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Comparison of hemodynamic response to tracheal intubation with Macintosh and McCoy laryngoscopes

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Comparison of Fentanyl and Nalbuphine in Total Intravenous Anaesthesia (TIVA)

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Abstract

Objective: To compare Nalbuphine and fentanyl as total intravenous anaesthesia with propofol infusion in laproscopic cholecystectomy cases.

Study design: Double blind randomised.

Methods: Changes in haemodynamic variables greater than twenty percent above or below the baseline and recovery profile were observed.

Results: Blood pressure remained within 20% of baseline in either group. Nine patients in fentanyl and fifteen in nalbuphine group required an additional bolus of propofol intraoperatively. Heart rate response after tracheal intubation was significantly higher in the nalbuphine group (25%). No difference was observed in the incidence of nausea and vomiting in the recovery room. Twenty-seven percent patients in the nalbuphine group required analgesia in the recovery in comparison to 87% in the fentanyl group. Patients in the fentanyl group required analgesia earlier (37 minutes vs. 62 minutes).

Conclusion: Fentanyl provided better intraoperative haemodynamic stability in comparison to nalbuphine when used as the analgesic component in total intravenous anaesthesia with propofol. The recovery profile with both drugs was similar. Lesser number of patients required analgesia in the recovery in the nalbuphine group (JPMA 52:459;2002).

Introduction

Use of total intravenous anaesthesia (TIVA) offers particular advantages in developing countries where there may be problems with availability of compressed gases¹, calibrated vaporizers and rotameters². Unpredictability in the availability of drugs is another problem for anaesthetists working in these countries and requires familiarity on their part in the use of alternatives to standard drugs. Fentanyl is generally used as the anaesthetic component in TIVA for inpatient settings because of its high therapeutic index and its pharmacokinetics properties but it may be associated with a variable amount of respiratory depression at conclusion of surgery³. Use of both nalbuphine and buprenorphine in TIVA was previously reported by us as a safe alternative⁴, but nalbuphine has the advantage of cardiovascular stability and rapid recovery⁵.

The purpose of this study was to test the hypothesis that 0.2ug.kg-1 of fentanyl and 0.2mg.kg-1 of nalbuphine will provide comparable suppression of intraoperative haemodynamic responses and similar recovery profile when used as narcotic analgesic component in TIVA.

Patients and Methods

The study was approved by the Human Subjects Protection committee of the hospital and informed consent was obtained from patients. The subjects were randomised by using sealed envelopes and study was double blind. Blindness was assured by using coded syringes prepared by anaesthetists unconnected with the study and those taking the recordings and assessing patients postoperatively were also blinded.

Sixty patients aged between sixteen and sixty years and of ASA status one and two undergoing

laproscopic cholecystectomy were entered in the trial, Patients taking medication likely to affect the cardiovascular system like antihypertensive and antidysrhythmic agents, beta blockers and calcium channel blockers were excluded. Obesity with body weight more than 30% of ideal, anticipated difficult intubation based on Mallampatti scoring were excluded and those presenting for emergency surgery were also excluded.

Patients enrolled in the trial received 7.5 mg of oral midazolam as premedication and were randomly divided into two groups; group 1 received an initial bolus of nalbuphine 0.2mgkg⁻¹ and group 2 received fentanyl 2 ug.kg⁻¹ intravenously. Both drugs were given five minutes before induction of anaesthesia and after taking baseline readings. Anaesthetic technique was standardized. After preoxygenation anaesthesia was induced with propofol 2 mgkg⁻¹ over thirty seconds followed by vecuronium 0.1 mgkg⁻¹ over fifteen seconds. An infusion of propofol was started immediately after induction according to the following regimen: 10 mgkg⁻¹hr⁻¹ for the first ten minutes, 8 mgkg⁻¹hr⁻¹ for the next ten minutes and 6 mgkg⁻¹hr⁻¹ for maintenance. An Imed-Gemini PC-i infusion pump was used. Tracheal intubation was performed three minutes after vecuronium injection. Patients' lungs were ventilated with an air-oxygen mixture maintaining an FIO₂ of 0.4 A nasogastric tube was inserted in all patients after tracheal intubation and removed before reversal of neuromuscular blockade. Patients were ventilated at an initial tidal volume of 10 mlkg⁻¹ and a respiratory rate of 10 breaths min⁻¹. These parameters were then adjusted to keep the EtCO₂ within 35-40 mm of Hg.

