DOI: 10.7860/JCDR/2023/66441.18845

Original Article

Anaesthesia Section

Comparison of Nalbuphine Hydrochloride and Fentanyl Citrate for Total Intravenous Anaesthesia in Short Surgical Procedures: A Randomised Control Study

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ABSTRACT

Introduction: Total Intravenous Anaesthesia (TIVA) with propofol is gaining acceptance for day care surgeries due to its advantages over inhalational agents. Opioids administered as premedication are known to enhance the hypnotic effect of propofol and provide intraoperative and postoperative analgesia.

Aim: To compare the effectiveness of Nalbuphine and Fentanyl for postoperative analgesia in short surgical procedures.

Materials and Methods: In present double-blinded randomised controlled trail conducted in the Department of Anaesthesia at the Gujarat Cancer and Research Institute, Ahmedabad, Gujarat, India, 60 patients aged 18 to 60 years, classified as American Soceity of Anaesthesiologists (ASA) Grade-I or II, and scheduled for elective short surgical procedures under TIVA were randomly assigned to two groups. Group N received Nalbuphine 0.05 mg/kg, and control Group F received 0.001 mg/kg Fentanyl intravenously before induction. Parameters studied included pain scores, first rescue analgesia, haemodynamics, and side effects. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA, version 19.0 for Windows). Parametric data were analysed using paired and unpaired t-tests.

Results: Data from a total of 60 patients (Group N mean age: 46.9±9.96 years and Group F mean age: 46.6±10.44 years) were collected and analysed. Both groups were comparable in terms of age, Body Mass Index (BMI), mean duration of surgery, and type of surgery (p>0.05). Pain scores on the Visual Analogue Scale (VAS) were not significant upto 15 minutes after surgery, but thereafter, the VAS score was significantly lower in the Nalbuphine group (p-value <0.05). Intraoperative episodes of significant hypotension were observed only in the Fentanyl group (p-value <0.05). The total dose of propofol required was significantly lower in the Fentanyl group (p-value <0.001). The time to the first rescue analgesia requirement (in minutes) was significantly shorter in the Fentanyl group (32.83±28.43) compared to the Nalbuphine group (56.37±25.31). Side effects such as postoperative sedation, nausea, and vomiting were observed in the Fentanyl group (p-value >0.05).

Conclusion: Nalbuphine provided superior postoperative analgesic effects compared to Fentanyl when used as an analgesic component in TIVA. Postoperatively, pain scores were lower, and the time to the first rescue analgesia was longer in the Nalbuphine group.

Keywords: Daycare, Opioids, Propofol, Visual analogue scale

INTRODUCTION

For day care surgeries, the choice of anaesthetic agent should allow for fast and smooth induction, rapid transitions in anaesthesia depth, quick recovery, and minimal postoperative side effects [1,2]. A shorter hospital stay minimises disruptions to the patient's and their relatives' daily activities, thereby reducing the risk of nosocomial infections [3]. Total Intravenous Anaesthesia (TIVA) offers advantages over inhalational anaesthesia, such as avoiding operating room pollution, minimal cardiac depression, reduced neurohormonal responses, decreased oxygen consumption, limited expansion of air-filled spaces within the patient's body, fewer instances of postoperative diffusion hypoxemia, and clear-headed awakening [1,4].

Propofol has proven to be the preferred intravenous anaesthetic agent for day care procedures due to its fast onset of action, rapid recovery, lower incidence of postoperative nausea, and minimal residual central nervous system effects [5].

The administration of opioids as premedication during anaesthesia induction is known to enhance the hypnotic effect of propofol, thus reducing the need for propofol and improving haemodynamic stability [6]. Fentanyl is commonly used as the opioid component in TIVA for inpatient settings due to its high therapeutic index and pharmacokinetic properties, although it may be associated with varying degrees of respiratory depression at the end of surgery [7]. Previous studies have reported the safe use of Nalbuphine in TIVA, highlighting its advantages of cardiovascular stability and rapid recovery [8,9].

