

### **DURATION OF POSTOPERATIVE ANALGESIA WITH INTRAVENOUS NALBUPHINE VERSUS INTRAVENOUS BUTORPHANOL IN PATIENTS UNDERGOING SHORT SURGICAL PROCEDURES UNDER TIVA.**

#### **ABSTRACT:**

**Aims And Objectives:** To compare the duration of post operative analgesia of nalbuphine 0.3mg/kg IV and butorphanol 0.04mg/kg IV in patients posted for short surgical procedures under TIVA. Also to observe the sedation score as well as the side effects like nausea, emesis, pruritis, hypotension, respiratory depression.

**Materials And Methods:** By closed envelope technique, sixty female patients of ASA Class I and II, aged 20-60 years, who were posted for short gynaecological surgeries under TIVA were randomly allocated into two groups: Group N (nalbuphine) and Group B (butorphanol). Just prior to surgery, Group N patients got IV Nalbuphine 0.3 mg/kg, while Group B patients received IV Butorphanol 0.04 mg/kg. Patients were asked to rate their pain intensity on a VAS scale in the course of the postoperative period, and the duration of postoperative analgesia was compared between the two groups. The Modified Ramsay sedation scale was exercised to assess sedation at the time of pain complaint, and patients were additionally monitored for 24 hours post the surgery for any adverse or side effects.

**Results:** In group N, 63.33% of patients had duration of pain relief ranging 31-50 minutes, with mean duration of analgesia being  $46.333 \pm 2.061$ . In group B, 60% of patients had duration of pain relief ranging from 11-30 minutes, with mean duration being  $19.167 \pm 1.68$  minutes. In group N, 63.33% of patients had score for sedation as 3 and rest (36.67%) had a score for sedation as 2. In group B, 80% of patients had a score for sedation as 2 and rest (20%) had a score for sedation as 1.

**Conclusion:** When compared to IV Butorphanol, intravenous Nalbuphine delivers a more effective post-operative analgesia with better sedation. IV Nalbuphine is recommended for post operative analgesia in patients undergoing short surgical procedures. Both the drugs did not cause any side effects.

**Keywords:** Postoperative analgesia, intravenous, Nalbuphine, Butorphanol

#### **INTRODUCTON:**

TIVA (Total intravenous anaesthesia) is a type of general anaesthetic used for short surgical procedures that involves a mix of drugs administered solely through the intravenous route, in the absence of inhalational anaesthetics (gas anaesthesia)<sup>1</sup>

Some of the potential benefits of total intravenous anaesthesia (TIVA) include reduced nausea and vomiting post operatively, more anticipated and prompt recovery, significant hemodynamic stability, hypoxic pulmonary vasoconstriction is preserved, lowering in intra cerebral pressure (ICP), as well as a lower risk of organ toxicity.

When utilised in circumstances where post-operative pain control is essential, TIVA (total intravenous anaesthesia) is merely an anaesthetic method.<sup>2</sup>

TIVA can be carried out using a single medication or in combination with other IV drugs. Hypnotics and short-acting opioids are two of the most regularly used medication classes.<sup>3</sup>

Propofol is the sole active intravenous drug (hypnotic) currently appropriate for anaesthesia induction as well as its maintenance. Many advantages of propofol-based TIVA include quick recovery of psychomotor function and consciousness, antiemetic action, and a reduced incidence of postoperative nausea and emesis.<sup>4</sup>

Many analgesics are used in premedication but the post operative analgesia is of short duration. Patient complaints of pain in post operative recovery room. Post operative pain is a troublesome and hence we need to take care of it.

For the majority of surgery patients, pain perception is a serious concern. Postoperative pain<sup>5</sup> is a type of acute pain that triggers a systemic stress response<sup>6</sup>, which includes neuroendocrine, immunological, and haematological reactions. Catabolism of stored body fuels is the overall metabolic effect.

Despite advances in pain relief management, most of the patients carry on to suffer from excruciating pain following surgery<sup>7</sup>. The novel anaesthetic aims not just in pain reduction but it also aims at the betterment of the quality of life of the sufferer and his/her speed recovery with lowering medical costs.

For a long time, opioids have been the go-to treatment for immediate postoperative pain, especially moderate to severe pain. Though, mu agonists such as morphine can cause major adverse effects such as delayed respiratory depression pruritus, increased frequency of micturition, poor bladder control (retention), nausea, vomiting, etc. These side effects could make patients uncomfortable and lengthen their stay in the hospital, limiting their effectiveness as a post-operative pain reliever.

