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Comparative Study of Nalbuphine and Fentanyl for Total Intravenous Anaesthesia in Short Surgical Procedures

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Abstract

Background: Total Intravenous Anesthesia (TIVA) can be defined as a technique of general anesthesia using a combination of agents given solely by the intravenous route and in the absence of all inhalational agents including nitrous oxide (Gas Anesthesia). Total intravenous anesthesia, based on the administration of Propofol combined with an opioid, has become a popular anesthetic technique. This study is to compare the analgesic effects of nalbuphine with fentanyl as well as associated side effects as adjuncts in TIVA along with propofol. *Aim:* To study the effect of nalbuphine and fentanyl when used as analgesic in total intravenous anesthesia along with propofol. *Methods:* This study was conducted on 60 adult patients belonging to American association of anesthesiologists (ASA) Grade I/II and posted for short minor surgical and gynecological procedures. They were divided into two equal groups of 30 each, using statistical table of random number: *Group N:* Preinduction medication with Inj. Nalbuphine 0.05 mg/kg; *Group F:* Preinduction medication with Inj. Fentanyl 1 mcg/kg. HR, BP, SPO_2, just before induction, immediately after induction and then at every 5 minute-intervals till 2 hours were recorded. Additionally, VAS scoring, Modified Aldrete scoring, Time for rescue analgesia, Respiratory rate were noted after 30 minutes. *Results:* Hemodynamic parameters like heart rate, systolic blood pressure, mean arterial pressure were controlled better in the fentanyl group at 5 min, 10 min, 15 min intraoperatively. Postoperative analgesia was better with nalbuphine group with reduced visual analogue scale with reduced respiratory depression. *Conclusions:* Fentanyl provided better intraoperative hemodynamic stability whereas, nalbuphine provided better postoperative analgesia with lesser respiratory depression.

Keywords: Total Intravenous Anesthesia (TIVA); Nalbuphine; Fentanyl.

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Introduction

Total Intravenous Anesthesia (TIVA) can be defined as a technique of general anesthesia using a combination of agents given solely by the intravenous route and in the absence of all inhalational agents including nitrous oxide (Gas Anesthesia).[1] TIVA has reduced incidence of postoperative nausea and vomiting, reduced atmospheric pollution, more predictable and rapid recovery, greater hemodynamic stability, preservation of hypoxic pulmonary

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vasoconstriction, reduction in intracerebral pressure and reduced risk of organtoxicity.

The most commonly utilized groups of drugs include hypnotics and short-acting opioids.[2]

Total intravenous anesthesia, based on the administration of Propofol combined with an opioid, has become a popular anesthetic technique. It allows independent modulation of the different components of anesthesia.[3]

Propofol is generally combined with an analgesic, the popular combination being either Propofol with Fentanyl or Ketamine, as pain relief to patient is an important constituent of balanced anesthesia.[4]

Fentanyl is a popular analgesic because of its relatively short-time to peak analgesic effect, rapid termination of effect and cardiovascular safety. Dose for achieving analgesia is 2-50 mcg/kg. Fentanyl decreases the anesthetic requirement for Thiopentone or Propofol by providing antinociceptive effects that the intravenous hypnotics do not provide.[5,6]

Nalbuphine is a member of the opioid family. It is an antagonist of μ receptor but agonist of kappa receptors.[7] It was synthesized in an attempt to produce analgesia without the undesirable side effects of alpha 1 agonist. Respiratory depression and abuse potential with nalbuphine is very less. Although very commonly used, fentanyl is costlier and needs narcotic licensing. Thus, this study is to compare the analgesic effects of nalbuphine with fentanyl as well as associated side effects.

Materials and Methods

Type of study:

Prospective Double blind Randomized Study.

Period required for data collection:

1.5 years.

Period required for data analysis:

Reporting: 6 months;

Sampl Size: 60 cases.

After approval from institution ethics committee, this study was conducted on 60 adult patients belonging to American association of anesthesiologists (ASA) Grade I/II and posted for short minor surgical and gynecological procedures under General Anesthesia.