Among the opioid group of drugs, Fentanyl or Nalbuphine, when used as a part of balanced anaesthesia, provide analgesia, reduce the response to airway manipulation, ensure haemodynamic stability, and minimise respiratory depression [10,11]. While Fentanyl, tramadol, and Nalbuphine have all been studied and recommended for analgesia during TIVA, there is a lack of direct comparison between these drugs and Fentanyl [12,13]. The present study aimed to establish the reliability and validity of the results when applied to different individuals and settings, address the limitations of previous research, and generalise the results. Additionally, it seeks to inspire new research by building upon previous findings and contributing to the existing body of knowledge in this field.

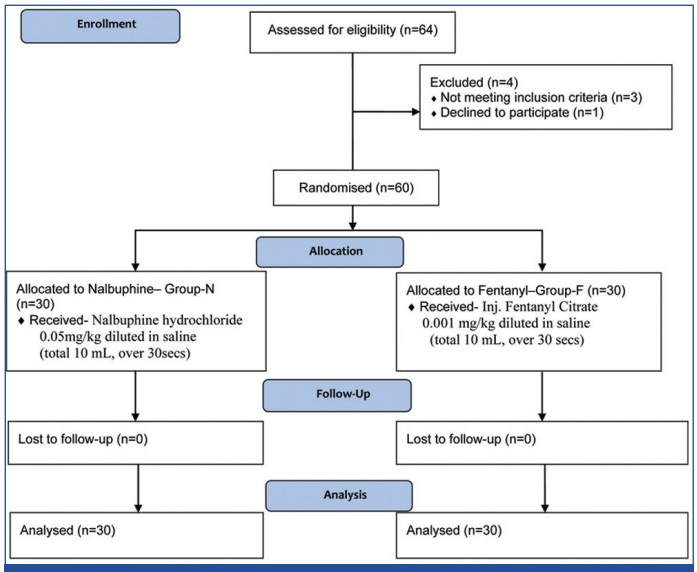
The present study hypothesised the superiority of Nalbuphine when comparing 0.001 mg/kg Fentanyl and 0.05 mg/kg Nalbuphine as premedication for postoperative analgesia, suppression of haemodynamic responses, and recovery profile in short surgical procedures.

MATERIALS AND METHODS

The present double-blind randomised controlled study was conducted at the Gujarat Cancer and Research Institute in Ahmedabad, Gujarat, India, from July 2022 to January 2023. The study was approved by the institutional ethical committee (IRC/12/2020/4740), and all participants provided prior written informed consent.

Inclusion and Exclusion criteria: The study included 60 patients belonging to ASA Grade 1 or 2, scheduled for surgical procedures lasting 30 minutes or less in the day care unit, without the need for muscle relaxants. Patients on sedatives or opioid medication, with a history of psychiatric or neurological diseases, or with allergies to any study drug were excluded.

The subjects were randomised into two groups using sealed envelopes [Table/Fig-1]. To ensure blindness, coded syringes prepared by anaesthetists not involved in the study were used, and those recording and assessing patients postoperatively were also blinded.



[Table/Fig-1]: Consolidated Standards of Reporting Trails (CONSORT) flowchart chart.

Sample size calculation: The sample size calculation was based on the Hardy-Weinberg principle, using the formula $n=4pq/E^2$ [14]. The prevalence of short surgical procedures (considered as 'p') was estimated to be 60%, with an allowable error (E) of 30% of the prevalence. The prevalence value was 60%, and the allowable error was calculated accordingly. By applying the formula, it was determined that 24 patients were needed for each group. However, to account for potential dropouts, 30 patients were included in each group, resulting in a total of 60 patients.

Study Procedure

Preanaesthetic consultations were conducted for all patients, including detailed history, examination, and necessary investigations. After confirming nil by mouth status, patients were transferred to the operating table, and standard monitors were attached. Intravenous access was secured, and baseline vital signs were recorded. Premedication was administered to all patients, including Inj. Glycopyrrolate 0.004 mg/kg, Inj. Ondansetron 0.01 mg/kg, and Inj. Ranitidine 1 mg/kg intravenously.