Both Butorphanol and Nalbuphine are partial agonist-antagonists, acting as agonists on the kappa receptor while acting as antagonists or partial agonists on the mu receptor. Analgesia with less undesired side effects, such as respiratory depression, are among the advantages of partial agonists. They can be administered intramuscularly, intravenously, epidurally, or transnasally. When compared to powerful opioids like morphine or fentanyl, they are commonly available and unrestricted.

## **AIMS AND OBJECTIVES**

**AIM:**To assess the efficacy of inj. Nalbuphine given intra venously with Intra venous inj. butorphanol in patients posted for short surgical procedures under Total Intravenous anaesthesia (TIVA)

### **OBJECTIVES:**

#### **PRIMARY OBJECTIVE**

To compare the duration of post operative analgesia of intra venous nalbuphine 0.3mg/kg and intra venous butorphanol 0.04mg/kg in patients posted for short surgical procedures under Total Intravenous anaesthesia (TIVA)

#### **SECONDARY OBJECTIVES**

To observe

- 1) The sedation score
- 2) Side effects like nausea, emesis, sedation, shivering, pruritis, depressed respiration.

## **MATERIAL AND METHODS**

After Institutional Ethical Committee clearance, the study was done in the Department of Anaesthesiology, Acharya Vinoba Bhave Rural Hospital, JNMC, Sawangi (Meghe), Wardha district, Maharashtra.

Sixty female patients undergoing short gynecological procedures under Total Intravenous anaesthesia (TIVA) were allocated randomly into two equal groups of 30 each by closed envelope technique. Group N, who were given intravenous Inj. Nalbuphine 0.3mg/kg and Group B, who were given intravenous Inj. Butorphanol 0.04mg/kg

After preoperative/ pre anaesthetic check up, patients were enrolled in the study as per following criteria

**Criteria for inclusion:**

1. Patients classified as ASA grade I and II
2. Female patients in age group of 20-60 years
3. Posted for surgeries short gynaecological procedures under Total Intravenous anaesthesia (TIVA)
4. Patients who gave consent to participate in study

**Criteria for exclusion:**

1. Patients who are allergic to the drugs.
2. Patients who are on
  - oral anticoagulant therapy.
  - neuroleptic agent.
  - Mono amino oxidase inhibitor.
3. Patients with
  - History of epilepsy/ seizure.
  - Increased intracranial tension.
  - History of motion sickness.
  - History of opioid use over the last 1 month.
4. Patients not willing to participate in study
5. Intraoperative sedation or analgesic given Intravenously or intra muscularly

On the day of operation, an informed written consent was obtained. The Visual analogue pain scale was taught to all of the patients (VAS) and pain descriptor terms in a language they understood..

The visual analogue scale, which is described below, was used to assess pain.

The Visual Analogue Scale (VAS) is a 10-centimeter line with two end points: "no pain" and "pain as bad as it gets." On this line, the patient is requested to make a mark reflecting the severity of the pain. The VAS score is calculated by measuring the distance in centimeters between the end of the scale that indicates "no pain" and the point indicated by the patient.<sup>8</sup>

**Fig 1: VISUAL ANALOGUE SCALE**

No pain 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10 Pain as bad as it can be

On the operating room table, baseline heart rate (HR), blood pressure (BP), respiration rate (RR), SPO<sub>2</sub> and temperature (in degree celcius) were noted.

Patients in both the groups were given intravenous Inj. Glyco 0.2mg, intravenous Inj. Midaz 1mg and study drug intravenously (nalbuphine or butorphanol) and intravenous Inj. Propofol 2mg/kg for induction and supplementation as required through out the procedure.

No other analgesics or sedatives drug were given intraoperatively. No inhalation agents were used intraoperatively.

Intraoperative haemodynamic monitoring was done as per conventional method.

Patients were sent to a post-operative recovery room after the surgery, where vital signs such as baseline heart rate (HR), blood pressure (BP), respiration rate (RR), SPO<sub>2</sub> and temperature (in degree celcius) were checked every 30 minutes.

When the patient complains of pain, VAS>4, the duration of postoperative analgesia was documented. (In the recovery room, the time interval between the onset of analgesia and the patient complaining of pain (i.e. VAS score >4) is regarded as the duration of analgesia.)

