Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/mw7a6b94

EFFECTS OF PREOPERATIVE NALBUPHINE ON MATERNAL HEMODYNAMICS AND NEONATAL OUTCOMES DURING ELECTIVE CESAREAN SECTION UNDER GENERAL ANESTHESIA

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Abstract

Background: Cesarean section demands that anesthesia control consciousness, muscle function and pain together. Opioids are important for control of pain but may cause breathing problems for the new born and can enter the bloodstream of the baby through the mother's placenta. Nalbuphine, an on-and-off opioid drug, may lower the risks to new borns.

Objective: This study looked at changes in maternal heart and the outcomes for the baby after nalbuphine was used just before the general anesthesia for elective cesarean section.

Methods: I gave 80 full-term pregnant women who were planning elective cesarean sections a study drug one minute ahead of anesthesia induction. Those in Group N were given nalbuphine diluted in normal saline and those in Group C were given normal saline only. Observation of both maternal heart rate and mean arterial pressure was started at the onset of labor, after intubation, throughout the operation and continued after the child was delivered. Researchers evaluated the outcomes at birth using the APGAR system at 1 and 5 minutes, the time for a infant to take its first breath and tests of the umbilical blood.

Conclusion: Stability in a mother's heart rate and blood pressure was greater among those in the nalbuphine group than the controls whenever and after anesthesia induced ($p < 0.05$). After delivery, the scores for nalbuphine patients were below average at 1 minute but returned to normal at 5 minutes. In Group N, time to sustained respiration was greater, though patients had no serious clinical problems. Fetal oxygenation and balance of acids in the blood were preserved, since the umbilical cord blood gases were identical in both groups. Nalbuphine use pre-anesthesia in planned cesarean sections improves the mother's blood pressure levels without jeopardizing the health of the baby. Because it floods the baby's system quickly, its withdrawal is almost instant which is why it can be used safely in child birth.

Keywords: Nalbuphine, Cesarean section, General anesthesia, Maternal hemodynamics, Neonatal outcomes

INTRODUCTION

Three important parts of anesthesia are hypnosis, muscle relaxation and analgesia. Losing an arm or a leg can seriously affect patients' lives. Awareness exists without hypnosis; without analgesia, pain leads to a rise in blood pressure, heart rate and pressure within the head. Different drugs are used to achieve outcomes in analgesia and hypnosis [1]. It is necessary to use opioids as part of anesthetic care for good results [2-4]. It is possible that placental transfer and neonatal difficulty breathing may happen with opioids, so they are not used during obstetric anesthesia. Since the arteries to the womb open extremely wide during full term pregnancy, catecholamine can limit blood flow and negatively affect the newborn. The administration of catecholamines will be limited after the patient is intubated and undergoes surgery. Synthetic opioid agonist-antagonist nalbuphine hydrochloride is a member of the nalbuphine hydrochloride class. It has the same analgesic effect as morphine. It is also used, in addition to balanced anesthesia, to relieve pain before and after surgery [5 - 8]. Researchers compared the quality of anesthesia, the mother's response to stress and outcomes for the newborn when nalbuphine was given ahead of anesthesia for cesarean delivery.

METHODS

The study involved giving participants who were scheduled for elective cesareans, according to established rules, the standard drug or the new one until they gave birth. Patients who did not consent, had fetal distress, were twin or triplet pregnancies or had emergencies were not part of this study. Women who met the criteria had come to term, had just one fetus and decided, together with their doctors, on having a cesarean delivery. They divided participants at random into two groups.

Group N: One minute before being put under general anesthesia, patients in Group N were given 10 ml of normal saline plus 0.2 mg/kg of nalbuphine.

Group C: Patients in this group received normal saline before they were given anesthesia.

The study used the double-blind approach. Eighty group envelopes were generated and included in the preparation. An unblinded senior nurse took care of sorting participants into the groups.

Anesthesia

Ranitidine at a dose of 150 mg was provided to patients two hours past the intended induction of anesthesia. Supine hypotension syndrome and aortic compression were prevented by setting the operating table to the left when the patient was brought in. Under sterile conditions, a big intravenous line was inserted and we measured the patient's vital signs.