They were divided into two equal groups of 30 each, using statistical table of random number:

Group N: Preinduction medication with Inj. Nalbuphine 0.05 mg/kg;

Group F: Preinduction medication with Inj. Fentanyl 1 mcg/kg.

Inclusion criteria:

1. ASA Grade I & II;
2. Ages between 18 and 60 of either gender;
3. Hemodynamically stable patients with normal laboratory investigations**;**
4. Patients willing to be a part of the study;
5. Surgery duration < 30 mins.

Exclusion criteria:

1. ASA Grade 3 and more;
2. Patients not willing to be a part of the study;
3. Patients on pain perception modifying drugs;
4. Patients with known sensitivity to any of the drugs understudy;
5. Surgery duration > 30 min.

Sample size:

By keeping the significance level of 5%, power of study at 95 %, the sample size was calculated by WinEpi Statistical Package. The minimum sample size required was 25 in each group. Keeping in mind dropouts or exclusions, we conducted the study in 60 patients after dividing 30 patients in each group.

Procedure and Conduct of Study Masking:

The anesthesiologist loading the drugs and administering the premedication was different than the one conducting the case and managing patients in postanesthesia care unit. Thus, both the anesthesiologists were blinded to the assignment.

Preop Evaluation

All patients were subjected to detailed preanesthetic evaluation and relevant laboratory investigations. Written informed consent was obtained from all the patients as per the hospital protocol given at appendix A. They were counseled with regards to sedation, general anesthesia as well as the operative procedure.

Intraoperative

On arrival in operation theatre, nil by mouth was confirmed and baseline vitals recorded.

Patient was premedicated with Inj. Ondansetron 4 mg, Inj. Glycopyrrolate 0.2 mg IV. Preoxygenation

done with 100% oxygen was done. Patient was given the randomly allotted drug (either Fentanyl or nalbuphine).

Propofol was administered 5 mins after the test drug fentanyl and nalbuphine were given as premedications to the participants.

It was given intermittently as per the vitals and clinical signs of the patient.

The initial bolus for induction was 0.8–1.2 mg/kg at the rate of 30 mg/10 sec till the desired clinical effect was achieved. 20–30 mg increment boluses were given to keep the patient deeply sedated.

Propofol was stopped 5–10 mins prior to the desired time of emergence.

Rescue analgesia was given when VAS is > 5. Inj. Diclofenac 75 mg IM was given as rescue analgesic.

All the intraoperative vitals were recorded and VAS score, Modified aldrete score, side effects and respiratory rate were noted in the postoperative period for 2 hours.

Patient was shifted to postanesthesia care unit and monitored for hemodynamic parameters, duration of analgesia, VAS & Modified Aldrete Scoring and adverse effects, if any, immediately on arrival in PACU & every 30 mins (till 2 hours) thereafter, till transfer to surgicalward.

Data analysis:

The comparison of quantitative data was done by using test of significance based on '*t*'-test. Unpaired *t*-test for intergroup & paired *t*-test for within the group comparisons. Qualitative parameters were analyzed by Chi-square test.

p - value ≤ 0.05 was taken as significant and *p* < 0.001 was taken as highly significant.

Results

The age and weight of the patients were comparable in both the groups and was found to be clinically insignificant.

Propofol given in fentanyl group was 151.6 ± 7.8 mg and in the nalbuphine group was 153.8 ± 6.9. There was no significant difference in the doses in both the groups.

The intraoperative heart rate is higher at 5, 10 ,15 minute in the nalbuphine group and is clinically significant, (Table 1).

The systolic Blood Pressure is lower at 1 minute, 2 minute, 5 minute, 10 minute, 15 minute and 30 minute in the fentanyl group and is clinically significant, (Table 2).

The mean diastolic blood pressure was comparable and there was no significant difference.

The mean arterial pressure was lower in the fentanyl group at 2, 5, 10, 15 minutes and was clinically significant, (Table 3).

The mean SpO_2 was on the lower side in fentanyl at 1 hour and 2 hour (postoperative) and was clinically significant, (Fig. 1).

