to the patient. Epidural administration of opioids can be used to provide postoperative analgesia as it gives better quality of analgesia than that achieved by systemically administered analgesics, has a lower incidence of side effects, improves surgical outcome and is associated with high level of patient satisfaction.[12] In spite of all the advantages of postoperative epidural analgesics with opioids, its use is also associated with many side effects like nausea, vomiting, pruritus, respiratory depression and urinary retention.

Our study was undertaken to compare the clinical profile of morphine and nalbuphine when administered epidurally for postoperative analgesia in elective lower segment caesarean section, following intra-operative intrathecal bupivacaine.

Fifty patients undergoing the above mentioned surgery were randomized into two groups (each group consisting of 25 patients) to receive the study drug. The demographic parameters such as age, body weight, height, ASA physical status along with the baseline systolic and diastolic blood pressure, pulse rate, SPO_2, respiratory rate in our study did not show any statistically significant difference and were comparable between the two study groups.

In studies conducted earlier[13-17] on epidural morphine and nalbuphine for post-operative analgesia, 2.5 to 5 mg of morphine and 3 to 10 mg of nalbuphine were used for postoperative epidural analgesia. Both morphine and nalbuphine are reported to have 1:1 equianalgesic doses.[7] So, in our study we compared epidural morphine and nalbuphine, with equivalent doses of 2 mg each, for the postoperative epidural analgesia following elective lower segment caesarean section.

In this study, onset time of first dose of epidural analgesia dose in Group N (7.48 ± 2.4 min) was faster than Group M (11.72 ± 3.0 min); (p< 0.001). However, in the study conducted by Ham BM and Lee SC,[16] the onset time of epidural analgesia with nalbuphine was 15-20 minutes, and also in the studies conducted by Devulapalli PK and Verma HR,[13] Parikh GP et al,[18] Vora KS et al,[19] the onset time of epidural analgesia with morphine were 34.76 ± 5.73, 62.5 ± 13.4 and 67 ± 1.5 min respectively which are not consistent with the finding of our study. This might be due to the use of 0.2% ropivacaine along with either morphine or nalbuphine in our study. Whereas in the other studies mentioned above only plain morphine or nalbuphine were used.

In our study, the duration of first dose of epidural analgesia was longer in Group M (935.40 ± 204.61 min) as compared to Group N (380.40 ± 60.48 min); (p<0.001). This result is consistent with the finding of other studies[13,14,18,19] where the duration of post-operative epidural analgesia with morphine were in the range of 709.75 ± 72.12 to 1158 ± 672 min and that of nalbuphine in the range of 294.68 to 380 ± 11.49 min.[17,20]

The total amount of epidural drug given during the first 24 hours was lesser in Group M as compared to Group N (p<0.001). Twenty-three patients from Group M received only 2 doses of epidural analgesia while the remaining 2 patients from the same Group received 3 doses of epidural analgesia. On the other hand, all the 25 patients from the Group N received 3 doses of epidural analgesia. This finding was consistent with the results of earlier studies conducted by Vora KS et al[19] and Chatrath V et al.[17]

The total number of rescue analgesia received in the form of Inj. diclofenac 75 mg IM during the first 24 hours was lesser in Group M as compared to Group N (p<0.001). Twenty-four patients from the Group M received only 1 dose of rescue analgesia while the remaining 1 patient received no rescue analgesia at all. On the other hand all the 25 patients in Group N received 2 doses of rescue analgesia during the first 24 hours. We didn't come across any study comparing the number or doses of rescue analgesia given after the post-operative epidural analgesia with morphine and nalbuphine.

All 25 patients in each Group M and Group N were observed hourly for 6 hours following the first epidural dose of analgesia for any sign of sedation using Ramsay Sedation Scale.[10] It was observed that there was not a single incidence of sedation (all patients having Ramsay Sedation Scale: 2) during the first 6 hours following the administration of study drugs. This is not in consistent with results from the earlier study conducted by Vora KS et al[19] where 20% of patients receiving epidural morphine of 4 mg were having sedation. Also, in the study conducted by Camann WR et al,[21] 50% of the patients receiving epidural nalbuphine of 30 mg were having sedation. The differences in the result between our study and the earlier studies might be explained by the lower doses of opioid analgesic used in our study which is 2 mg each of morphine and nalbuphine as compared to 4 mg and 30 mg of morphine and nalbuphine used respectively in the earlier studies.

In this study, all the patients in each group were observed for respiratory depression, every hourly for first 12 hours following the first dose of epidural analgesia. It was observed that there was no incidence of respiratory depression in both groups during the first 12 hours. Our findings are consistent with the studies conducted earlier.[21,22] Whereas, in one study,[13] respiratory depression was found in 0.25% of the patients (characterised by respiratory rate less than 10 times/min) who received more than 4 mg of epidural morphine. The differences in the finding might be explained by the higher doses of epidural morphine in their study. Also, in our study, no observation for delayed respiratory depression was made.

In our study, systolic and diastolic blood pressure, respiratory rate, pulse rate in both the Group M and Group N were comparable for first one hour following the first dose of epidural analgesia. But there were significant ($p<0.05$) intragroup fall in haemodynamic parameters in each group in line with other studies.[18,23] This might be explained by the onset of pain relief following study drug administration which decreases the haemodynamic parameters of the patient.

Other potential side effects such as pruritus, anxiety, nausea and vomiting were also considered in our study. Only nausea was found in 20.5% of patients in Group M and in 8% of Group N which was statistically insignificant ($p>0.05$). In one study,[16] it was concluded that epidural nalbuphine was a better agent than epidural morphine in terms of complications like nausea, vomiting and pruritus. In our study, no side effects were found in either group except for the nausea, which might be due to the relatively smaller dose of study drug used as compared to other studies. Also, the premedication with Injection metoclopramide IV might have reduced the incidence of nausea and vomiting. Lastly, we were not able to study urinary retention as a side effect in our study as all the patients were catheterised with indwelling catheter during the post-operative period.

CONCLUSIONS

Epidural morphine when given for post-operative analgesia provides longer duration of analgesia as well as requires less rescue analgesia as compared to that of epidural nalbuphine. The onset time of analgesia was faster with nalbuphine.

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