Depth of anaesthesia was assessed during the intraoperative period by observing a variation of more than 20% above or below the baseline in systolic arterial pressure or heart rate measurements.

Lacrimation and sweating during anaesthesia were also noted. If any two of the above signs were present a supplemental bolus of propofol 10 mg was given. If the signs persisted for more than three minutes after the bolus the rate of infusion was again increased to 8 mgkg⁻¹hr⁻¹ for another ten minutes. Half the preinduction dose of analgesic was repeated from a coded syringe if the criteria for light anaesthesia persisted. Regular hourly analgesia/placebo top-ups were given in both groups from coded syringe to keep the study blind. Group I (Nalbuphine group) patients received saline bolus whereas fentanyl 1.0 ug.kg⁻¹ diluted to similar volume was given in group 2 (Fentanyl group) patients. The size of tracheal tube and the type of laryngoscope blades were standardized. The infusion of propofol was stopped at the time of last stitch and the neuromuscular blockade was reversed with atropine 0.02 mgkg⁻¹ and neostigmine 0.05 mgkg⁻¹.

The ECG was monitored continuously using lead II. Noninvasive blood pressure, oxygen saturation, FIO₂ and ETCO₂ were monitored using the Datex Cardiocap monitor. Blood pressure and heart rate were noted five minutes before and two minutes after the study drug, at one minute interval after induction for three minutes and at one minute interval after tracheal intubation for five minutes, one and two minutes after the dosage of propofol was altered and after termination of infusion and extubation.

At the time of reversal, response to eye opening on command and any sign of the patient being in pain were noted. In the recovery room patients' ability to tell name and any complaints of pain, nausea and vomiting were noted down. Patients were discharged from the recovery room when they fulfilled the routine discharge criteria of our unit (PAR scoring). The time of requirement of first postoperative dose of analgesic was also noted. Postoperative interview took place the next day. Every patient was asked regarding any recall of events inside the operating room and any specific problems experienced after anaesthesia.

A sample size and power analysis had shown that thirty patients per group were required to demonstrate a twenty percent difference in blood pressure or heart rate value at a 0.05 and a power of eighty percent. Variables were analyzed using the Epi info-6 statistical package. Analysis of variance was used to compare the mean changes in systolic, diastolic, mean blood pressure and heart rate. The incidence of untoward effects and other qualitative data was assessed by Chi-Square analysis. A p value of less than 0.05 was taken as significant.

Results

Demographic data

Both groups were comparable for age, weight, preinduction systolic blood pressure, heart rate and duration of anaesthesia (Table).

Table. Demographic and baseline haemodynamic data. Mean±SD

Group	n	Age (years)	Weight (kg)	Duration of anaesthesia (min)	Preinduction values			
					SBP	DBP	MAP	HR
Group 1 (Nalbuphine)	30	38.9± 6.4	60.3±6.0	87.4±15.3	126.8±10.1	*76.2±6.4	*93.1± 9.9	83.3±10
Group 2 (Fentanyl)	30	39.6± 5.9	59.0±5.4	88.2±13.7	129.1±7.5	82.8±6.2	99.8±9.8	86.3±8.2

Systolic blood pressure, SBP; diastolic blood pressure, DBP; mean arterial pressure, MAP; heart rate, HR.

*Significant difference between groups (p<0.05)

There was a significant difference in the baseline diastolic and mean pressure within the groups with the pressures in the nalbuphine group being lower.

