INTRAOPERATIVE OPIOD ANALGESIA FOR EMERGENCY OBSTETRICS

A COMPARISON BETWEEN PETHIDINE AND NALBUPHINE

DR. G. MONIZ, MBChB (NAIROBI)

THIS DISSERTATION IS SUBMITTED
IN PART FULFILMENT FOR THE REQUIREMENTS OF
THE DEGREE OF MASTER OF MEDICINE IN ANAESTHESIA
OF THE UNIVERSITY OF NAIROBI. 1988

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This dissertation is my original work and has not, to my knowledge, been presented for a Degree in any other University.

GERALD C. MONIZ, MBChB(Nairobi)

This Dissertation has been submitted for examination with my approval as a University Supervisor.

DR.P.O.HUMA, F.F.A.R.C.S. (Eng.)
Senior Lecturer in Anaesthesia
University of Nairobi, Kenya

ACKNOWLEDGEMENTS

My sincere thanks go to the following:-

- Dr.P.O. Huma for his invaluable guidance and supervision.

- The Director, Kenyatta National Hospital for his permission to carry out this study.

- All my colleagues for their assistance and encouragement.

- The Nursing staff of the Kenyatta Hospital especially those in the Maternity Unit and Wards for their cooperation.

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SUMMARY

Pain relief in Emergency Operative Obstetrics under General Anaesthesia was studied in 300 patients at Kenyatta National Hospital. Three separate groups of 100 patients each differed only in the intraoperative analgesic component used.

Inclusion and Exclusion Criteria.

The patients were females between the ages of 15 and 45 years of A.S.A. classes I to III and were all in the first stage of labour scheduled for Emergency Caesarean Sections for a variety of reasons.

None of the patients had received any Opiods or Sedatives during labour, or as part of the premedication. Those who had received the above drugs were excluded as were patients not in established labour, or those with evidence of any contraindicating Systemic diseases.

The basic Anaesthetic techniques were the same for the three groups, but only varied in the Intraoperative analgesic used, on clamping the umbilical cord. Patients in Group I received Pethidine (0.8 mg/kg). Patients in Group II received Nalbuphine (0.15 mg/kg). Patients in Group III (Controls) - No opiods used.

Pancuronium was used as the Non depolarising muscle relaxant and all patients received 67% Nitrous Oxide in Oxygen with 0.5% Halothane post delivery.

The vital signs, Tidal and Minute Volumes, which had been measured preoperatively were again evaluated after the patients had regained consciousness fully. Patients were also questioned on the adequacy of pain relief according to the scale given (Appendix). Patients subjectively assessed the degree of analgesia. Any side effects such as sedation, vomiting or twitching were also noted. Patients were visited in their Wards after 12 to 24 hours and questioned about any other side effects, intraoperative awareness, or recall. In addition the time of demand for postoperative analgesia was noted.

It was found that 34.7% of patients were in pain on awakening. However of these only 2% in Group I and 3% in Group II were not relieved of pain, whereas 99% of the Control group (Group III) were in pain; these patients were also the first to demand postoperative analgesia. In contrast patients in Groups I and II did not ask for analgesia for mean times of over two and a half hours postoperatively, and were generally calmer and less agitated.

As far as Ventilatory depression was concerned, all patients studied showed a decrease in both Tidal Volume and Minute Volume after operation. Group III (Control) patients showed the smallest depression with Groups I and II showing similar but larger degrees of depression.

Among side effects sedation was the most common but was not disturbing and patients were stable enough to go to the wards.

Between the two groups studied Nalbuphine offered marginal advantages over Pethidine in the doses used. Although both drugs showed similar degrees of Analgesia and Ventilatory depression, Nalbuphine showed better Haemodynamic stability and less Nausea and Vomiting.

INTRODUCTION

Various studies have been conducted on General Anaesthesia for Caesarean Sections. (1, 8, 9, 10, 20, 28, 29, 34). Most emphasize the need for Intraoperative analgesia, a technique that has not been overwhelmingly popular at Kenyatta National Hospital for many reasons.

As is common in busy Maternity Units in developing countries, the Recovery Ward facilities are meagre and patients have to be fully awake and "safe" enough to be sent to the wards soon after operation.

A recent study at Kenyatta Hospital (1) showed that postoperative pain was the commonest complaint with 84.1% of patients listing it as the worst thing about their peri-operative period. None of the 400 patients in that study had received any intraoperative analgesia.

This study attempts to emphasize the need for intra-operative analgesics and compare the effects of 2 opiod analgesics - Pethidine and Nalbuphine. Studies on the analgesic effects of Nalbuphine (3, 7, 11, 12) have shown it to be equipotent with morphine. However there are no published studies comparing Nalbuphine with Pethidine.

Another problem in Obstetric Anaesthesia is that of awareness. Previous studies carried out at Kenyatta Hospital have shown rates of between 4.3% and 5% (1, 29). Studies have also shown that the awareness rate for Caesarean Sections may be reduced by inhalational agents and also by Narcotics (20, 32, 33, 20, 28).

Ventilatory dynamics are known to be physiologically altered in pregnancy (18,43). However actual values for the above in Labour are not available in literature. Tidal and Minute Volumes are found to be increased preoperatively and so were respiratory rates. Ventilatory depression using the three different techniques were then compared, by re-evaluation of the parameters postoperatively.