Chart 1: Sedation assessment was done using the 'Modified Ramsay' scale for sedation, which is as follows.<sup>9</sup>

Definition	Score
Anxiousness, restlessness, agitation	01
Cooperative, orientate, calm	02
Responds only to orders	03
Response on light glabellar tapping being brisk or strident noise	04
Response on light glabellar tapping being sluggish or strident noise	05
Un responsiveness	06

Any adverse effects like nausea, emesis, pruritis, hypotension, respiratory depression and others were recorded.

#### OBSERVATION:

- a) **Duration Of Analgesia:** When the patient complains of pain, VAS>4, the duration of postoperative analgesia was documented.

63.33% of patients in group N were having a range of 31-50 minutes of analgesic duration, with a mean analgesic duration being  $46.333 \pm 2.061$  minutes with minimum of 21-30 minutes analgesic duration was seen in 10% of group N participants and a maximum analgesic duration of 61-70 minutes was seen in 6.67% of group N participants.

60% of patients in group B were having a range of 11-30 minutes of analgesic duration, with a mean analgesic duration being  $19.167 \pm 1.68$  minutes with minimum analgesic duration of 5-10 minutes was seen in 30% of group B participants and a maximum analgesic duration of 31-40 minutes was seen in 10% of group N participants.

**Table 1: Analgesic duration**

Analgesic duration (MINUTES)	Group N No of cases (%)	Group B No of cases (%)
5-10	0 (0)	9 (30)
11-20	0 (0)	12 (40)
21-30	3 (10)	6 (20)
31-40	11 (36.67)	3 (10)
41-50	8 (26.66)	0 (0)
51-60	6 (20)	0 (0)
61-70	2 (6.67)	0 (0)

When comparing groups N and B, a statistical analysis using a student unpaired t-test revealed that group N had a statistically significant increase in analgesia duration. (t=55.9594 with df=31, p<0.0000001)

**b) Assessment of sedation:** It was done using Modified Ramsay sedation

In group N, 63.33% of patients were having a sedation score of 3 and rest (36.67%) were having a sedation score of 2.

In group B, 80% of patients were having had a sedation score of 2 and rest (20%) had a sedation score of 1.

**Table 2: Sedation score**

Sedation score	Group N Number of cases (in %)	Group B Number of cases (in %)
1	0 (0)	6 (20)
2	11 (36.67)	24 (80)
3	19 (63.33)	0 (0)
4	0 (0)	0 (0)
5	0 (0)	0 (0)
6	0 (0)	0 (0)

**c) Side effects:**

*Patients were also observed for 24 hours post operatively for any side effects .None of the patients participated in the study showed any of the side effects like nausea , vomiting, pruritis, respiratory depressions , hypotension or others.*

**Result and Discussion:**

In our study, 63.33% of patients in group N were having a range of 31-50 minutes of analgesic duration , with a mean analgesic duration being  $46.333 \pm 2.061$  minutes with minimum of 21-30 minutes analgesic duration was seen in 10% of group N participants and a maximum analgesic duration of 61-70 minutes was seen in 6.67% of group N participants. 60% of patients in group B were having a range of 11-30 minutes of analgesic

duration, with a mean analgesic duration being  $19.167 \pm 1.68$  minutes with minimum analgesic duration of 5-10 minutes was seen in 30% of group B participants and a maximum analgesic duration of 31-40 minutes was seen in 10% of group N participants

Regarding the sedation, In group N, 63.33% of patients were having a sedation score of 3 and rest (36.67%) were having a sedation score of 2. In group B, 80% of patients were having a sedation score of 2 and rest (20%) had a sedation score of 1.

Both the drugs used in our study did not show any of the side effects like nausea, vomiting, pruritis, respiratory depressions, hypotension etc.

Vidhya N et al after comparing the efficacy of butorphanol with nalbuphine for balanced anaesthesia and post-operative analgesia in patients posted for laparoscopic surgery concluded that Butorphanol is more efficacious as an analgesic with better hemodynamic stability than Nalbuphine.<sup>10</sup>

Swapna Banerjee and Shaswat Kumar Pattnaik compared post operative analgesia with epidural nalbuphine, butorphanol and fentanyl in lower abdominal surgeries concluded that fentanyl produces the faster onset of analgesia and Butorphanol gives longer duration of analgesia.<sup>11</sup>

V.V Lokeswari et al compared intra muscular nalbuphine with intramuscular butorphanol for postoperative pain relief concluded that intramuscular nalbuphine group patients were haemodynamically stable with better post operative analgesia.<sup>12</sup>