Table 1: Comparison of mean heart rate between Fentanyl and Nalbuphine at different time internal

Time interval	Fentanyl (Mean ± SD)	Nalbuphine (Mean ± SD)	*p* - Value
Baseline	72.63 ± 8.54	73.13 ± 8.41	0.820
1 Minute	71.90 ± 7.59	72.70 ± 8.09	0.694
2 Minute	70.53 ± 7.50	73.70 ± 8.09	0.121
5 Minute	69.13 ± 7.31	74.10 ± 8.30	0.017
10 Minute	68.30 ± 6.58	77.47 ± 8.06	0.000
15 Minute	69.90 ± 7.18	74.93 ± 8.17	0.014
30 Minute	71.20 ± 8.04	71.87 ± 8.40	0.755
1 Hour	72.63 ± 8.54	71.67 ± 6.77	0.629
2 Hour	72.33 ± 8.51	71.30 ± 5.93	0.587

Table 2: Comparison of mean systolic blood pressure between Fentanyl and Nalbuphine at different time internal

Time interval	Fentanyl (Mean ± SD)	Nalbuphine (Mean ± SD)	*p* - Value
Baseline	117.47 ± 7.60	123.37 ± 14.66	0.055
1 Minute	115.40 ± 8.08	123.30 ± 13.94	0.009
2 Minute	113.30 ± 7.42	125.00 ± 13.35	< 0.001
5 Minute	111.53 ± 7.28	125.40 ± 13.29	< 0.001
10 Minute	110.67 ± 6.78	128.17 ± 12.69	< 0.001
15 Minute	112.67 ± 7.04	123.40 ± 12.48	< 0.001
30 Minute	114.50 ± 7.85	120.23 ± 13.30	0.047
1 Hour	117.70 ± 8.30	117.67 ± 10.75	0.989
2 Hour	116.73 ± 8.39	116.47 ± 9.89	0.989

Table 3: Comparison of mean arterial pressure between Fentanyl and Nalbuphine at different time internal

Time interval	Fentanyl (Mean ± SD)	Nalbuphine (Mean ± SD)	*p* - Value
Baseline	92.00 ± 5.91	92.67 ± 10.17	0.757
1 Minute	89.87 ± 5.95	92.60 ± 9.98	0.203
2 Minute	88.73 ± 5.53	93.73 ± 9.91	0.019
5 Minute	87.33 ± 5.43	93.93 ± 9.84	0.002
10 Minute	86.53 ± 5.14	95.67 ± 9.65	< 0.001
15 Minute	88.27 ± 5.15	92.87 ± 9.57	0.024
30 Minute	90.00 ± 5.62	90.77 ± 9.85	0.713
1 Hour	92.00 ± 5.91	91.97 ± 9.89	0.987
2 Hour	92.00 ± 5.91	91.97 ± 9.65	0.987