Circulatory stability was also compared in this study. Pulse rates and Mean Arterial blood pressures were evaluated at various stages. Pethidine when used along with inhalational agents is known to cause Hypotension, both by Myocardial depression and also through peripheral vasodilatation; this is accompanied by tachycardia (35, 36, 37, 38). Initial evaluation of Nalbuphine has demonstrated negligible adverse haemodynamic effects (2, 3, 4).

Other drawbacks to the Intra-operative use of opiods have been those of Sedation (30, 31) and Nausea or Vomiting (5, 30, 31, 39, 40, 41, 42). Nausea and Vomiting are further influenced by Pregnancy itself (41, 42). In this study the above side effects have been evaluated against a control group where opiods were not used.

In addition other minor side effects were also compared. These include Psychotomimetic effects such as hallucinations, delusions and depersonalisation. Miller (31) has shown these to be not as frequent with Nalbuphine as with other opiods.

Other minor effects reported (5, 31) include headache, vertigo, sweatiness and dry mouth, all of which were enquired for on recovery of consciousness after operation.

AIMS AND OBJECTIVES

(i) To compare the efficacy and side effects of Pethidine and Nalbuphine and to emphasize the need for Intraoperative analgesics for Caesarean Section.

(ii) To observe the Physiological changes in respiratory dynamics during labour and to compare the respiratory depressant effects of Pethidine and Nalbuphine.

METHODS AND MATERIALS

Informed consents both written and verbal were obtained from a total of 300 patients of A.S.A. Classes I - III scheduled for Emergency Caesarean Section. Patients were randomly allocated to one of the three groups under study and had been premedicated with Atropine 0.6 mg intramuscularly half an hour before operation, or intravenously just before induction. None of the patients studied had received any opiod analgesic or other sedative during labour. In addition the patients were all in Active phase of Labour established First Stage) and did not have any contraindicating systemic diseases.

Patients were placed on the operating table tilted 15^{o} to the Left. An infusion of 5% Dextrose or Normal Saline was set up. While the patient was being prepared for operation she was preoxygenated (a period of at least 5 minutes). At this time the Vital Signs i.e. Pulse, Blood Pressure and Respiratory Rate were recorded. In addition the Preoperative Tidal and Minute Volumes were evaluated with the help of a Wrights Respirometer - attached to a well fitting transparent anaesthetic mask. Care was taken to ensure accurate measurement over a full minute and also that the measurements were not made during an active contraction.

After the patient had been draped Anaesthesia was induced with Thiopentone (4 mg/kg) and Suxamethonium (i.5 mg/kg) while applying Cricoid pressure. A cuffed and lubricated endotracheal tube of internal diameter 7.5 mm to 8.5 mm was passed, and Cricoid pressure was released

after Cuff inflation. The lungs were mechanically ventilated by means of a Manley Pulmovent (Medishield Model MPT). Tidal Volume was set at the preoperative measured value which worked out at approximately 10-12 ml/kg body weight. The Minute Volume delivered was 8-10 litres per minute hence giving a Resultant respiratory rate of 10-12/Minute.

Antenatally maintenance of Anaesthesia was with 50% N_2O in Oxygen and 0.5% Halothane. Pancuronium at a dosage of 0.08 mg/kg was used as the long acting Muscle Relaxant. There was no Nitrous Oxide washout before delivery of the baby.

Immediately after delivery of the baby and on clamping the Umbilical cord, Syntocinon 10 Units was administered intravenously along with the analgesic depending on the study group - as follows:

Group I - received Pethidine 0.8 mg/kg (50 mg)
Group II - received Nalbuphine 0.15 mg/kg (10 mg)
Group III - did not receive either drug (CONTROL).
In addition Maintenance of Anaesthesia was with 67% N_2O in Oxygen with Halothane remaining at 0.5% until the end.

At the end of operation patients were ventilated with 100% Oxygen and the effects of Muscle Relaxants were reversed with Neostigmine 2.5 mg and Atropine 1.2 mg (TABLE 1). The patients were extubated in the lateral position after spontaneous ventilation was adequate and oro-pharyngeal suction has been carried out.

The following times were noted to the nearest minute; Times of Induction, Clamping the Umbilical Cord, Extubation, Response to Name and also time when full conciousness was regained. (This was taken as the time when the patient was able to converse or to pronounce her name).

When fully conscious the Vital signs (ie. Pulse, Blood Pressure and Respiratory Rates) were recorded. The Tidal and Minute Volumes were re-evaluated with the Respirometer. At this time patients were also questioned as to the adequacy of analgesia.

Patients were interviewed within 24 hours in their wards, when any other points were enquired about e.g. Awareness, Nausea, Confusion, Hallucination etc. In addition the time of demand for postoperative analgesia was also noted (Appendix 1).

RESULTS

AGE

All 300 patients studied were females between the ages of 14 and 45 years.

The largest number of patients (90 patients - 30%) fell between 20 and 24 years, followed by 86 patients (28.7%) between 25 and 29 years. Hence 58.7% of patients in the study fell between 20 and 29 years (Tables 2 and 3).

The distribution of patients by age per group under study is fairly even and all three groups showed a predominance of patients between 20 and 29 years. (Table 4).

A.S.A. CLASS

Out of the 300 patients studied 232 (77.3%) were of A.S.A. Class I, 60 patients (20%) fell into A.S.A. Class II with only 8 patients (2.7%) in A.S.A. Class III. (Table 5).

As with age distribution there were no remarkable differences in A.S.A. class between the three study groups.

WEIGHT

The weight of the patients ranged from 51 kg to 112 kg. Out of the 300 patients studied 128 patients (42.7%) weighed between 61 and 70 kg, 81 patients (27%) weighed between 71 and 80 kg. The remaining 30.3% of patients were those weighing less than 60 kg and those above 80 kg. (Table 6).