Both groups received their respective study drugs five minutes before anaesthesia induction:

1) Group N: Inj. Nalbuphine hydrochloride 0.05 mg/kg diluted in saline (total 10 mL, over 30 secs) [5].
2) Control Group F: Inj. Fentanyl Citrate 0.001 mg/kg diluted in saline (total 10 mL, over 30 secs) [5].

Patients received 100% oxygen at 8 L/min via a face mask attached to a Bain's (Mapleson D) circuit with a 2 L reservoir bag for 2-3 minutes before induction. Anaesthesia was induced with Inj. Propofol 2 mg/kg with 2% lidocaine 2 mL intravenously, slowly administered over 30 seconds. Additional doses of propofol (20 mg increments) were given if required.

Intraoperatively, the depth of anaesthesia was assessed by observing a variation of more than 20% above or below the preoperative Systolic Blood Pressure (SBP) or Heart Rate (HR). If lacrimation occurred during anaesthesia, a supplemental bolus of propofol 20 mg was given. Patients breathed spontaneously with 100% O_2 via a mask, and Intermittent Positive Pressure Ventilation (IPPV) was administered if required. Ringer lactate was administered during the procedure. After the surgery, propofol infusion was stopped. Patients were shifted to the recovery room once they were able to follow verbal commands, and this time was considered as time 'zero' for calculating the recovery time. Recovery time was calculated as the time taken to achieve a modified Aldrete score ≥9. Any emergence events such as breathe holding, coughing, restlessness, or shivering were recorded. Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), mean blood pressure, SpO_2, and respiratory rate were recorded at various time intervals.

The primary outcome variable was to compare the analgesic effect between Fentanyl and Nalbuphine, while the secondary outcome was to study the haemodynamic responses and recovery profile. Postoperative pain was assessed using the Visual Analogue Scale (VAS) score, where '0' represented no pain and '10' represented the worst imaginable pain. When the VAS score was recorded as ≥4, Inj. Diclofenac 75 mg was administered intravenously as a rescue analgesic. Incidences of side effects were also noted.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS Inc., Chicago, IL, USA, version 19.0 for Windows. Parametric data were analysed using paired and unpaired t-tests. Qualitative or categorical variables were compared using the Chi-square test or Fisher's-exact test. All statistical tests were two-sided and were conducted at a significance level of $\alpha=0.05$.

RESULTS

The present study included 60 adult patients classified as ASA 1 and 2 who underwent short surgical procedures. They were randomly assigned to two groups, with 30 patients in each group. [Table/Fig-2] demonstrates that both groups were comparable in terms of age, sex, BMI, mean duration of surgery, and type of surgery. There was no statistical difference between the groups ($p>0.05$). To ensure uniformity, present study focused on limited types of procedures, specifically peripheral surgeries that did not require muscle relaxants in either group.

Parameters		Group N (n=30)	Group F (n=30)	p-value
Age (years)		46.9±9.96	46.6±10.44	0.91
Gender (Male/Female)		16/14	16/14	1
BMI		20.75±1.56	21.41±1.96	0.14
Duration of surgery (Minutes)		26.3±3.62	24.53±5.81	0.15
Type of surgery	Urethral stricture dilatation	5	5	1
	Orchidectomy	5	5	1
	D&C	6	4	0.73
	EUA and biopsy of cervix	4	6	0.73
	UGI scopy	6	4	0.73
	Colonoscopy	4	6	0.73

[Table/Fig-2]: Demographic data (Student's t test).
*BMI: Body mass index; D&C: Dilatation and Curettage; EUA: Examination under anaesthesia, UGI scopy: Upper gastrointestinal endoscopy

The pulse rate was comparable between the two groups at baseline and during the procedure depicated in [Table/Fig-3]. The pulse rate in the Nalbuphine group remained slightly higher compared to the Fentanyl group, but this difference was not statistically significant (p-value >0.05).