Praveen P.V.V.S.B et al when IM nalbuphine, butorphanol, and pentazocine were tested for post-operative analgesia in participants having abdominal hysterectomy, concluded that nalbuphine and butorphanol offered superior analgesia than pentazocine<sup>13</sup>

JJ Wang et al. compared analgesic efficacy of epidural butorphanol, nalbuphine, Meperidine and morphine concluded that both epidural nalbuphine and butorphanol demonstrated a very similar analgesic profile and when compared to morphine they exhibit faster onset of action with shorter duration.<sup>14</sup>

Viviane et al after comparing nalbuphine and butorphanol, either alone or in conjunction with acepromazine, it was found that butorphanol provided superior sedation than nalbuphine when used alone or in combination with acepromazine.<sup>15</sup>

Zucker et al in 1987 compared nalbuphine with butorphanol to assess the respiratory depression in patients undergoing procedure under general anaesthesia. They concluded that butorphanol caused significantly pronounced respiratory depression compared to that caused by nalbuphine<sup>16</sup>

J Malek et al in 1988 compared the post-operative analgesic efficacy of injectable Tramadol (100 mg), Butorphanol (2 mg), Nalbuphine (20 mg), and Buprenorphine (0.3 mg) in adult patients who had had cholecystectomy under GA. They came to the conclusion that all of the medicines were effective in the treatment of post-operative pain. Buprenorphine and tramadol had a longer duration of analgesia and fewer side effects than other opioids.<sup>17</sup>

Babu S et al in 2017 did a study for comparing the post operative analgesic quality as well as the side-effect properties of butorphanol and nalbuphine which are epidurally administered as an adjuvant to 0.2 percent ropivacaine, and it was discovered that ropivacaine with nalbuphine administered via thoracic epidural route is more effectual than ropivacaine with butorphanol for instant post operative pain mitigation in patients subjected for exploratory laparotomy under emergency.<sup>18</sup>

Kim DH and Park CH in 1998 conducted a study to find out the analgesic efficacy, dose requirement and adverse reactions of butorphanol and nalbuphine when given via patient controlled analgesia (PCA) along with ketorolac after TAH (total abdominal hysterectomy). They determined that butorphanol and nalbuphine were both effective for PCA for post operative pain relief, and that ketorolac 180 mg with butorphanol 9 mg or nalbuphine 70 mg could be effective for 48-hour pain relief.<sup>19</sup>

Priti M Chawda et al in 2010 investigated the efficacy of nalbuphine in reducing increases in heart rate (HR) and mean arterial pressure in response to laryngo-scopy and oro-tracheal intubation. Patients received a 0.2 mg/kg IV bolus dose of saline or nalbuphine 5 minutes before laryngoscopy. They found that a dose of 0.2 mg/kg of Nalbuphine avoided a significant increase in heart rate (HR) and mean arterial pressure (MAP) during laryngo-scopy and oro-tracheal intubation.<sup>20</sup>

Ahsan-ul-Haq et al in 2005 did a study to see how effective nalbuphine is at preventing heart rate (HR) and blood pressure (BP) increases while laryngo-scopy and oro-tracheal intubation. They came to the conclusion that 0.2 mg/kg of IV Nalbuphine could avoid a significant increase in HR (heart rate) and MAP(mean arterial pressure) during laryngo-scopy and oro-tracheal intubation.<sup>21</sup>

Tariq MA et al in 2014 investigated the effectiveness of nalbuphine in avoiding a haemodynamic response to laryngo-scopy and oro-tracheal intubation. Subjects undergoing general anaesthesia received a 0.2 mg/kg IV bolus dose of saline or nalbuphine 5 minutes before to laryngoscopy. After laryngo-scopy and oro-tracheal intubation, the nalbuphine group had a considerably lower increase in mean arterial pressure (MAP) and heart rate (HR) than the control group.<sup>22</sup>

## Conclusion:

Intravenous Nalbuphine provides longer duration of analgesia and better sedation when compared to intravenous Butorphanol. Both intravenous Nalbuphine and intravenous Butorphanol are safe as no side effects were observed. This study recommends intravenous Nalbuphine as an analgesic for short gynecological procedures under Total intravenous anaesthesia (TIVA).