As with A.S.A. distribution and Age distribution, the Weight distribution was fairly even within the groups studied.

RESPIRATORY DYNAMICS.

In labour the Respiratory Rate, Tidal Volume and Minute Volume were all found to be increased over published values in Pregnancy (18). Before operation there were no major differences in Respiratory dynamics between the three groups. (Table 7).

After operation all patients showed a decrease in Tidal and Minute Volumes. The decrease in Tidal Volume ranged from 25.5% to 33.7%, whereas Minute Volumes decreased by 22.4% and 34.2%. (Table 7).

HAEMODYNAMIC DATA.

Pulse Rate.

The preoperative mean pulse rate was 84 for Group I and 85 for Groups II and III. These pulse rates were taken after Atropine premedication.

The mean postoperative pulse rates were 80, 78 and 86 for the three groups respectively. (Table 8).

Mean Arterial Pressure: (M.A.P.)

The Mean Arterial pressure was calculated from the Systolic and Diastolic Blood pressures. The preoperative mean arterial pressures were 103 for Group I, 100 for Group II and 103 for Group III.

The Mean Arterial Pressures intraoperatively were lowest (80 mm Hg) for Group I patients and were 83 mm Hg for Groups II and III. After operation the M.A.P. in Group I was 83 mm Hg. In Group II it was 93 mm Hg and in Group III it remained at the preoperative level of 103 mm Hg. (Table 9).

ANALGESIA.

On awakening 98% of patients in Group I, 97% in Group II but only 1% in Group III had adequate analgesia. Pain relief was defined as adequate if patients said they were pain free or complained of only slight pain (Table 10).

At the other end of the scale 27% of patients in Group III complained of severe pain and 20% were in unbearable pain. In contrast none of the patients in Groups I or II were in unbearable pain and only 1% in each group were in severe pain.

The duration of analgesic effect was calculated from the time of administration of drug (on clamping the Umbilical Cord) to the time when the patient first demanded post-operative analgesia.

The mean times in minutes were 187, 204 and 80 minutes respectively for the three groups I, II and III. (Table 11).

The mean durations of Analgesia after operation were less than the above values by about 45 minutes since the quoted values include the operative time from delivery to end of operation.

SIDE EFFECTS.

Among the side effects Sedation was the most frequently occurring, with a total of 83 patients (27.7%) sedated postoperatively. 43% of patients in Group I (Pethidine) were sedated, whereas 30% of Group II (Nalbuphine) and 10% of Group III (Controls) were sedated.

Nausea and vomiting were the next group of side effects. 26 patients showed either nausea or vomiting (8.7%). Group I patients (Pethidine) showed a 12% rate of nausea or vomiting. The Controls (Group III) showed 8% rate of nausea whereas the Nalbuphine group (II) showed only 6%.

3% of the Control group were agitated after operation. None of the patients given analgesia were agitated. (Table 12).

The Pethidine group showed 5% of patients with Post-Operative Hypotension. This was however easily corrected by intravenous fluids.

Other minor side effects included burning at injection site, dizziness, headache and sweating. The Nalbuphine group (II) showed a 5% incidence of these effects and the Pethidine group (I) 3%, whereas the Controls only had 2% of patients who experienced these effects.

AWARENESS.

The awareness rate overall was 1.66% with 5 out of the 300 patients admitting that they were aware or could recall certain intraoperative events. All of these patients however admitted to remember events only uptil the baby was delivered.

Groups I and II patients had an awareness rate of only 1% each whereas the Control Group (III) had 3% of patients aware at any one time intraoperatively. Awareness was defined as the ability of the patient to recall any intraoperative event with or without prompting. (Table 13).

TIME FACTORS.

Times between extubation and first response to name were compared (to the nearest minute), with the Controls (Group III) responding to their names the soonest, with mean times of 1.5 minutes. The range of times were 1.4 minutes for Group III.

Group I and II patients showed similar time ranges of 2-6 minutes, however the Pethidine group (I) took a mean time of 4.5 minutes whereas the Nalbuphine group (II) took a mean time of 4.2 minutes. (Table 14).

The times between extubation and recovery of consciousness were also compared. This was when the patient was able to pronounce her name or to converse. Once again the patients in Group III (Controls) were the first to regain consciousness within a mean time of 5.5 minutes after extubation and within a range of 4-8 minutes.

Group II patients (Nalbuphine) regained consciousness within a mean time of 7.8 minutes and within a range of 3-12 minutes, whereas Group I patients (Pethidine) took longer (9.5 minutes mean) to wake up with a wider range of 3-20 minutes. (Table 15).

DISCUSSION

ANALGESIA.

Various studies have been conducted on General Anaesthesia for Caesarean Section. The need for Intraoperative analgesia has been emphasized (1, 8, 9, 10, 20, 28, 29, 34). In a recent study at Kenyatta National Hospital, Were (1) showed that postoperative pain was the most distressing complaint with 84.1% of patients complaining of severe pain on awakening from anaesthesia. None of the patients in his study had received intraoperative analgesic supplements.

The need for intraoperative analgesia has been confirmed in this study, where Pethidine was being compared with Nalbuphine. 98% of patients who received intraoperative Pethidine and 97% of those who received Nalbuphine were adequately free of pain on recovery from General Anaesthesia. In sharp contrast only 1% of patients who did not receive analgesics (Control group) were adequately free of pain.