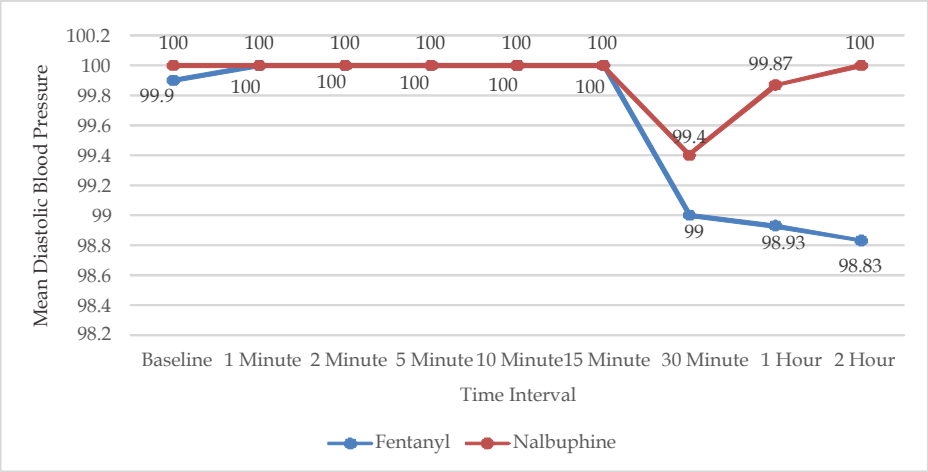

Fig. 1: Comparison of SpO_2 in both groups

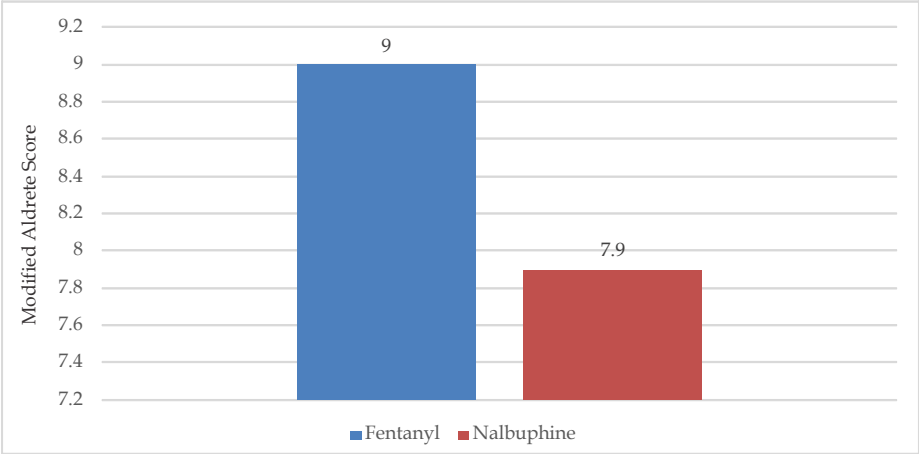

Fig. 2: Comparison of modified aldrete score in both the groups

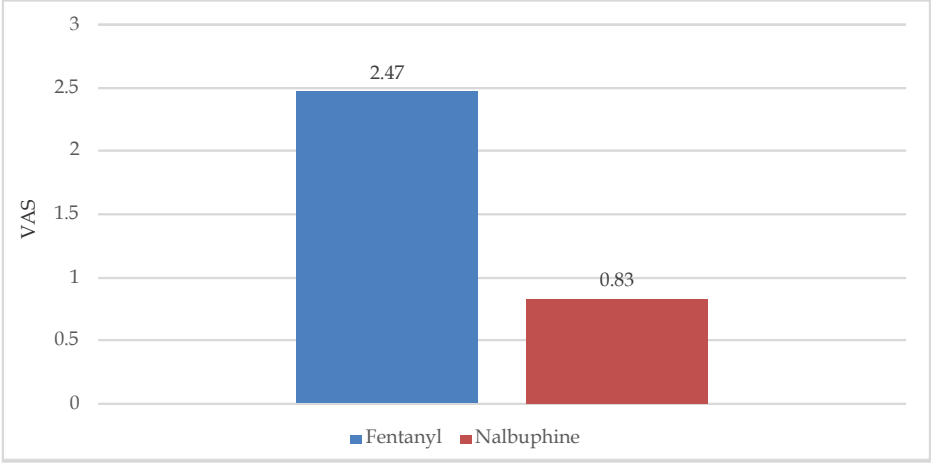

Fig. 3: Comparison of visual analog scale in both the groups

Modified aldrete score was lower in nalbuphine group in the postoperative period and the difference was clinically significant, (Fig. 2).

The visual analog scale was lower in the postoperative period in the nalbuphine group and was clinically significant, (Fig. 3).

Rescue analgesia time was significantly higher in the nalbuphine group with fentanyl needing rescue analgesia at 65.30 ± 8.82 minutes and nalbuphine at 139.87 ± 8.99 minutes.

The respiratory rate was on the lower side in the fentanyl group and it was clinically significant as per (Fig. 4).

No difference was found in the incidence of nausea in both the groups;

Vomiting was observed in one patient in nalbuphine group;

Pruritis was observed in 3 patients in fentanyl group.