Haemodynamic data

Figure 1 shows the mean changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) in relation to time. Because of significant difference in the baseline values of DBP and MAP percentage change from baseline was also calculated rather than the absolute change. Both groups exhibited a decrease of less than 15% after induction. The rise after tracheal intubation was not significant compared to the baseline in either group. The blood pressure was maintained within 20% of baseline after incision and at the time of emergence and extubation. A significant difference in SBP was observed between the two groups at two, three and five minutes post intubation, after decreasing propofol infusion to maintenance levels and at the time of incision when higher levels were observed in the nalbuphine group (Figure 1).

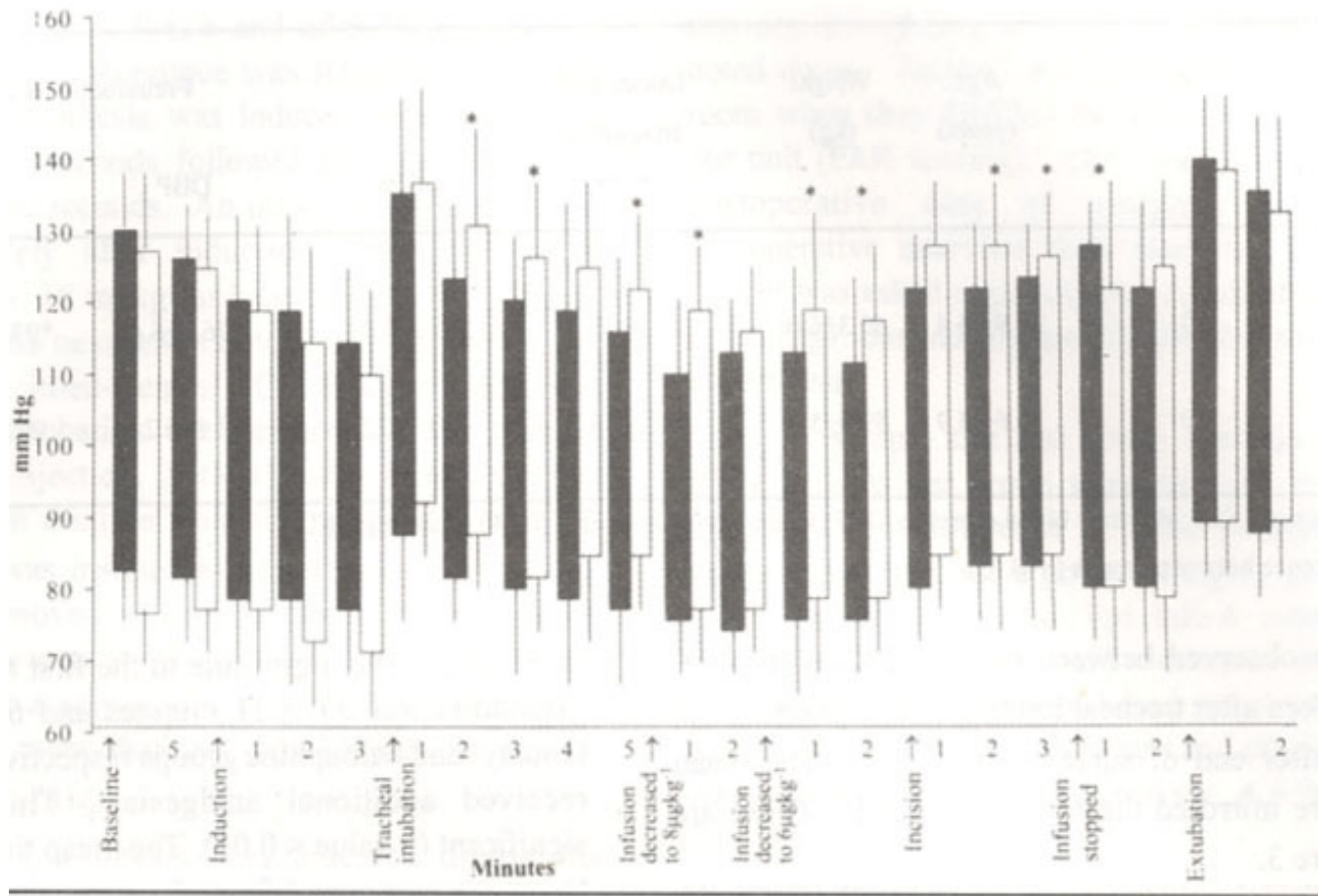


Figure 1. Changes in systolic and diastolic blood pressure (mean±SD).
 ■ = Fentanyl, □ = Nalbuphine
 * = Statistical difference between the two groups (p<0.05)

The changes in DBP are shown in Figure 2. DBP fell after induction. After tracheal intubation it rose to a maximum of 13% in the nalbuphine group versus 3% in fentanyl. The pressures remained within 20% of the baseline in all the observed readings. A significant difference was observed between the two groups after all the readings taken after tracheal intubation except one taken two minutes after end of surgery (Figure 2).

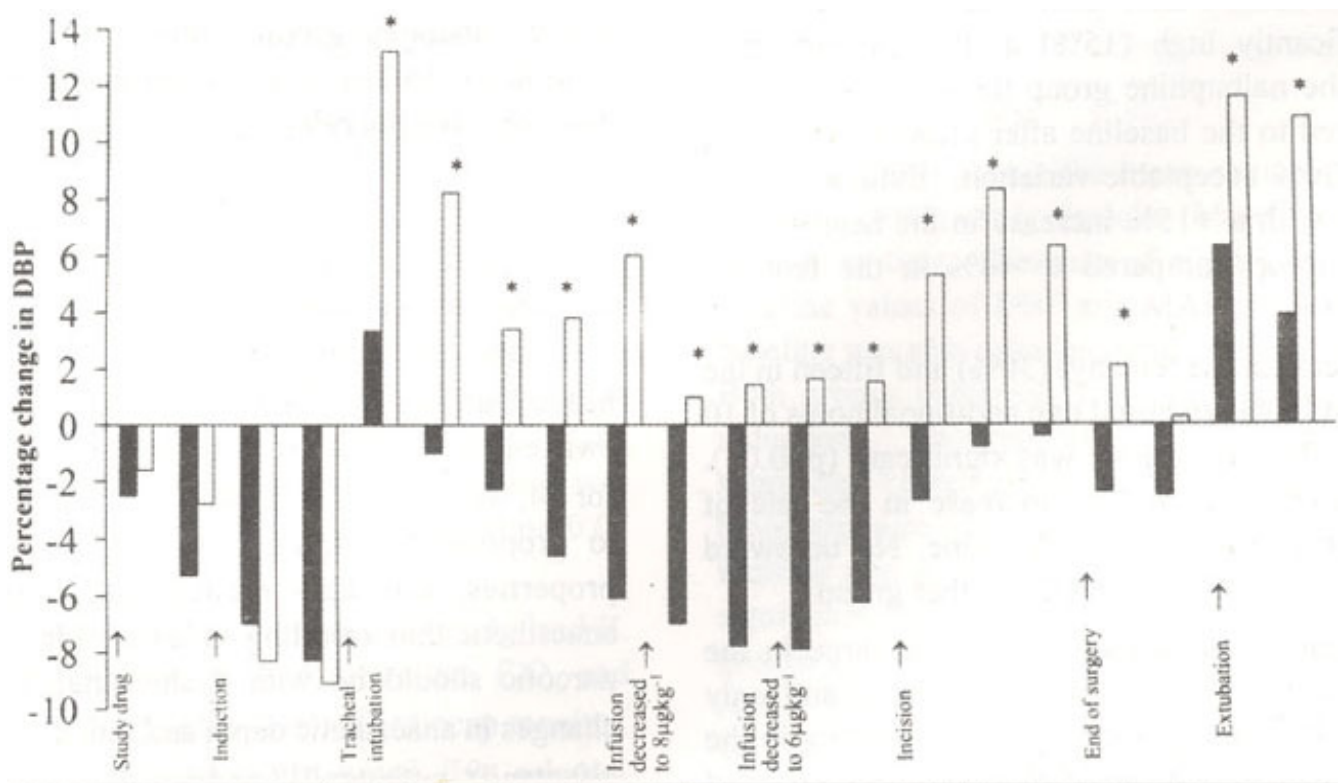


Figure 2. Percentage changes in diastolic blood pressure compared to baseline.