On analysing the results there was a statistically significant difference between the Patients in Group III (Control) versus the other two groups which received analgesics. There was however no statistically significant difference between the Pethidine group and the Nalbuphine group. None of the patients in Groups I or II were in Unbearable pain although 2.5% of patients complained of Moderate or Severe pain inspite of intraoperative analgesia.

There are at present no published studies comparing Pethidine with Nalbuphine. There are however several comparing

Nalbuphine with Morphine. Fahmy (3) reported a double blind comparative study of Nalbuphine and Morphine in balanced anaesthesia and concluded that the two drugs had similar analgesic effects.

Beaver et al (7) however have shown that when both intensity and duration of analgesia were considered, Nalbuphine was found to be only 0.7 to 0.8 times as potent as Morphine when used Intramuscularly. Nalbuphine was also shown to have a longer duration of action at equianalgesic doses.

When compared with other agonist/antagonist analgesics such as Pentazocine, studies by Houde et al (11) and Tammisto et al (12) have shown that

(i) Nalbuphine is about 3 times as potent as Pentazocine

(ii) the time of peak effect (39 minutes) was similar after intravenous administration

(iii) the duration of action of Nalbuphine is somewhat longer than Pentazocine or Morphine.

In this study the duration of analgesia was taken as the time between clamping the umbilical cord and demand for postoperative analgesia. Patients in Group III (Controls) demanded analgesics soonest after delivery, within a mean time of 80 minutes after delivery or approximately 35 minutes postoperatively. On the other hand the patients given analgesics did not demand any more for a mean time of 187 minutes and 204 minutes respectively for Groups I and II, corresponding to 142 minutes and 159 minutes postoperatively.

Magruder et al (5) have also reported similar findings for Balanced Anaesthetic techniques using opiods and have further reported that the duration of action of Nalbuphine increases with increasing dosage. At higher doses of 2 mg/kg (total) Lake et al (14) found that plasma Nalbuphine levels nine hours postoperatively were still above the analgesic threshold of 20 ng/ml.

Kay et al (15) found that 20 mg Nalbuphine given intravenously postoperatively provided adequate analgesia for most patients and subsequent demands for analgesia were infrequent.

Other studies on duration of action have shown that when administered intravenously, usual therapeutic doses of Nalbuphine have a rapid onset of action within two minutes, provide peak analgesia in thirty minutes and have a duration of action of between 2 and 6 hours (2, 3, 12, 16, 17).

In this study Nalbuphine was used at an Intravenous dose of 0.15 mg/kg after clamping the Umbilical Cord. 70% of patients were completely pain free on awakening, 27% complained of only slight pain, 2% of moderate pain and 1% of severe pain.

These findings were similar in the Pethidine group of patients where 0.8 mg/kg of pethidine intravenously resulted in 68% of patients completely pain free on awakening, 30% complained of slight pain, 1% of moderate pain and 1% of severe pain. In neither of the two groups (I & II) given analgesia did patients complain of unbearable pain.

There was no significant difference in the degree of analgesia obtained with the two drugs - but there was a marginal difference as far as duration was concerned with Nalbuphine appearing to have a longer duration of action (mean of three hours and twenty-four minutes) versus Pethidine with a mean duration of three hours and seven minutes. There was a significant difference between patients in Group III and the other two groups. Group III patients (Controls) had 20% who complained of Unbearable pain, 27% of Severe pain, 52% of Moderate pain, 1% of Slight pain, but there weren't any patients who were absolutely pain free. Thus it was shown that intraoperative analgesia is absolutely essential and should be administered after delivery of the baby.

RESPIRATORY DYNAMICS.

The mean preoperative respiratory rate was 22 per minute. All the patients were in the first stage of labour. Respiratory rate is increased by 15% during pregnancy and even further during labour (18, 43). This study has shown that the respiratory rate increases by a mean value of 37.5% during labour. Part of this increase is attributable to unrelieved pain, as none of the patients studied had received preoperative analgesics during labour (Table 16).

Preoperative Tidal Volumes were also elevated. The mean Tidal Volume was 741 ml. This worked out at 11.4 ml/kg Body weight (Mean body weight of patients was 65 kg). Tidal volume during labour increases by 5.9% over that found during pregnancy (which is 40% greater than during the nonpregnant state) (Table 13A).

As a result of the large increase in respiratory rate, as well as the smaller increase in tidal volume, the mean minute volume was 16.3 litres per minute. This represents a 55.2% increase in minute volume during labour (Table 16) when compared to expected values for pregnancy.

Previous studies on respiratory effects of Nalbuphine have proved equivocal. In some patients no respiratory depression was detected (19, 20, 21, 22), whilst in others definite respiratory depression was induced (3, 13, 23, 24). The explanation may lie in the dosage involved. Generally it appears that respiratory depression occurs with Nalbuphine doses of over 0.1 mg/kg. Gal et al (25) reported that respiratory depression was not further increased by Nalbuphine doses higher than 30 mg/70 kg. This is called the "Ceiling effect" for respiratory depression. Romangoli et al (26) reported similar values with maximum respiratory depression occurring with doses of 0.45 mg/kg. However Julien et al (27) demonstrated that the "Ceiling effect" was different in healthy volunteers, where the maximum respiratory depression was produced by Nalbuphine doses of 0.1 mg/kg.

In this study Nalbuphine was used intraoperatively in doses of 0.15 mg/kg. Postoperatively the Minute Volume and Tidal Volume were decreased. Tidal Volume (mean) showed a 34.2% decrease and Minute Volume also showed a 34.2% decrease.