Discussion

Demographic Profile

The demographic data age, weight, and type surgery in both the groups were comparable. The difference between both groups was statistically insignificant.

The nature of the procedure in the study was same. Any procedure extending beyond 30 minutes were excluded from the study.

Kay and Rolly[8] introduced Propofol in 1977 during their search for an ideal intravenous anesthetic agent. There was lack of analgesic properties of Propofol which led to development of use of supplementary agents during TIVA, like Ketamine and Fentanyl.

In our study, we are comparing propofol-fentanyl and propofol-nalbuphine and studying the efficacy of nalbuphine as adjunct.

Comparison of hemodynamic stability

Comparison of Heart Rate

Both in nalbuphine group and in fentanyl group the heart rate was within 20 percent of the baseline with nalbuphine showing intraoperative increase in heart rate which was clinically significant at 5 min, 10 min and 15 min and postoperative reduction of heart rate which was not clinically significant.

Similar findings were found in a study conducted by *FA Khan in 2002,*[9] when nalbuphine was compared to fentanyl in total intravenous anesthesia where nalbuphine showed a much higher positive variation compared to fentanyl group especially after incision. The study was conducted in 60 ASA 1 patients undergoing laparoscopic cholecystectomy. Both the drugs, nalbuphine 0.2 mg/kg and fentanyl 2 mcg/kg were given 5 minutes before induction. Anesthesia was induced with propofol 2 mg/kg followed by vecuronium 0.1 mg/kg.

Another study conducted by *Khanday et al. in 2019,*[10] where they compared fentanyl *versus* nalbuphine for attenuation of hemodynamic response to laryngoscopy and endotracheal intubation in general anesthesia. In this study, the variation was more in nalbuphine group than fentanyl but the difference was statistically insignificant.

Thus, both the studies had similar findings as ours.

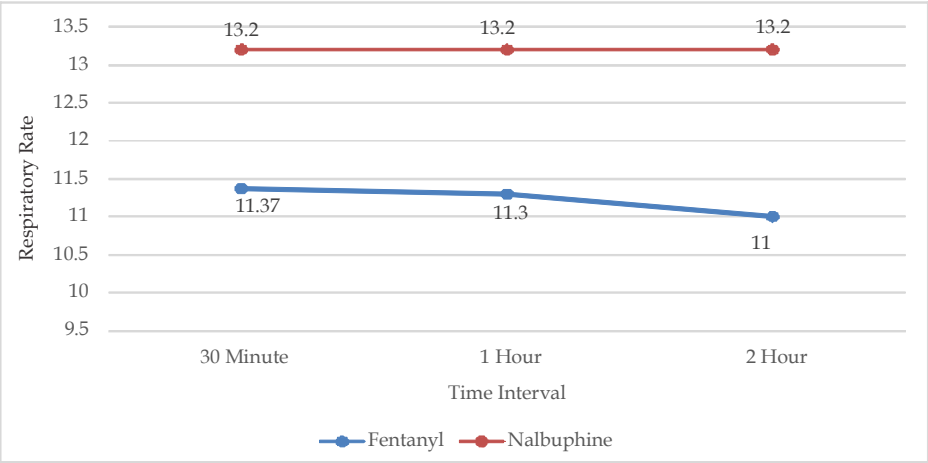

Fig. 4: Comparison of respiratory rates in both the groups

Comparison of Systolic Blood Pressure

There was significant difference in the systolic blood pressure at 5 min, 10 min, 15 min postinduction with increase in the systolic blood pressure in the nalbuphine group which later falls in the postoperative period but is not clinically significant. There was a fall in systolic blood pressure in the fentanyl group at 5, 10, 1 5 min which was statistically significant. However, the variation was within 20 percent of baseline at all times.

Similar findings were found in the study conducted by *Khan et al. in 2002*[9] where there was a significant difference in systolic blood pressure at 2, 3 , 5 minutes postinduction when the maintenance doses of propofol was started and at the time of incision with higher values in the nalbuphine group.