■ = Fentanyl □ = Nalbuphine

* Statistical difference between the two groups ($p < 0.05$)

The mean arterial pressure mirrored the changes in DBP. These are shown in Figure 3.

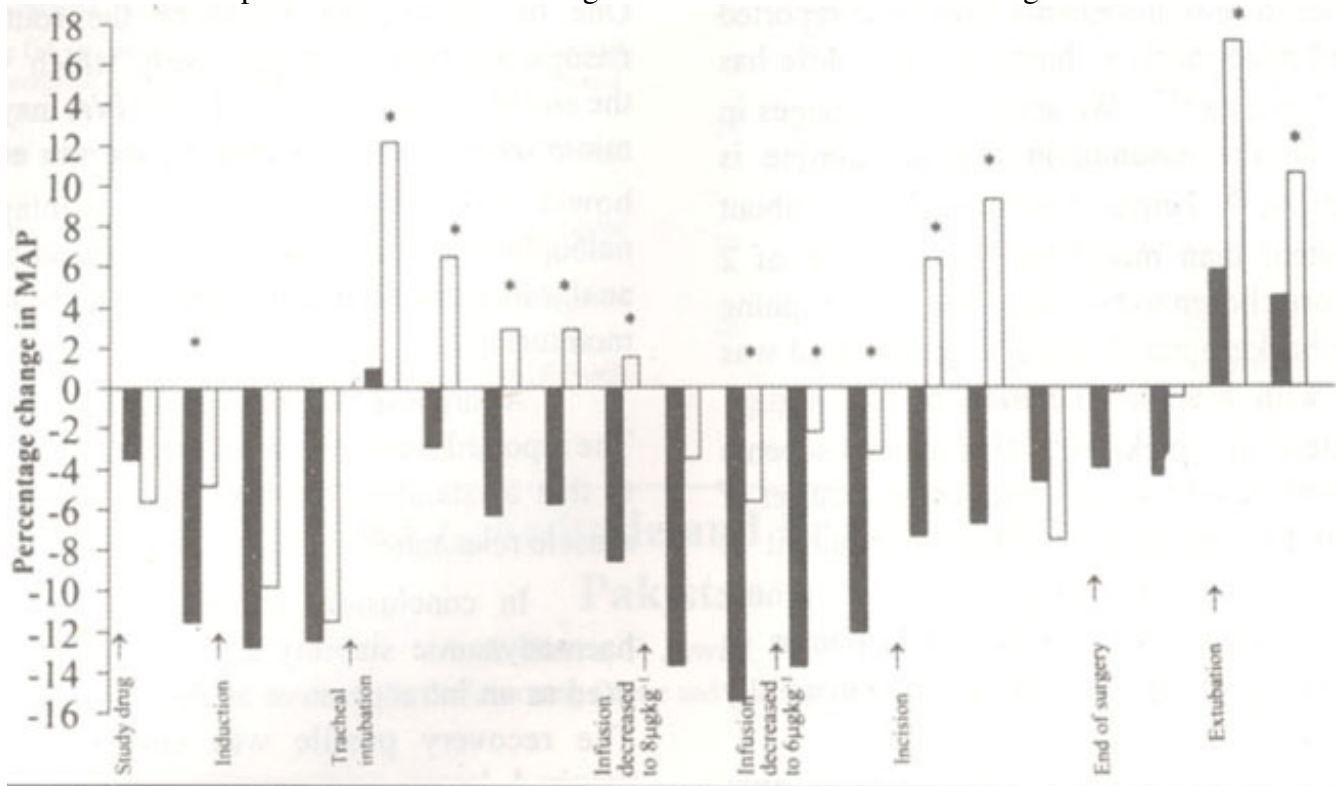


Figure 3. Percentage change in mean arterial pressure compared to baseline.