Pethidine (0.8 mg/kg) showed similar decreases with the Tidal Volume decreasing by 33.8% and the Minute Volume by 30.8%.

The Control group showed smaller degrees of respiratory depression with a 25.5% decrease in Tidal Volume and a 22.4% decrease in Minute Volume. These patients were hyper-ventilating, possibly due to unrelieved pain and hence the Minute Volumes were not as low as the other two groups. (Table 17).

Inspite of the decrease in Tidal Volume, respiration was clinically adequate in all the patients. None of the patients had a Tidal Volume of less than 350 ml and Narcotic antagonists were not required in any patient.

HAEMODYNAMIC EFFECTS.

There was no significant difference between preoperative pulse rates between the three groups, the mean pulse rate being 85/min. This was after Atropine premedication. Wylie and Churchil Davidson (18) quote a 15% increase in pulse rate during pregnancy and further increases in labour. This has also been quoted in Anaesthesia (43).

This study has revealed that the Pulse rate increase is 18% during labour and hence only about 3% of an increase from the average pre-labour values.

After operation there were differences in pulse rate between groups with Group III (Controls) patients showing the highest mean pulse rate (86/min), whereas Group I (Pethidine) had a mean rate of 80/min and Group II (Nalbuphine) a mean of 78/min. None of the patients showed either intraoperative or postoperative bradycardia or tachycardia, although Pethidine is known to cause tachycardia (35, 36).

Mean Arterial Pressures (M.A.P.) were calculated from systolic and diastolic pressures. (Table 18). Patients in Group I (Pethidine) showed a certain degree of Intraoperative Hypotension with the mean value of M.A.P. being 80 mmHg corresponding to values of 100/70 mmHg. However in some patients intraoperative blood pressures were as low as 90/60 mmHg (M.A.P. 70 mmHg), but were easily corrected by Intravenous fluids. After operation the M.A.P.'s in Group I were again lower than the others, with a mean value of 83 mmHg - corresponding to 110/70 mmHg.

In Group II (Nalbuphine) the blood pressure remained relatively stable, with mean intraoperative values of 83 mmHg for M.A.P. This corresponds to 110/70 mmHg. The postoperative M.A.P. for these patients was 93 mmHg (120/80 mmHg).

In Group III patients (Control) blood pressures remained relatively elevated during and after operation, with the M.A.P. postoperatively being 103 mmHg (130/90 mmHg). This again could be attributed to unrelieved pain.

Previous clinical studies on Nalbuphine demonstrate that it is associated with little or no adverse haemodynamic effects (3, 4). This has been confirmed in this study and it appears to have definite haemodynamic advantages over Pethidine, which was associated with hypotension both intraoperatively as well as postoperatively.

SIDE EFFECTS.

Among the side effects, sedation was the most common (Table 12). In the dosages used Pethidine seemed to have a greater sedative effect with 43% of patients drowsy after operation, whereas Nalbuphine showed only 30% of patients sedated. The Control group showed only 10% of patients who were drowsy. This data compares well with previously published works on Nalbuphine which showed sedation in 36% of patients (Errick and Heel - 30). Miller (31) comments that sedation occurs in 30-40% of Nalbuphine recipients and concludes that it does not occur more frequently than with other opiods and also that a dose-response relationship was not evident.

The next group of side effects was nausea and vomiting. 10% of Pethidine recipients complained of nausea and 2% vomited postoperatively. In contrast only 6% of Nalbuphine recipients were nauseous and none vomited. The Controls were intermediate with 8% of patients complaining of nausea. (Table 9). Other studies on side effects have shown that nausea and vomiting occur in 5-6% of Nalbuphine recipients (39, 31). Beaver et al (7) revealed an incidence of only 2.3% with Nalbuphine but 8.9% with Morphine. These results were however with the Intramuscular route of administration.

Other infrequent side effects with a total incidence of less than 5% included confusion, twitching, sweating, dizziness, headache, psychotomimetic reactions and thrombophlebitis. (Table 9).

An interesting point to note is that the Awareness rates in Groups I and II were found to be only 1% each, whereas in the Controls it was 3%. Awareness was defined as the ability of the patient to recall any event occurring during the period when the patient was believed to be unconscious. Narcotics given after delivery of the baby are known to alleviate awareness (32, 33). Barr et al (19) managed to decrease the awareness rate to 1.7% for Caesarean section by using Pethidine 25 mg and Benzodiazepine after delivery of the baby, with the intention of causing retrograde amnesia.

TIME FACTORS.

Group III (Control) patients were the first to respond to their names, the mean times after extubation being 1.5 minutes. The patients given opiods took longer to respond with a mean time of 4.5 minutes for the Pethidine group and 4.2 minutes for Nalbuphine recipients. (Table 11).

In addition Group I (Pethidine) patients took longer to regain consciousness fully - within a mean time of 9.5 minutes after extubation. Nalbuphine recipients took a mean time of 7.8 minutes whereas the Control (Group III) were fully conscious within a mean time of only 5.5 minutes. (Table 12).

It is however emphasized that although the patients given analgesics (Groups I & II) took slightly longer to regain consciousness fully they were as "safe" as the Controls as far as protective reflexes, haemodynamic and respiratory parameters were concerned.

CONCLUSIONS AND RECOMMENDATIONS.

This study has shown that intraoperative analgesia is essential for Caesarean Sections, and should be administered on clamping the umbilical cord. Analgesics with long duration of action are recommended so that the patient is pain free on awakening and during the immediate postoperative period, when further analgesics may be administered intramuscularly on demand.