Time	Group N	Group F	p-value
Baseline (0)	89.16±7.94	86.43±9.75	0.23
3 min	90.03±5.94	90.2±8.09	0.24
5 min	91.96±7.15	89.36±5.34	0.09
10 min	89.2±7.13	86.63±7.24	0.17
15 min	88.8±7.17	87.69±7.71	0.58
30 min	90.04±5.84	87.73±8.03	0.1

[Table/Fig-3]: Comparison of pulse rate (min) at induction and intraoperative period (Student's t-test).

During the intraoperative period, the mean blood pressure at three minutes, five minutes, and 10 minutes was significantly lower in the Fentanyl group compared to the Nalbuphine group (p-value=0.0017, 0.0021, and 0.0023, respectively) [Table/Fig-4]. For the rest of the time, the mean blood pressure was comparable between both groups.

Time	Group N	Group F	p-value
Baseline (0 min)	95.32±4.08	96.82±6.58	0.32
3 min	93.95±3.7	85.7±4.05	0.0017*
5 min	95.45±3.53	86.7±3.63	0.0021*
10 min	96.67±5.3	84.4±3.53	0.0023*
15 min	94±4	93.9±4.5	0.05
30 min	89.2±4.96	87.1±1.01	0.14

[Table/Fig-4]: Comparison of mean blood pressure (mmHg) at induction and intraoperative period.
(Student t-test, p-values with *are significant)

The SpO_2 levels were comparable in both groups at baseline and during the intraoperative peroid [Table/Fig-5].

The requirement of Propofol was significantly higher in the Nalbuphine group (p-value <0.05) [Table/Fig-6]. The requirement for the first rescue analgesia was significantly earlier in the Fentanyl group (p-value <0.05), while the recovery profile, assessed using the modified Aldrete score, remained comparable in both groups (p-value=0.1).

Time	Group N	Group F	p-value
Baseline (0 min)	99.36±0.96	99.26±1.01	0.69
3 min	99.60±0.67	99.84±0.55	0.21
5 min	99.53±0.67	99.78±0.59	0.29
10 min	99.43±0.62	99.84±0.40	0.05
15 min	99.55±0.57	99.82±0.40	0.07
30 min	99.57±0.67	99.87±0.35	0.13

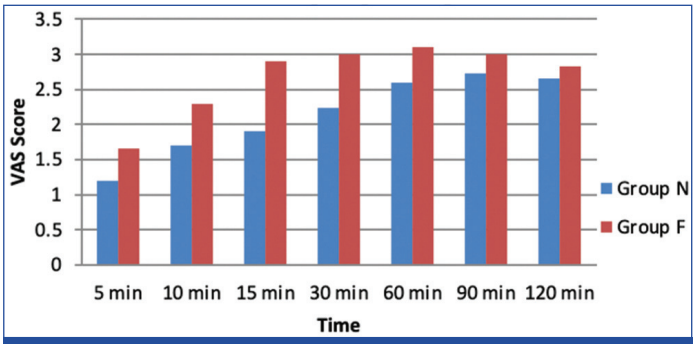
[Table/Fig-5]: Comparison of SpO_2 (in %) at induction and intraoperative period.
(Student t-test, p-values with *are significant)

Parameters	Group N	Group F	p-value
Total dose of propofol required (mg)	609.66±43.11	568.33±40.83	0.00036*
Requirement of 1st rescue analgesia (min)	56.37±25.31	32.83±28.43	0.046*
Time to achieve modified aldrete score ≥9 (min)	10.00±4.39	11.70±3.58	0.1

[Table/Fig-6]: Comparison of intraoperative propofol, postoperative analgesia and recovery.
(Student t-test, p-value marked as *is significant)

In the postoperative period, pulse rate, mean blood pressure, SpO_2, and respiratory rate were observed at five minutes, 10 minutes, 15 minutes, 30 minutes, 60 minutes, 90 minutes, and 125 minutes, and they were found to be comparable in both groups (p-value >0.05).