## REFERENCES:

1. Total intravenous anaesthesia using target controlled infusion – A pocket reference, College of Anesthesiologists, Academy of medicine Malasia (retrieved 07.05.15)
2. Aunac, S., Carlier, M., Singelyn, F., & De Kock, M. (2002). The analgesic efficacy of bilateral combined superficial and deep cervical plexus block administered before thyroid surgery under general anesthesia. *Anesthesia & Analgesia*, 95(3), 746-750.
3. Nora, Fernando Squeff. (2008). Total intravenous anesthesia as a target-controlled infusion: an evolutive analysis. *Revista Brasileira de Anestesiologia*, 58(2), 179-192. Retrieved October 07, 2015, from [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0034-70942008000200011&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-70942008000200011&lng=en&tlng=en). 10.1590/S0034-70942008000200011.
4. Absalom A & Struys M. An Overview of TCI & TIVA. Second Edition., 2011; Gent: Academia Press
5. Joshi G, Ogunnaike B. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiology Clinics of North America*. 2005;23(1):21–36.
6. [2]. J. P. Desborough, "The stress response to trauma and surgery," *British Journal of Anaesthesia*, 2000;85(1):109-117.
7. [3]. Apfelbaum J, Chen, Mehta S, Gan T. Postoperative Pain Experience: Results from a National Survey Suggest Postoperative Pain Continues to Be Undermanaged. *Anesthesia & Analgesia* 2003;97(2):534–540.
8. Kumar P. Methods of clinical pain assesment. In ;A Text Book of Pain first edition, New Delhi; Modern publishers; 2005:43-48.
9. Sciencedirect.com ; 2019 Elsevier B.V.
10. Comparative efficacy of butorphanol versus nalbuphine for balanced anaesthesia and post-operative analgesia in patients undergoing laparoscopic surgery :Vidhya N, Prakash V, Irshad B, V. S. Senthil Kumar

11. A comparative between epidural butorphanol , nalbuphine and fentanyl for post operative analgesia in lower abdominal surgeries ; SWARNA BANERJEE, SHASWAT KUMAR PATTNAIK
12. A comparative study of intra muscular nalbuphine with intramuscular butorphanol for the relief of postoperative pain ; Dr.V.VLokeswari. Dr. B.AnnapurnaSarma, Dr.D.B.V.Madhusudhana Rao.
13. A prospective , randomized , double blind , comparative study of intramuscular nalbuphine hydrochloride, butorphanol tartrate and pentazocine lactate for post operative pain relief following abdominal hysterectomy; Praveen P.V.V.S.B., Vijaya Chandra Reddy Konda , Lohit K
14. Comparative analgesic efficacy of epidural nalbuphine, butorphanol, Meperdine and morphine; JJ Wang, MS Mok and M Lippmann
15. Comparison of the sedative effects of nalbuphine and butorphanol , alone or in combination with acepromazine in dogs ; Viviane et al.
16. Zucker JR, Neuenfeldt T, Freund PR. Respiratory effects of nalbuphine and butorphanol in anesthetized patients. *Anesth Analg*1987;66:879-81.
17. Malek, J., &Pocta, J. (1988). Comparative study of the new analgesics Tramadol, Butarphanol, Nalbuphine and Buprenorphine. *ActaAnaesthesiologicaMelitensis*, 1(6), 6-11.
18. Babu S, Gupta BK, Gautam GK. A comparative study for post operative analgesia in the emergency laparotomies: Thoracic epidural ropivacaine with nalbuphine and ropivacaine with butorphanol. *Anesthesia, essays and researches*. 2017 Jan;11(1):155.
19. Kim DH, Park CH. A effectiveness of butorphanol and nalbuphine as utilized with ketorolac in patient controlled analgesia after total abdominal hysterectomy. *The Korean Journal of Pain*. 1998;11(2):263-7.
20. Priti M Chawda, Mayuresh K Pareek, and Ketan D Mehta.Effect of Nalbuphine on Haemodynamic Response to Orotracheal Intubation. *Journal of anaesthesiology clinical pharmacology*.2010 Oct-Dec; 26(4): 458–460
21. Ahsan-ul-Haq M, Kazmi EH and Rao ZA .Nalbuphine prevents haemodynamic response to endotracheal intubation.*Journal of the College of Physicians and Surgeons--pakistan : JCPSP*, 01 Nov 2005, 15(11):668-670
22. AM, Iqbal Z, Qadirullah . Efficacy of nalbuphine in preventing haemodynamic response to laryngoscopy and intubation. *Journal of postgraduate medical institute* 2014;28(2):211-216

UNDER PEER REVIEW