On comparing the two opiod analgesics Pethidine and Nalbuphine, it is evident that both drugs produce similar degrees of analgesia although Nalbuphine has a slightly longer duration of action. Both drugs produce similar degrees of ventilatory depression, but of little clinical significance in the doses used. Narcotic antagonists were not required for any of the patients in this study. Pethidine was associated with higher incidences of Hypotension, Nausea, Vomiting and Sedation. Nalbuphine also showed sedation but inspite of this, the patients were easily arousable. This is an important factor at Kenyatta Hospital since recovery ward facilities are meagre in the Maternity Unit, as in common in many developing countries.

In addition this study has revealed some interesting values for patients in labour. Pulse Rate, Blood Pressure, Respiratory Rates, Tidal Volumes and Minute Volumes were all increased during labour when compared to values in late pregnancy (pre-labour). These data have to be kept in mind during the design of apparatus for inhalational analgesia

during labour, which should be capable of accurate performance when subjected to high Minute Volumes and Inspiratory flow rates.

Nalbuphine should be considered the analgesic of choice where haemodynamic stability is essential or in patients with compromised cardiac function where wide fluctuations in pulse or blood pressure could be detrimental. It also has a place where frequent demands for postoperative analgesia are anticipated, since it has a definite ceiling for respiratory depression, unlike most other available opiods. It would also be useful in patients who require postoperative analgesia and are known to be prone to nausea or vomiting. However the cost of the drug is to be considered if use on a routine basis is contemplated.

TABLE 1. ANAESTHETIC TECHNIQUES USED:

GROUP ⟶	GROUP I (PETHIDINE)	GROUP II (NALBUPHINE)	GROUP III (CONTROL)
PREMEDICATION	Injection Atropine 0.6 mg IV/IM	Injection Atropine 0.6 mg IV/IM	Injection Atropine 0.6 mg IV/IM
INDUCTION	Thiopentone 4 mg/kg IV Suxamethonium 1.5 mg/kg	Thiopentone 4 mg/kg IV Suxamethonium 1.5 mg/kg	Thiopentone 4 mg/kg IV Suxamethonium 1.5 mg/kg
MAINTENANCE (ANTENATAL)	N_2O : O_2 : HALOTHANE 50% : 50% : 0.5% Pancuronium 0.08 mg/kg	N_2O : O_2 : HALOTHANE 50% : 50% : 0.5% Pancuronium 0.08 mg/kg	N_2O : O_2 : HALOTHANE 50% : 50% : 0.5% Pancuronium 0.08 mg/kg
MAINTENANCE (POSTNATAL)	N_2O : O_2 : HALOTHANE 63% 37% : 0.5% Pethidine 0.8 mg/kg	N_2O : O_2 : HALOTHANE 63% : 37% : 0.5% Nalbuphine 0.15 mg/kg	N_2O : O_2 : HALOTHANE 63% : 37% : 0.5%
REVERSAL	Neostigmine 2.5 mg Atropine 1.2 mg 100% O_2	Neostigmine 2.5 mg Atropine 1.2 mg 100% O_2	Neostigmine 2.5 mg Atropine 1.2 mg 100% O_2

TABLE 2. OVERALL AGE DISTRIBUTION

AGE IN YEARS	NUMBER OF PATIENTS	PERCENTAGE OF TOTAL
14 to 19	40	13.3
20 to 24	90	30.0
25 to 29	86	28.7
30 to 34	42	14.0
35 to 39	37	12.3
40 and over	5	1.7
TOTAL	300	100.0

TABLE 3. HISTOGRAM OF AGE DISTRIBUTION

(Age taken to the nearest year)