Until ten minutes after shifting to the recovery room, the VAS score was comparable in both groups [Table/Fig-7]. However, there was a subsequent rise in the VAS score at 15 minutes, 30 minutes, and 60 minutes in Group F, which was statistically significant (p-value=0.00056, 0.00048, and 0.026, respectively).



[Table/Fig-7]: Comparison of VAS score in postoperative period.

[Table/Fig-8] reveals that among patients receiving Nalbuphine, only 3.33% experienced episodes of intraoperative bradycardia, while 3.33% experienced postoperative sedation. In the Fentanyl group, 6.66% experienced episodes of intraoperative bradycardia, postoperative nausea, and sedation, while 3.33% of patients had coughing and hypotension. None of the patients experienced vomiting, pruritus, dizziness, or any allergic reactions.

Side-effects	Group N n (%)	Group F n (%)	p-value
Nausea	0	2 (6.66%)	0.49
Coughing	0	1 (3.33%)	1
Hypotension	0	1 (3.33%)	1
Bradycardia	1 (3.33%)	2 (6.66%)	1
Postoperative sedation	1 (3.33%)	2 (6.66%)	1

[Table/Fig-8]: Intraoperative and postoperative side-effects.
(Student t-test, n=number of patients)

DISCUSSION

A day care procedure is an elective procedure performed on selected patients, in which the patient is operated on and discharged home on the same day [15]. In day care procedures, a discharge scoring system is designed to address the readiness of patients to go home in a simple and clear manner [16]. For day care procedures, it is recommended to use anaesthetics that provide rapid and smooth induction, allow fast changes in intensity while maintaining anaesthesia, and promote early recovery with minimal postoperative adverse effects [17].

General anaesthesia with Total Intravenous Anaesthesia (TIVA) is widely accepted due to the availability of short-acting hypnotics, opioids, and improved intravenous systems. In the case of ambulatory patients, short-acting drugs are necessary for TIVA to ensure prompt recovery. Propofol is a logical choice as it allows for rapid changes in anaesthetic depth, has no cumulating effect, and enables rapid clearheaded awakening [1].

When a narcotic agent is added to propofol, it reduces the dose of intravenous anaesthetic, resulting in fewer adverse effects. Ideally, the narcotic should have a short half-life, allowing for rapid changes in anaesthetic depth and quick recovery. Fentanyl and various other narcotics have been studied and recommended for analgesia during TIVA, but their effects have not been directly compared with Fentanyl [12,13].

Nalbuphine, which has chemical similarity to naloxone, provides a ceiling effect for respiratory depression [8]. Fentanyl is commonly used as an anaesthetic adjuvant in TIVA for inpatient settings due to its high therapeutic index and pharmacokinetic properties. However, there are chances of variable amounts of respiratory depression

at the end of surgery [18]. The present study was conducted to examine the haemodynamic effects and postoperative pain relief provided by Nalbuphine and Fentanyl when added to TIVA.

During the intraoperative period, both Nalbuphine and Fentanyl initially caused a fall in blood pressure and heart rate, followed by an increase in blood pressure and heart rate in the Nalbuphine group. In the Fentanyl group, heart rate and blood pressure remained lower than baseline but within 20% of baseline. Only one patient (3.33%) in present study experienced an episode of hypotension (>20% of baseline) with Fentanyl, which was treated with a 250 mL Ringer's lactate bolus.

The initial fall in all haemodynamic parameters in the Nalbuphine group is due to its strong and predominant kappa agonist action. Surgical stress-induced sympathoadrenal stimulation causes a rise in haemodynamic parameters [19]. As a pure mu agonist, Fentanyl causes a decrease in arterial blood pressure, heart rate, systemic vascular resistance, and blood catecholamine levels. It also depresses myocardial contractility and decreases cardiac workload, which may explain the steady fall in all haemodynamic parameters in the Fentanyl group [10]. These mechanisms support results, which are consistent with a study by Khan FA and Hameedullah, comparing Nalbuphine and Fentanyl in TIVA for laparoscopic cholecystectomy [12].