All the usual patient monitoring equipment was used for the anesthesia. The area around the stomach was cleaned and covered and patients breathed only oxygen 100% for three minutes before the operation. Participants in Group N got nalbuphine in saline, but Group C only received saline.

Immediately one minute before the anesthesia was given, we gave the study drug through injection. I gave 5 mg/kg of thiopental and 1.5 mg/kg of succinylcholine during the anesthesia induction. With a 30-second direct laryngoscopy, I set the patient's end-tidal CO2 at 35 mmHg by keeping them at 1% isoflurane and 0.25 mg of atracurium.

Both induction to delivery and the time from a uterine cut to delivery were logged. Morphine was given by IV to the control group at a dose of 0.1 mg/kg following delivery and the nalbuphine group received saline instead.

The first group got 2 mg of midazolam through an IV and 5 units of oxytocin within three minutes. A solution with oxytocin in 500 ml of Ringer's solution was also given. There, I reversed the residual neuromuscular blockade by giving neostigmine and atropine.

Maternal Monitoring

All four measurements were taken at induction, five minutes after intubation, in the middle of the operation and at delivery of the fetus.

Neonatal Evaluation

Neonates were assessed by a pediatrician without information about their mothers' group. Babies had APGAR scores taken at one and five minutes following their birth. We took samples of blood from the umbilical vessels for gas analysis. Immediately after delivery and for six hours after, we kept an eye on the newborn's oxygen, heart and respiratory rates. When needed, we stimulated the newborn with vibration, delivered oxygen by blowing into a mask over the mouth and performed bag-mask ventilation. For cases of very low breathing rate, we supplied oxygen under pressure. Few factors carried risk; APGAR values ≤3 were classified as critical, 4-6 as low and those 7-10 as normal. Newborns with initial low scores were assessed again at both one and five minutes after they were born.

Statistical Analysis

We decided on the sample size by looking at the main outcome. We determined that in order to detect a reduction of 20% in heart rate and blood pressure with 80% power in each group, 26 patients would have to participate. Each study group balanced the risk of error by using 30 patients.

Results are reported using data as means and standard deviations. All statistical analysis was performed using SPSS. Data on infant demographics, blood gas and APGAR scores were compared by using unpaired t-tests and the Mann-Whitney U test respectively. Repeated determines were used to analyze serial changes in hemodynamics. Results with a P-value less than 0.05 were viewed as statistically significant.

RESULTS

We found that participants in both groups had similar ages, weights, gestational ages, times to induction, length of uterine delivery and their babies' birth weights (Table 1). In Group N, women's average age was 29.8 years (with a standard deviation of 4.2), compared to 28.1 years (with a standard deviation of 5.5) for women in Group C. Maternal weight, age at delivery and the time spent inducing and delivering the uterus were similar in both groups. The rates of birth were uniform, since Group N infants had an average weight of 4.8 kg and Group C infants had one of 4.4 kg.

Before anesthetic induction, mothers in both groups had heart rates similar to each other: Group N average heart rate was 79.7 bpm and Group C was 77.2 bpm. Once anesthesia began and through surgery, Group C showed that their heart rates were higher than those of Group N, suggesting nalbuphine may help keep a woman's heart rate stable under anesthesia. When we looked at the groups after delivery, the rates in both were close, though those in Group C were still slightly higher (Table 2).

The trend in mean arterial blood pressure was much the same. We found that the average blood pressure of both groups was nearly the same prior to induction. Throughout surgery and following induction, patients in Group C (nalbuphine) had significantly higher mean arterial pressures compared to Group N, indicating that nalbuphine may preserve stable blood pressure during a cesarean under general anesthesia. Immediately after delivery, the differences in blood pressure between the groups lessened, but Group C blood pressure was still higher (see Table 3).

There were no infants in either group whose APGAR score was 3 or below at one minute. A higher number of infants in Group N had scores between 4 and 6 at one minute, but Group C showed better adaptation with more scoring 7 to 10 at this age. Five minutes after the birth, APGAR values improved for all babies, but Group C infants' scores were better. Out of the neonates, most babies from both groups scored 9 or higher at five minutes. It was clear that neonates in Group C resumed stable breathing faster (Table 4).