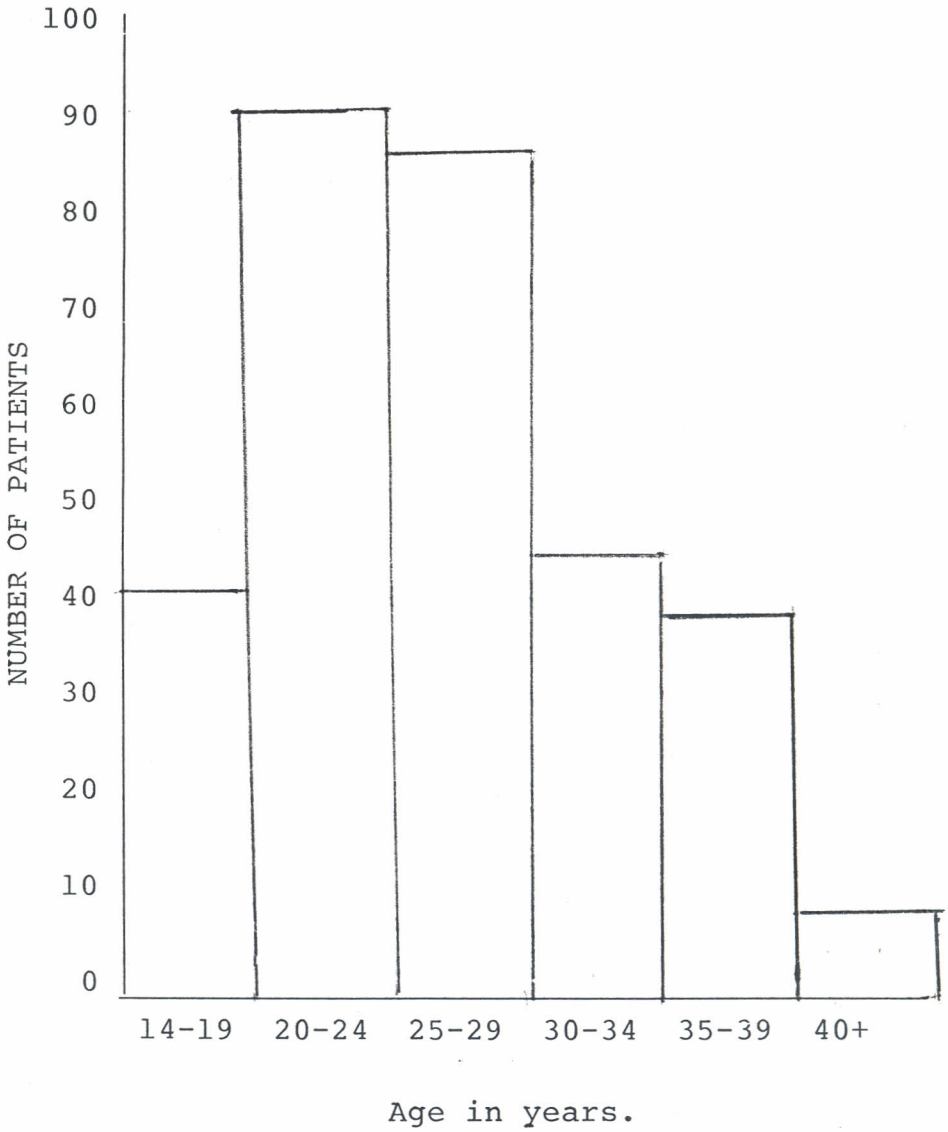

TABLE 4 AGE DISTRIBUTION ACCORDING TO GROUP.

AGE IN YEARS → / GROUP ↓	14-19	20-24	25-29	30-34	35-39	40+	TOTAL
GROUP I (PETHIDINE)	20	35	20	12	13	0	100
GROUP II (NALBUPHINE)	7	22	38	15	14	4	100
GROUP III (CONTROL)	13	33	28	15	10	1	100
TOTAL	40	90	86	42	37	5	300

TABLE 5 A.S.A. CLASS DISTRIBUTION

A.S.A. CLASS → / GROUP ↓	A.S.A. I	A.S.A. II	A.S.A. III	TOTAL
GROUP I (PETHIDINE)	75	22	3	100
GROUP II (NALBUPHINE)	75	21	4	100
GROUP III (CONTROL)	82	17	1	100
TOTAL	232	60	8	300
%	77.3%	20.0%	2.7%	100.0%

TABLE 6 WEIGHT DISTRIBUTION ACCORDING TO GROUP

WEIGHT KG → / GROUP ↓	50-60 Kg	61-70 Kg	71-80 Kg	81-90 Kg	Over 90 Kg	TOTAL
GROUP I (PETHIDINE)	10	50	25	12	3	100
GROUP II (NALBUPHINE)	9	40	30	16	5	100
GROUP III (CONTROL)	19	38	26	15	2	100
TOTAL	28	128	18	43	10	300
PERCENTAGE OF TOTAL	12.7%	42.7%	27.0%	14.3%	3.3%	100.0%

TABLE 7 RESPIRATORY DYNAMICS BEFORE AND AFTER OPERATION

STUDY GROUP	RESPIRATORY RATE/MIN	TIDAL VOLUME ML	MINUTE VOLUME L/MIN	RESPIRATORY RATE/MIN	TIDAL VOLUME ML	MINUTE VOLUME L/MIN	% DECREASE TIDAL VOLUME	% DECREASE MINUTE VOLUME
GROUP I (PETHIDINE)	22	740	16.28	23	490	11.27	33.7%	30.7%
GROUP II (NALBUPHINE)	21	760	15.96	21	500	10.5	34.2%	34.2%
GROUP III (CONTROL)	24	725	17.40	25	540	13.5	25.5%	22.4%

TABLE 8. CHANGES IN PULSE RATE (MEAN)

GROUP	Preoperative Pulse/Min	Postoperative Pulse/Min	% Change in Pulse Rate
GROUP I (Pethidine)	84	80	- 4.76%
GROUP II (Nalbuphine)	85	78	- 8.20%
GROUP III (Control)	85	86	+ 1.17%

TABLE 9. CHANGES IN MEAN ARTERIAL PRESSURE (M.A.P.) mm Hg.

GROUP	Preoperative M.A.P. mmHg	Intraoperative M.A.P. mmHg	Postoperative M.A.P. mm/Hg	% Change in M.A.P.
GROUP I (Pethidine)	103	80	83	- 19.4%
GROUP II (Nalbuphine)	100	83	93	- 7.0%
GROUP III (Control)	103	83	103	NO CHANGE

TABLE 10. ADEQUACY OF PAIN RELIEF ON AWAKENING

ANALGESIA SCALE → / GROUP ↓	1 NO PAIN	2 SLIGHT PAIN	3 MODERATE PAIN	4 SEVERE PAIN	5 UNBEARABLE PAIN	TOTAL NUMBER OF PATIENTS
Number of patients in Group I (Pethidine)	68	30	1	1	0	100
Number of patients in Group II (Nalbuphine)	70	27	2	1	0	100
Number of patients in Group III (Control)	0	1	52	27	20	100
TOTAL PATIENTS	138	58	55	29	20	300

TABLE 11. DURATION OF ANALGESIA.