Changes in mean arterial pressure reflect the autoregulatory responses of the heart, brain, and kidneys. The Fentanyl group reported a greater decrease compared to the Nalbuphine group at three minutes, five minutes, and ten minutes after administering the study drugs. The difference was statistically significant (p-value <0.05). The present study results align with those of Shah RJ et al., who compared Nalbuphine and Fentanyl in TIVA for laser surgeries of the larynx [20]. A study by Joshi S and Jacob SS, also reported similar haemodynamic changes when comparing Fentanyl and Nalbuphine in TIVA [5].

Pulse rate and blood pressure changes have always been a better predictors of the stress response to surgery. Reddy BAP et al., concluded that ketamine provided better haemodynamic stability compared to Fentanyl, along with pleasant and safe pain relief and only a few untoward side effects [21]. Nalbuphine was compared to Fentanyl by Wang P et al., who reported comparable haemodynamic stability [22]. Similar results were reported by Khan FA and Hameedullah, when comparing Nalbuphine with buprenorphine in TIVA [12]. Siddiqui KM and Chohan U, were able to reproduce similar results regarding comparable haemodynamic stability with Nalbuphine and tramadol in TIVA for dilation and evacuation procedures [13].

With regard to the study requirements, the total dose of propofol was significantly higher in the Nalbuphine group compared to the Fentanyl group, likely due to the hypotension observed in the Fentanyl group, which may worsen with a higher dose of propofol. Therefore, the Nalbuphine group required higher doses of propofol to maintain an adequate level of sedation and haemodynamic stability. This reduced propofol requirement with Fentanyl is supported by another study by Siddiqui TH et al., where they compared Fentanyl with dexmedetomidine [18]. However, opposing results were noted by Turgut N et al., who observed a higher dose of propofol requirement in the Fentanyl group compared to the dexmedetomidine group in TIVA [23].

In present study, authors observed that the requirement for rescue analgesia was significantly earlier in the Fentanyl group (p-value 0.046), suggesting better postoperative analgesic potency of Nalbuphine compared to Fentanyl. A study by Khan FA and Hameedullah, in 2002 also observed a lower analgesic requirement in the recovery room in the Nalbuphine group [12]. When Nalbuphine was compared with morphine by Akshat S et al., it was found that Nalbuphine provided less intraoperative analgesia compared to morphine but had equivalent postoperative analgesia [24]. The equivalent postoperative analgesic effect of Nalbuphine and Fentanyl was demonstrated by Wang P et al., [22]. Shah RJ et al., also found similar results when comparing Nalbuphine and Fentanyl in laser surgeries of the larynx under TIVA with intravenous propofol [20]. Deng C et al., demonstrated that Nalbuphine provides adequate analgesia and less respiratory depression compared to sufentanyl [25].

In present study, the time to achieve a modified Aldrete score ≥9 was prolonged in the Fentanyl group, but the difference was not statistically significant (p-value 0.1), suggesting a comparable recovery profile with both drugs. Khan FA et al., also observed a comparable recovery profile when comparing Nalbuphine with buprenorphine [23]. Regarding postoperative sedation, only two patients (6.66%) in the Fentanyl group had postoperative sedation evaluated by the Ramsey sedation score, while in the Nalbuphine group, only 1 (3.33%) experienced postoperative sedation. Nalbuphine produces less respiratory depression than other opioids at equivalent analgesic doses, partly due to its ceiling effects where respiratory depression does not increase with the dose. Chung W et al., observed respiratory depression leading to dangerous consequences in the recovery room with the use of pure agonist opioids. On the contrary, Nalbuphine, being an agonist-antagonist opioid, activates supraspinal and spinal kappa receptors, causing less respiratory depression [26]. Haytural C et al., showed that opioids used as adjuvants to propofol provide more effective and reliable sedation for short procedures; however, they can still cause respiratory depression leading to hypoxia [27]. Wang P et al., also found similar results when comparing Nalbuphine with Fentanyl in propofol sedation for Endoscopic Retrograde Cholangiopancreatography (ERCP), where they observed an increased incidence of respiratory depression in the Fentanyl group [22]. In present study, authors found a similar incidence of respiratory depression, which was 6.66% in the Fentanyl group.