No difference was found in acid-base status during delivery between the two groups as measured by umbilical artery blood gas. Although the mother used nalbuphine, PaO2, bicarbonate, pH and PaCO2 were all comparable for both conditions and show that fetal oxygen was still stable after birth.

In addition, comparing results from the umbilical vein revealed pH, CO2 tension, oxygen pressure and bicarbonate levels were the same between both groups, adding support to the security of delivering nalbuphine into the neonatal blood through the umbilical vein.

Generally, these results indicate that nalbuphine given after the first anesthetic injection and before induction of anesthesia for elective cesarean section improves a mother's heart activity and at the same time is safe for the newborn.

Table 1: Baseline Demographic Characteristics of Participants

Parameter	Group N	Group C
Age (Years)	29.8 ± 4.2	28.1 ± 5.5
Weight (kg)	77.1 ± 10.1	78.9 ± 11.6
Gestational Age (weeks)	39.0 ± 2.4	39.3 ± 2.9
I D (min)	15.3 ± 4.8	16.6 ± 4.3
U D (sec)	83 ± 34	84 ± 41
Weight at Birth (kg)	4.8 ± 0.6	4.4 ± 0.6

Figure 1: Baseline Demographic Characteristics

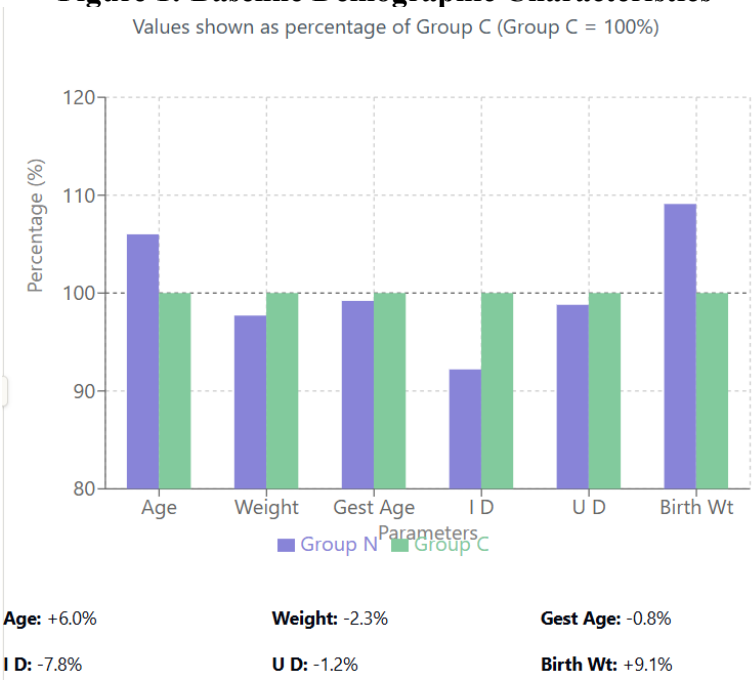


Table 2: Maternal Heart Rate Variations During the Study.

Time Point	Group N Mean ± SD	Group C Mean ± SD
Prior to induction	**79.7 ± 4.1**	**77.2 ± 4.5**
After induction	**81.4 ± 5.1**	**89.5 ± 5.6***
During surgery	**83.3 ± 3.8**	**91.5 ± 3.6***
After delivery	**83.1 ± 5.0**	**85.8 ± 4.2**

Figure 2:

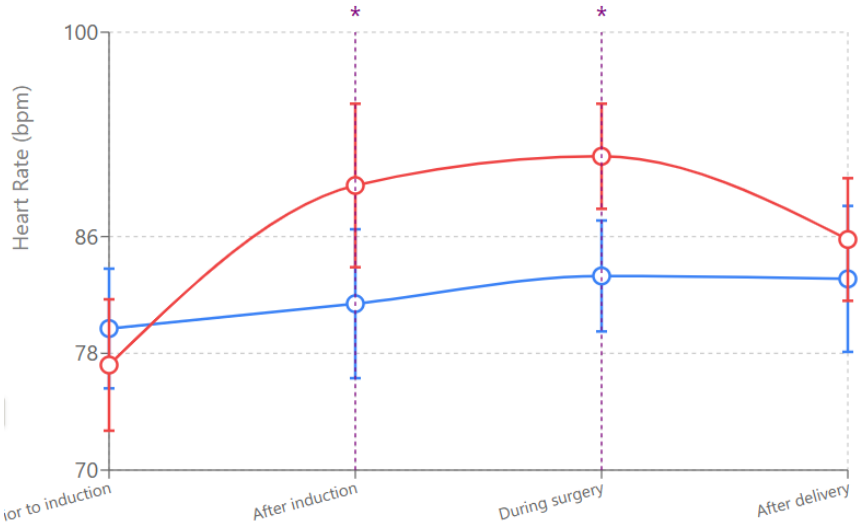


Table 3: Maternal Mean Arterial Blood Pressure Changes Across Groups.

Time Point	Group N Mean ± SD	Group C Mean ± SD
Prior to induction	87.1 ± 6.60	89.7 ± 6.50
After induction	89.9 ± 7.15	101.2 ± 7.40*
During surgery	91.8 ± 3.10	99.3 ± 3.05*
After delivery	86.8 ± 6.35	89.9 ± 6.00

Table 4: Neonatal APGAR Score Comparison Between Groups

APGAR	Group N	Group C
At one min		
3 or less	None	None
4–6	17	5
7–10	43	55
Mean ± SD at five min	7.8 ± 3.1†	9.4 ± 0.80
9–10	59	61
Mean ± SD	10.6 ± 0.60	10.9 ± 0.30
Time to sustained respiration (sec)	80.5 ± 50.2*	37.3 ± 28.1

Table 5: Umbilical Artery Blood Gas Analysis at Delivery (Mean ± SD)

Umbilical Artery Blood Gas	Group N	Group C
pH	8.2 ± 0.6	8.35 ± 0.5
PaCO2 (mmHg)	53.8 ± 11.2	52.1 ± 9.7
PaO2 (mmHg)	26.5 ± 7.5	25.9 ± 6.1
HCO3 (mEq/L)	23.8 ± 3.4	23.3 ± 3.8

Table 6: Umbilical Vein Blood Gas Analysis at Delivery (Mean ± SD)

Umbilical Vein Blood Gas	Group N	Group C
pH	8.30 ± 0.55	8.36 ± 0.58
PaCO2 (mmHg)	50.2 ± 7.2	47.9 ± 4.8
PaO2 (mmHg)	38.2 ± 7.7	36.7 ± 9.3
HCO3 (mEq/L)	24.7 ± 2.7	23.4 ± 3.7