■ = Fentanyl □ = Nalbuphine

* Statistical difference between the two groups ($p < 0.05$)

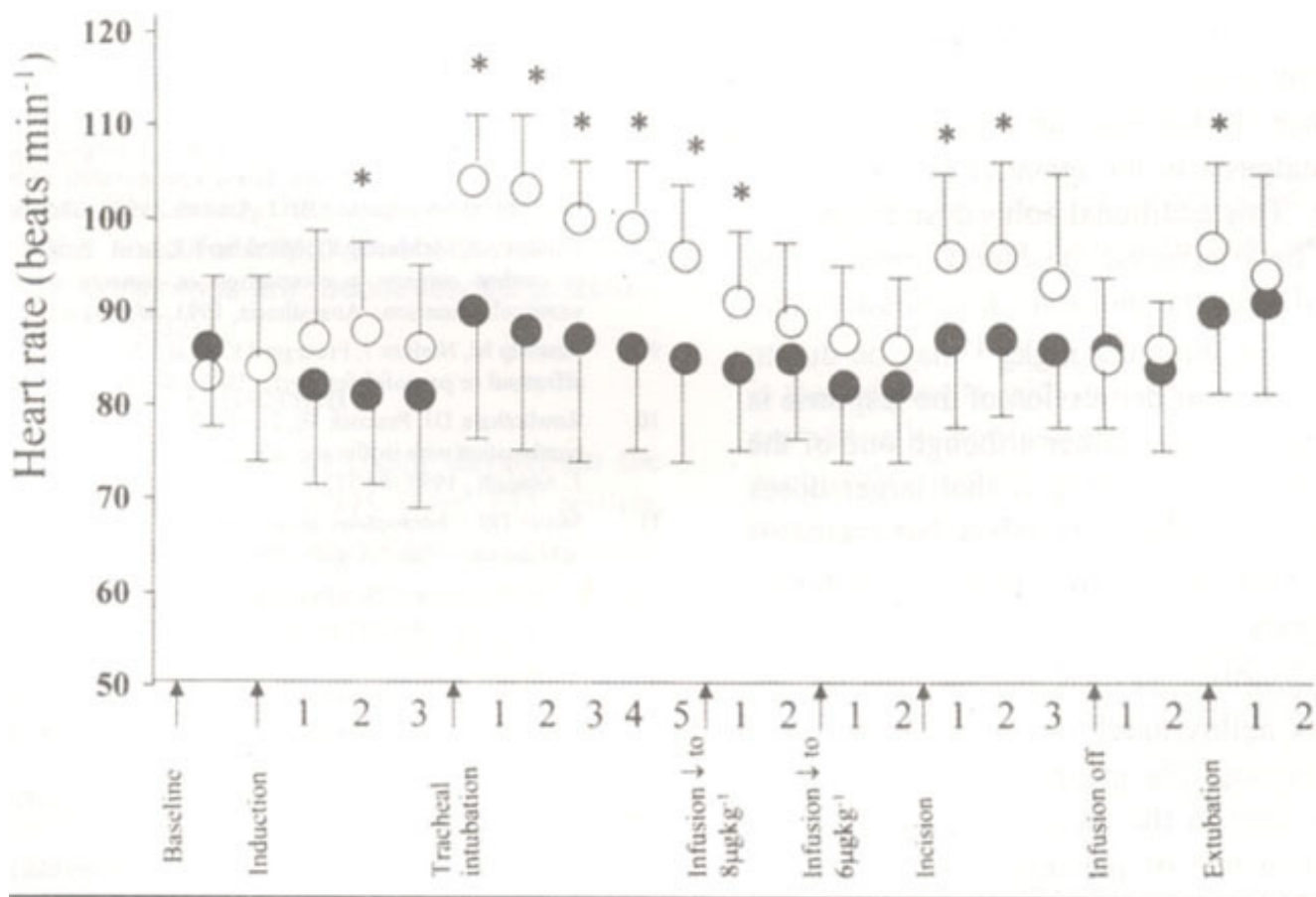


Figure 4. Changes in heart rate (mean + SD)
 ■ = Fentanyl □ = Nalbuphine
 * Statistical difference between the two groups (p<0.05)

Figure 4 shows the changes in heart rate. The maximum positive or negative change observed during the study period in the fentanyl group was 6.4%. The heart rate in the nalbuphine group showed a much higher positive variation compared to the fentanyl group. In this group the maximum response seen after tracheal intubation was a 25% change one minute after intubation. The heart rate remained significantly high (15%) at five minutes post intubation. In the nalbuphine group there was significant increase compared to the baseline after incision (16%) but this was within 20% acceptable variation. Extubation was again associated with a +15% increase in the heart rate in the nalbuphine group compared to +4% in the fentanyl group (Figure 4).

Nine patients in the fentanyl (30%) and fifteen in the nalbuphine group (50%) required one additional bolus of 10 mg of propofol. This difference was significant (p<0.01). None of the patients required an increase in the rate of propofol infusion or additional nalbuphine. No untoward intraoperative effects were observed in either group.

One patient in the fentanyl (3%) and three in the Nalbuphine group (10%) complained of nausea and only one in fentanyl (3%) group complained of vomiting in the recovery room. No significant difference was observed between the groups. None of the patients were excessively sedated.

First analgesic dose in the postoperative period was given on patient demand. Twenty six patients in the fentanyl (87%) and eight in the nalbuphine (27%) group needed postoperative analgesia in the recovery room pressure, MAP; heart rate, HR. (p<0,001). The mean time to the first analgesic dose after extubation was 37 ± 11 minutes and 62 ± 35 minutes in fentanyl and nalbuphine groups respectively in patients who received additional analgesia. This difference was significant (p value <0.01). The mean