Limitation(s)

A possible limitation of the study could be that the authors only monitored patients in the postoperative period for two hours, so any delayed side effects of the study drugs could not be observed. Additionally, the study only compared opioids with propofol, and the interaction of opioids with other induction agents may be different.

CONCLUSION(S)

Nalbuphine provided superior postoperative analgesia compared to Fentanyl. It resulted in lower pain scores and reduced analgesic requirements in the postoperative period compared to Fentanyl, thus supporting the hypothesis. The requirement for the first rescue analgesic was delayed in the Nalbuphine group. Nalbuphine was associated with a lower incidence of postoperative sedation. It provided acceptable intraoperative and postoperative haemodynamic stability. Nalbuphine can be considered a reasonable alternative to Fentanyl for patients undergoing short surgical procedures under TIVA.

REFERENCES

[1] Ahuja H, Abraham V, Abraham J, Liddle D. Ideal anesthetic agents for day-care gynecological procedures: A clinical trial comparing thiopentone with ketamine as adjuncts to propofol. Adv Biomed Res. 2015;4:81.
[2] Bailey CR, Ahuja M, Bartholomew K, Bew S, Forbes L, Lipp A, et al. Guidelines for day-case surgery 2019. Guidelines from the Association of Anaesthetists and the British Association of Day Surgery. Anaesthesia. 2019;74(6):778-92.
[3] Patel N, Patel MM, Patel MV. Comparison of cardiovascular and respiratory changes during induction, maintenance, and recovery with sevoflurane and propofol in paediatric day care anaesthesia. J Chem Pharm Res. 2013;5(11):562-65.
[4] Bajwa SJ, Bajwa SK, Kaur J. Comparison of two drug combinations in total intravenous anaesthesia: Propofol-ketamine and propofol -fentanyl. Saudi J Anaesth. 2010;4(2):72-79.
[5] Joshi S, Jacob RR. Comparative study of nalbuphine and fentanyl for total intravenous anaesthesia in short surgical procedures. Indian J Anaesth Analg. 2020;7(1) (Part-II):347-53.
[6] Mandal M. Opioids as co-induction agents-the pros and cons. Int J Crit Illn Inj Sci. 2017;7(2):77-78.
[7] Matsuda C, Sato J. Postoperative Apnea induced by fentanyl and other multiple respiratory-modulating factors. Open Journal of Anaesthesiology. 2014;4(8):177-82.