Figure 3: Maternal Mean Arterial Blood Pressure Changes

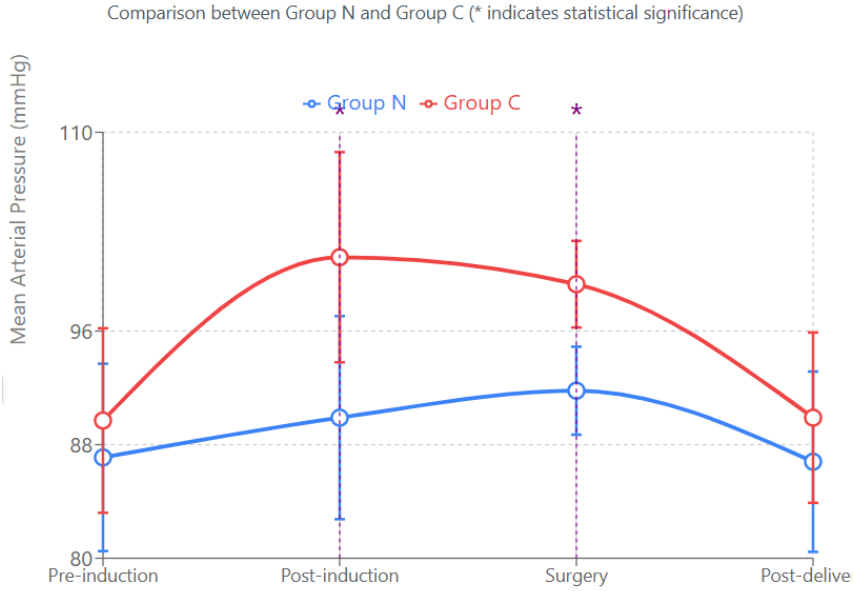


Figure 4: Neonatal APGAR Score Comparison

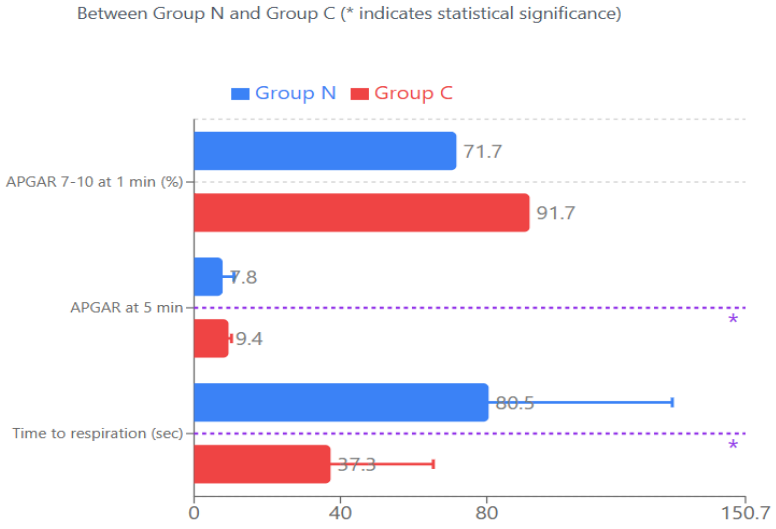


Figure 5: Umbilical Artery Blood Gas Analysis

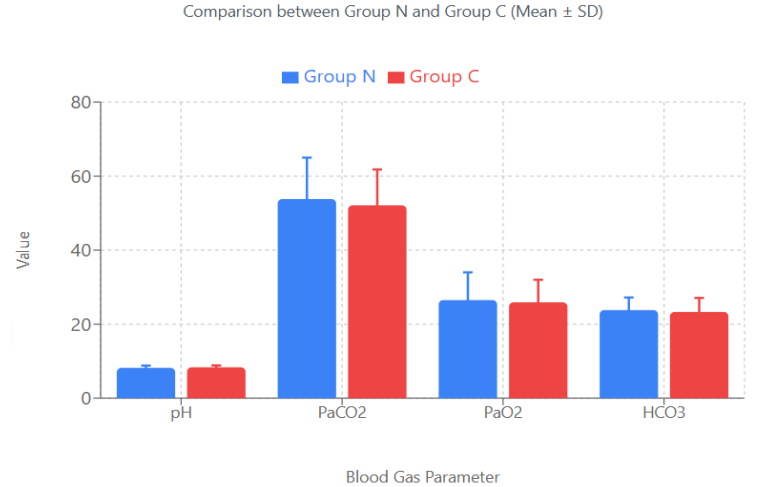
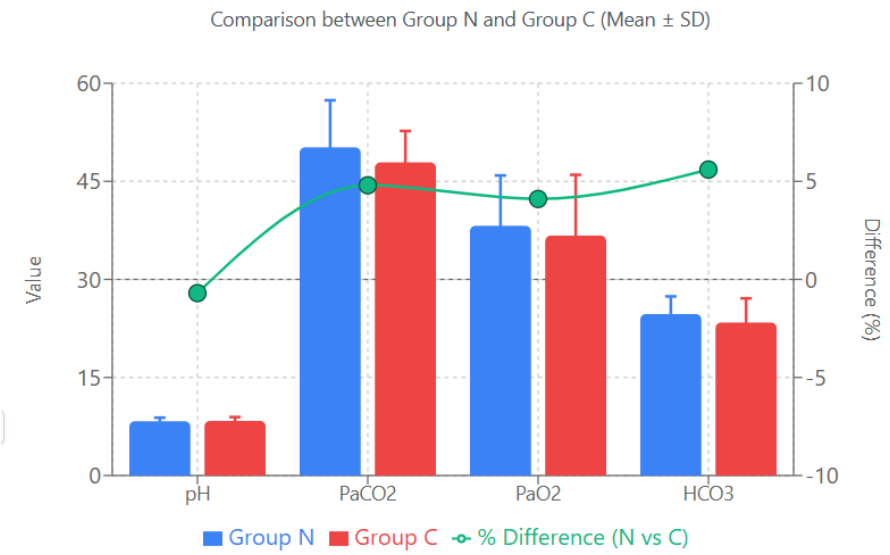


Figure 6: Umbilical Vein Blood Gas Analysis



DISCUSSION

When a woman's pregnancy is threatened, intubation, surgery and taking in more catecholamines can harm both her and her child [9-11]. Doing anything to prevent the stress response is better than putting the patient through intubation and surgery.