GROUP	DURATION OF ANALGESIA (MEAN)
GROUP I (Pethidine)	187 MINUTES
GROUP II (Nalbuphine)	204 MINUTES
GROUP III (Control)	80 MINUTES

TABLE 12 SUMMARY OF SIDE EFFECTS

SIDE EFFECTS STUDIED	GROUP I (PETHIDINE)	GROUP II (NALBUPHINE)	GROUP III (CONTROL)	TOTAL
Sedation	43	30	10	83
Nausea	10	6	8	24
Vomiting	2			2
Agitation			3	3
Confusion	1			1
Twitching				
Hypotension	5			5
Sweating				
Awareness	1	1	3	5
Other Complaints	3	5	2	10
TOTAL	65	42	26	133

TABLE 13. AWARENESS RATE

GROUP STUDIED	Number of Patients Aware	Percentage of Total in Group
GROUP I (Pethidine)	1	1.0%
GROUP II (Nalbuphine)	1	1.0%
GROUP III (Control)	3	3.0%
TOTAL	5	1.66%

TABLE 14. TIMES BETWEEN EXTUBATION AND RESPONSE TO NAME

STUDY GROUP → / TIME ↓	GROUP I (Pethidine)	GROUP II (Nalbuphine)	GROUP III (Control)
Mean Time in Minutes Between Extubation and Response to Name	4.5	4.2	1.5
Range of Times (Minutes)	2-6	2-6	1-4

TABLE 15. TIMES BETWEEN EXTUBATION AND REGAINING FULL CONSCIOUSNESS

STUDY GROUP → / TIME ↓	GROUP I (Pethidine)	GROUP II (Nalbuphine)	GROUP III (Control)
Mean Time in Minutes Between Extubation and Regaining Full Consciousness	9.5	7.8	5.5
Range of Times (Minutes)	3-20	3-12	4-8

TABLE 16. RESPIRATORY CHANGES IN PREGNANCY AND LABOUR

	NON-PREGNANT	PREGNANT (PRE-LABOUR)	% INCREASE	DURING LABOUR	% INCREASE
RESPIRATORY RATE PER MINUTE	14	16	+15%	22	+37.5%
TIDAL VOLUME (ML)	500	700	+40%	741	+ 5.9%
MINUTE VOLUME L/MIN.	7	10.5	+50%	16.3	+55.2%

TABLE 17. DECREASE IN TIDAL AND MINUTE VOLUMES AFTER OPERATION

	PREOPERATIVE		POST OPERATIVE		% CHANGE	
Study Group	Mean Tidal Volume (ml)	Mean Minute Volume(L/Min)	Mean Tidal Volume (ml)	Mean Minute Volume(L/Min)	Tidal Volume	Minute Volume
GROUP I (Pethidine)	740	16.28	490	11.27	-33.8%	-30.8%
GROUP II (Nalbuphine)	760	15.96	500	10.50	-34.2%	-34.2%
GROUP III (Control)	725	17.40	540	13.50	-25.5%	-22.4%

TABLE 18.

CONVERSION OF ARTERIAL BLOOD PRESSURES (SYSTOLIC/DIASTOLIC) TO MEAN ARTERIAL PRESSURES (M.A.P.) mm Hg.

Formula used

M.A.P. (mm Hg) = Diastolic pressure + 1/3 Pulse pressure.

SYSTOLIC / DIASTOLIC	Pressure (mm Hg) Diastolic + 1/3 Pulse Pressure	Mean Arterial Pressure (M.A.P.) mm Hg (To the nearest mm Hg)
140/90	(90 + 16.6)	107
130/90	(90 + 13.3)	103
120/90	(90 + 10)	100
120/80	(80 + 13.3)	93
120/70	(79 + 16.7)	87
110/80	(80 + 10)	90
110/70	(70 + 13.3)	83
100/70	(70 + 10)	80
100/60	(60 + 13.3)	73
90/60	(60 + 10)	70
90/50	(50 + 13.3)	63

APPENDIX I.

A COMPARATIVE STUDY OF NALBUPHINE AND PETHIDINE FOR INTRAOPERATIVE USE IN EMERGENCY OBSTETRICS

Questionnaire

Name of Patient: _____

Unit No._____.

Age in Years _____.

Weight in Kilogrammes _____.

A.S.A. Physical Status _____.

Preoperative Signs

Pulse _____/min B.P. _____ mm Hg.

Respiratory Rate _____/min. Tidal Volume _____ml.

Time of induction _____.

Time of clamping Umbilical Cord _____.

Analgesic drug / Placebo used

Tick here.

Pethidine (0.8 mg/kg) 50 mg. to 60 mg. ____

Nalbuphine (0.1 mg/kg) 6 mg. to 7 mg. ____

Control (Normal Saline) ___

Mean Intraoperative Signs

Time of Extubation _____ Pulse _____/min

Time of first response to Name _____ BP _____ mm Hg

Time at which FULL Consciousness regained (Patient able to pronounce name or converse) _____.

All the following are after the patient is awake.

Tidal volume _____ ml. Respiratory Rate _____/min.

Pulse _____/min. B.P. _____ mm Hg.

ANALGESIA: 1. No Pain: ___ 2. Slight Pain: ___ 3. Moderate Pain: ___

4. Severe Pain: ___ 5. Unbearable Pain: ___.

Postoperative Side Effects noted:

Sedation ___; Nausea ___; Vomiting ___; Agitation ___;

Confusion ___; Twitching ___; Hypotension ___;

Sweating ___; Intraoperative recall ___; Others(Specify) ____.

Time of first demand for analgesia _____.

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