[8] Hari Prasad K, Ram Kumar PA, Rajagokilam R, Varadarajan V. A comparative study of analgesic potential of nalbuphine versus fentanyl during general anaesthesia. International Journal of Contemporary Medical Research. 2016;3(10):2815-18.
[9] Chawda PM, Pareek MK, Mehta KD. Effect of nalbuphine on haemodynamic response to orotracheal intubation. J Anaesthesiol Clin Pharmacol. 2010;26(4):458-60.
[10] Khanday SB, Mir AH, Sofi KP, Lone AQ, Shah AN. Evaluation and comparison of fentanyl versus nalbuphine for attenuation of hemodynamic response to laryngoscopy and endotracheal intubation in general anaesthesia. Anaesth Essays Res. 2019;13(1):111-18.
[11] Chen C, Tang W, Ye W, Zhong W, Li Y. ED50 of propofol combined with nalbuphine on the sedative effect in painless hysteroscopy. Pain Ther. 2021;10(2):1235-43.
[12] Khan FA, Hameedullah. Comparison of fentanyl and nalbuphine in total intravenous anaesthesia (TIVA). J Pak Med Assoc. 2002;52(10):459-565.
[13] Siddiqui KM, Chohan U. Tramadol versus nalbuphine in total intravenous anaesthesia for dilatation and evacuation. J Pak Med Assoc. 2007;57(2):67-70.
[14] Solanki NM, Engineer SR, Vecham P. Comparison of epidural versus systemic analgesia for major surgeries in neonates and infants. J Clin Neonatol. 2017;6(1):23-28.
[15] Lee JH. Anaesthesia for ambulatory surgery. Korean J Anaesthesiol. 2017;70(4):398-406.
[16] Valasareddy SK, Segaran SK, George SK, Ranjan R, Titu OG, Anil PR. Recovery profile using modified aldrete score in post anaesthesia care unit after sevoflurane or desflurane anaesthesia: A prospective randomised study. J Clin of Diagn Res. 2018;12(9):UC01-UC04.
[17] Shetty A, Raveendra US. Anaesthesia for day care surgery. Nitte University Journal of Health Science. 2015;5(2):97-103.
[18] Siddiqui TH, Choudhary N, Kumar A, Kohli A, Wadhawan S, Bhadoria P. Comparative evaluation of dexmedetomidine and fentanyl in total intravenous anaesthesia for laparoscopic cholecystectomy: A randomised controlled study. J Anaesthesiol Clin Pharmacol. 2021;37(2):255-60.
[19] Singh M. Stress response and anaesthesia altering the peri and post-operative management. Indian J Anaesth. 2003;47(6):427-34.
[20] Shah RJ, Kapdi M, Prajapati V, Joshi Y. Comparison of nalbuphine/fentanyl as opioid adjuvant to propofol based TIVA for laser surgery of larynx. International Journal of Science and Research (IJSR). 2021;10(4):741-46.
[21] Reddy BAP, Girija Kumari B, Ananta KV. A comparative study of ketamine and propofol versus fentanyl and propofol in total intravenous anaesthesia for short surgical procedures. Medpulse International Journal of Anaesthesiology. 2019;12(3):238-243.
[22] Wang P, Chen Y, Guo Y, Cao J, Wang H, Mi W, et al. Comparison of propofol-nalbuphine and propofol-fentanyl sedation for patients undergoing endoscopic retrograde cholangiopancreatography: A double-blind, randomized controlled trial. BMC anesthesiology. 2022;22(1):47.
[23] Turgut N, Turkmen A, Gökkaya S, Altan A, Hatiboglu MA. Dexmedetomidine-based versus fentanyl-based total intravenous anesthesia for lumbar laminectomy. Minerva Anestesiol. 2008;74(9):469-74. PMID: 18762754.
[24] Akshat S, Ramachandran R, Rewari V, Chandralekha, Trikha A, Sinha R. Morphine versus nalbuphine for open gynaecological surgery: A randomised controlled double blinded trial. Pain Research and Treatment. 2014;204:727952.
[25] Deng C, Wang X, Zhu Q, Yanming Kang, Yang J, Wang H. Comparison of nalbuphine and sufentanyl for colonoscopy: A randomised controlled trial. PLoS ONE. 2017;12(12):e0188901
[26] Chung W, Ko Y, Yoon H, Lee J. Effect of Nalbuphine on hemodynamic values and bispectral indices during Total Intravenous Anaesthesia (TIVA) with propofol and remifentanil. Korean J Anesthesiol. 2007;53(6):S7-11.
[27] Haytural C, Aydinli B, Demir B, Bozkurt E, Parlak E, Disibeyaz S, et al. Comparison of propofol, propofol-remifentanil, and propofol-fentanyl administrations with each other used for the sedation of patients to undergo ERCP. Biomed Res Int. 2015:465465.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 12, 2023
- Manual Googling: Oct 13, 2023
- iThenticate Software: Nov 03, 2023 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 08, 2023**
Date of Peer Review: **Sep 29, 2023**
Date of Acceptance: **Nov 06, 2023**
Date of Publishing: **Dec 01, 2023**