Labor analgesic use for nalbuphine has been proven helpful for delivery, but as a medicine given before a cesarean section, no studies are currently available. Both blood pressure and heart rate were markedly higher in the control group than in the nalbuphine group after the anesthesia was started.

Time taken with induction was the same as that with incision and likely the reason for lower APGAR scores in the nalbuphine group is that the drug reaches the baby from the placenta.

Because nalbuphine moves rapidly through the placenta, [12,13] it is removed from the system of the baby more quickly than meperidine is in neonates which takes between 7 and 32 hours.As a result, newborn babies will experience fewer side effects with nalbuphine than with meperidine.

Bolus meperidine was found by Wilson et al., [12] to cause lower APGAR and neonatal neurobehavioral scores for babies whose mothers were given nalbuphine for pain relief in labor. Additional studies have shown that nalbuphine does not normally affect neonatal results.

A researcher looked at nalbuphine as a painkiller for labor, with intubation followed by the drug once hemodynamics were stable in the mother. Neonatal blood levels were not linked to the baby's APGAR scores.

Plenty of studies mention using opioids, like fentanyl, alfentanil and remi fentanyl, before cesarean section. Giving an 10 mg/kg dosage of alfentanil to mothers 1 minute ahead of inducing anesthesia decreased their stress, but also tended to counter early neonatal depression. The authors found no link between giving fentanyl and midazolam to mothers before spinal anesthesia and any bad effects on the newborns. Before putting a patient under general anesthesia, giving 1g/kg of remifentanil prevented most changes in their blood flow, heart rate and blood pressure. Sometimes, remifentanil can enter a newborn's system from the mother's bloodstream and lead to mild depression in the newborn.

Nicolle et al. [14] point out that neonates receive a good deal of nalbuphine from the placenta and that the drug remains in their system longer than it does in adults. At 1 minute, the APGAR scores for each baby were low: one had 8 and already rose to 10 at 5 minutes and the other had 3.

Conclusion

The study shows that a dose of nalbuphine given one minute before anesthesia is induced during elective cesarean sections improves how stable the mother's heart is without putting the baby at risk. Nalbuphine control was associated with a drop in heart rate and blood pressure in women after

anesthesia induction and throughout surgery, while placebo treatment did not achieve this reduction in maternal stress responses. Fluctuations in a pregnant woman's blood pressure and heart rate during anesthesia can negatively affect the health of her child and can trigger problems for her.

Fortunately, the newborn outcomes observed here were encouraging. At both one minute and five minutes after birth, scores between the groups were similar and none of the neonates reached very low scores. Although neonatal apgar scores at one minute and respiration time in the nalbuphine group took longer than those in the control group, all signs suggested full recovery by five minutes. In addition, examination of blood samples from the umbilical artery and vein revealed nothing to suggest nalbuphine harmed the baby's oxygen or metabolic status at birth.

Why these results are seen may lie in the fast transfer of nalbuphine to the placenta and how fast it is cleared in the neonate which is why prolonged neonatal breathing problems typical of other opioids are reduced. Other opioids are often avoided for cesarean anesthesia due to worries about neonates, but nalbuphine's effect is effective in the mother and safe in the baby. Such findings are in keeping with earlier work that shows nalbuphine is safe for birth pain management and does not strongly influence the health of newborns as much as meperidine.

Nalbuphine can be added during general anesthesia for cesarean delivery to ease discomfort for the mother and control blood pressure swings, but young mothers are not put at greater risk. This matters most where patients are given general anesthesia, as opposed to regional techniques. Future research can focus on the best possible way to give nalbuphine, when it should be given and if it works better than other opioid drugs for use in obstetric anesthesia. So, giving nalbuphine before starting anesthesia for elective cesarean sections is safe and effective, improves maternal heart function and maintains outcomes for the newborns, making it suitable for widespread use in obstetric anesthesia.

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