Comparison of Diastolic Blood Pressure

Nalbuphine group showed an increase in the diastolic blood pressure till 10 minutes which was not found to be statistically significant and later a fall in diastolic blood pressure after 30 mins. Fentanyl group showed a fall in Diastolic Blood Pressure (DBP) which was not found to be statistically significant.

In a study, conducted by *Neha Sharma et al. in 2014,*[11] group nalbuphine had a significant rise in systolic and diastolic blood pressure compared to fentanyl postintubation with a maximum rise in systolic blood pressure and diastolic blood pressure to be 14.9 % and 8.9% in nalbuphine group and 4.8 % and 4.5% in fentanyl group. The rise in nalbuphine group lasted longer in nalbuphine group than fentanyl.

Our findings were similar.

Comparison of Mean Arterial Pressure

In our study, there was a fall in mean arterial pressure in the fentanyl group which was found to be statistically significant at 2, 5, 10, 15 minutes. Nalbuphine showed a fall in mean arterial pressure in the immediate postoperative period after 30 mins which was similar to fentanyl.

In *Khan et al. in 2002*[9] study, the changes in mean arterial pressure was similar to their diastolic blood pressure findings, where the variation was within 20 % in both the groups but there was a much higher rise in nalbuphine which was found to be statistically significant. These findings were congruous to our study.

Channaiah et al. in 2008[12] noted in their study that inter group MAP yielded significant attenuation in the Fentanyl group for all recorded time periods and it was similar to our study.

Recovery Profiles

Comparison of modified Aldrete Score

We used modified aldrete score in our study to compare the recovery profile and to compare the safety in discharging patients from postanesthesia care unit. The modified aldrete score was lower in the nalbuphine group than in fentanyl, showing a better and earlier recovery in the fentanyl group.

According to *Khan et al. in 2002,*[9] the recovery profile was same in both the groups but an earlier recovery was noted in the fentanyl group.

Comparison of Visual Analog Scale

We used the Visual analog scale to compare the postoperative analgesia, and nalbuphine provided better analgesia in the postoperative period than fentanyl and it was statistically significant.

These findings were similar to *Khan et al. in 2002*[9] study.

Comparison of Rescue Analgesia Time

The rescue analgesia time was significantly higher in the nalbuphine group with a mean of 139 minutes in the nalbuphine group and 65 mins in the fentanyl group.

Similar findings were found in *Khan et al. in 2002*[9] study.

Comparison of respiratory depression in postoperative period

Fentanyl produced a lower saturation level than nalbuphine at one hour and two hour without Oxygen supplement which was found to be statistically significant.

The mean respiratory rate at 30 min, 1 hour and 2 hour was lower in fentanyl group which was 11.3 per minute and nalbuphine was 13.2 per min. This difference was statistically significant.

Similar findings were found in a study conducted by *Rawal et al. in 1990*[13] where within the first 15 min following recovery, increasing $Paco_2$ and $ETco_2$ as well as respiratory rates below 10/min were noted considerable patients in fentanyl group.

Side effects

The incidence of nausea was 10% in nalbuphine group and vomiting was 3%. Fentanyl reported of nausea in 10%. So, nausea was comparable in both the groups.

A study conducted by Bone E et al. (1988)[14] found no significant difference in the incidence of nausea and vomiting in the study Comparison of nalbuphine with fentanyl for postoperative pain relief following termination of pregnancy under day care anesthesia, which is congruous to our findings.

Pruritis occurred in 10 percent patients of fentanyl group in the postoperative period. Similar findings were found in the study conducted by Hari Prasad et al.[15] (2016) in the study Comparative Study of Analgesic Potential of Nalbuphine *versus* Fentanyl during General Anesthesia. Pruritis was not reported in the nalbuphine group.

Side effects like shivering, headache, bradycardia were not noted in our study.

Conclusion

Based on this study we can conclude that,

1. Fentanyl had better control on intraoperative hemodynamics as compared to nalbuphine;
2. Nalbuphine had better analgesia in the postoperative period;
3. Fentanyl showed earlier and better recovery;
4. Respiratory depression was more in the fentanyl group in the postoperative period, which is undesirable.

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