time from extubation to eye opening was 4.2 ± 0.4 minutes in fentanyl and 5.2 ± 0.6 minutes in the nalbuphine group. This difference was non-significant. The mean time from extubation to the patients' ability to tell their name was 14.2 ± 2.6 minutes in fentanyl and 21.8 ± 4.8 minutes in the nalbuphine group ($p < 0.05$). Mean discharge time from recovery room was 90 ± 22 minutes in the fentanyl group and 99.9 ± 27 minutes in the nalbuphine group. None of the patients answered in affirmative to the three specific questions asked in the postoperative interview.

Discussion

Several drugs could be used to achieve total intravenous anaesthesia. Propofol allows rapid changes in the anaesthetic depth, lack of cumulation and rapid clearheaded awakening⁶ and is a logical choice. Speed of awakening was shown to be unaffected by infusion given for 24, 48, 72 and 96 hours⁷. Addition of a narcotic agent to propofol is required, as propofol has no analgesic properties; this also reduces the dose of intravenous anaesthetic thus resulting in lesser side effects. Ideally the narcotic should be with a short half-life allowing rapid changes in anaesthetic depth and quick recovery. Fentanyl⁸, alfentanil⁹, sufentanil¹⁰ and remifentanyl^{11,12} have all been used or recommended for analgesia during TIVA.

Resource variability is a major problem in developing countries and working conditions may vary from excellent to poor. One of the challenges of working in these places is the non-availability or sudden shortages of newer short acting drugs forcing anaesthetists to look for safe alternatives. Longer acting narcotics, like pethidine antagonist or partial agonist drugs offer a degree of safety in and morphine, have been used in TIVA¹³, Agonist above mentioned circumstances because of the ceiling effect on respiration, and are especially beneficial in situation where recovery facilities are lacking. Both buprenorphine and nalbuphine have been used in TIVA^{4,14} and found to be safe alternatives. However, effect of these drugs has not been directly compared with fentanyl.

Nalbuphine is chemically related to naloxone. It has a ceiling effect for respiratory depression and is said to cause less nausea and vomiting compared to morphine, pethidine or pentazocine¹⁵. Our dosage selection of the two drugs is open to critique however equipotent doses of these drugs have not been fully established. The ED₅₀ of nalbuphine in rats was found to be 1.2 mg.kg^{-1} compared to 0.98 mg.kg^{-1} for morphine indicating its potency to be 0.7-0.8 times that of morphine¹⁶. Higher dose requirements have been reported for use in balanced anaesthesia in humans where dose has ranged from $0.15\text{-}2 \text{ mg.kg}^{-1}$ ¹⁷. We selected the dosages in our study based on the assumption that nalbuphine is equipotent to morphine¹⁸. Fentanyl on an mg basis is about 80 times more potent than morphine¹⁹ and a dose of 2 was therefore chosen to be equipotent to nalbuphine 0.2 mg.kg^{-1} . The background Propofol regimen used was Robert's regimen with a slight alteration of a 2 mg.kg^{-1} ²⁰ induction dose instead of 1 mg.kg^{-1} ²⁰. This manual scheme was designed to achieve a blood propofol concentration of $3\text{-}4 \text{ ug.kg}^{-1}$ within five minutes and then maintain it at constant level²¹. The use of manual regimens is now replaced by Target Controlled Infusion (TCI) pumps in developed countries²² but again these are not generally available in the developing world.

A difference was observed in the blood pressure response between the two drugs. The response after tracheal intubation and incision was higher in the nalbuphine group. A significant difference was also observed in heart rate response with the response being significantly lower in the fentanyl group after induction, tracheal intubation and incision.

Thirty percent patients in the fentanyl compared to 50% patients in the nalbuphine group required supplemental propofol bolus. Both narcotic and propofol bolus have been found to be equally effective in controlling haemodynamic and hormonal response to surgical stimuli during TIVA²³. All patients in

the fentanyl group received additional analgesia one hour following the induction dose. This was done in a blind manner. It was considered unethical not to provide additional analgesia in the fentanyl group because of its shorter half life. This additional bolus dose because of its timing could not have affected the blood pressure and heart rate readings till after the incision. It is possible that inadequate effect of nalbuphine 0.2 mg kg^{-1} may be due to insufficient dosage and further depression of the response is possible by increasing the dose further although one of the disadvantages suggested for this drug is that larger doses may contribute little to the analgesic effect but increases sedation²⁴. Fentanyl 2 mg kg^{-1} given at induction therefore provided better analgesia.

The recovery profile was the same for both groups except for the patients' ability to tell their name, which was earlier in the fentanyl group. The incidence of postoperative nausea and vomiting seen in the recovery room was very low. The reported incidence of postoperative nausea and vomiting in laproscopic cholecystectomy is high with approximately 50% of the patients requiring antiemetics²⁵, This low incidence was also seen in our previous study.

One of the reasons could be the routine insertion of nasogastric tube intraoperatively which was removed at the end of the procedure. Use of TIVA may also account for minimizing emesis by eliminating the effect of N 20 on bowel distension. An added advantage seen in the nalbuphine group was that lesser number of patients needed analgesia in the recovery room and hence the need for lesser monitoring.

Awareness was not reported in any of our patients. The reported incidence of awareness in TIVA is comparable to that of standard balanced anaesthesia techniques using muscle relaxants²⁶.

In conclusion, nalbuphine group provided lesser haemodynamic stability in comparison to fentanyl when used as an intraoperative analgesic in TIVA with propofol. The recovery profile was similar. Nalbuphine group required lesser postoperative analgesia in the recovery room.

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