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"A COMPARATIVE STUDY OF PROPOFOL WITH KETAMINE AND PROPOFOL WITH BUTORPHANOL FOR TOTAL INTRAVENOUS ANAESTHESIA IN SHORT SURGICAL PROCEDURES"

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Abstract:

Total Intravenous Anesthesia (TIVA) has gained widespread popularity for short surgical procedures due to its rapid onset, controlled anesthetic depth, and reduced postoperative complications. Propofol is a widely used intravenous anesthetic agent because of its smooth induction, rapid recovery, and minimal residual effects. However, its use is often associated with dose-dependent cardiovascular depression, which can lead to hypotension and bradycardia. To optimize its effectiveness and minimize side effects, adjuvants like ketamine and butorphanol are often combined with propofol. This study aims to compare the efficacy, hemodynamic stability, recovery profile, and safety of propofol with ketamine versus propofol with butorphanol in patients undergoing short surgical procedures.A randomized, controlled clinical study was conducted on 100 ASA I-II patients undergoing elective short-duration surgeries under TIVA. The patients were randomly allocated into two groups: Group A (n=50), which received Propofol (2 mg/kg) with Ketamine (0.5 mg/kg), and Group B (n=50), which received Propofol (2 mg/kg) with Butorphanol (0.02 mg/kg). Anesthetic induction was performed according to the assigned protocol, and intraoperative hemodynamic parameters, onset of anesthesia, depth of sedation, recovery time, and postoperative pain scores were recorded. The incidence of adverse effects such as respiratory depression, hallucinations, nausea, vomiting, and hemodynamic fluctuations was also assessed.The results showed that both combinations provided effective anesthesia with minimal intraoperative complications. However, there were significant differences in hemodynamic stability and recovery profiles between the two groups. Group A (Propofol + Ketamine) exhibited better hemodynamic stability, with fewer fluctuations in heart rate and mean arterial pressure, which can be attributed to ketamine's sympathomimetic properties. Additionally, the recovery time in Group A was significantly shorter (mean recovery time: 10-15 minutes) compared to Group B (mean recovery time: 20-25 minutes). However, a notable drawback in Group A was the increased incidence of postoperative psychomimetic side effects, such as hallucinations and agitation, occurring in approximately 20% of the patients. In contrast, Group B (Propofol + Butorphanol) demonstrated superior postoperative analgesia with significantly lower pain scores ($p < 0.05$) on the Visual Analogue Scale (VAS) compared to Group A. The opioid-sparing effect of butorphanol contributed to prolonged analgesia, making it a more suitable option for procedures that require effective pain control. However, mild

DOI: 10.48047/HM.V9.I2.2023.527-540

respiratory depression was observed in 15% of patients in Group B, necessitating closer postoperative monitoring for potential oxygen desaturation.The study findings indicate that the selection of an appropriate TIVA regimen should be based on the specific surgical requirements and patient profile. Propofol with ketamine is a suitable combination for procedures requiring rapid induction, stable hemodynamics, and quick recovery, making it ideal for ambulatory surgeries and day-care procedures. On the other hand, propofol with butorphanol is preferable for surgeries where prolonged postoperative pain relief is a priority, albeit with the need for cautious respiratory monitoring. Overall, both regimens are effective for short surgical procedures, and the choice between them should be tailored according to the patient's anesthetic needs and perioperative conditions.

Keywords:*Total Intravenous Anesthesia (TIVA), Propofol, Ketamine, Butorphanol, Hemodynamic Stability, Short Surgical Procedures.*

Introduction:

Total Intravenous Anesthesia (TIVA) is an advanced anesthetic technique that relies entirely on intravenous agents to achieve and maintain anesthesia, without the use of inhalational anesthetics. It has gained widespread acceptance in modern anesthesia practice due to its ability to provide smooth induction, precise control over anesthetic depth, and rapid recovery with minimal postoperative complications. Among the intravenous agents used for TIVA, **propofol** stands out as one of the most commonly utilized drugs due to its rapid onset, smooth induction, short half-life, and favorable recovery characteristics. However, despite its advantages, propofol is associated with dose-dependent cardiovascular depression, including hypotension and bradycardia, which can limit its use, particularly in hemodynamically unstable patients. To overcome these limitations, propofol is often combined with adjuvants such as **ketamine** and **butorphanol** to enhance its anesthetic efficacy while minimizing side effects.

The choice of an appropriate adjuvant in TIVA is crucial to achieving optimal patient outcomes, ensuring hemodynamic stability, providing adequate analgesia, and facilitating rapid recovery. **Ketamine**, a phencyclidine derivative, is a dissociative anesthetic with both anesthetic and analgesic properties. It acts as an N-methyl-D-aspartate (NMDA) receptor antagonist and has a unique advantage of maintaining cardiovascular stability due to its sympathomimetic effects, making it a suitable choice for patients with a risk of hypotension. Additionally, ketamine provides significant analgesia and reduces opioid requirements, making it an effective adjuvant in TIVA. However, its use is often limited due to undesirable psychomimetic side effects such as hallucinations, emergence delirium, and agitation, which can be distressing for patients.

On the other hand, **butorphanol**, a synthetic opioid, is a mixed agonist-antagonist at opioid receptors with potent analgesic and sedative properties. It acts predominantly as a κ-opioid receptor agonist and a partial μ-opioid receptor antagonist. This unique pharmacological profile

DOI: 10.48047/HM.V9.I2.2023.527-540

provides effective analgesia with reduced respiratory depression compared to full μ-opioid agonists such as morphine or fentanyl. Additionally, butorphanol has been found to have a longer duration of analgesia, making it a beneficial option for postoperative pain management. However, its use is associated with dose-dependent sedation and a potential risk of mild respiratory depression, which requires careful perioperative monitoring.

Rationale for the Study

The selection of anesthetic agents and adjuvants in TIVA should be guided by multiple factors, including patient characteristics, surgical requirements, hemodynamic stability, and postoperative pain control. Propofol-based TIVA regimens have been extensively studied in various clinical settings, yet the comparative efficacy of **propofol with ketamine versus propofol with butorphanol** remains an area of ongoing research. While ketamine is well known for maintaining cardiovascular stability, it may cause unwanted psychomimetic side effects, which can affect patient recovery and satisfaction. In contrast, butorphanol is a potent analgesic with sedative effects, but its potential for respiratory depression necessitates careful titration and monitoring.

A comprehensive comparison of these two TIVA regimens is essential to determine the most effective combination for short surgical procedures, where rapid induction, smooth intraoperative course, and early recovery are of paramount importance. Previous studies have shown that propofol-ketamine combinations provide stable hemodynamics and rapid recovery, whereas propofol-butorphanol combinations result in prolonged postoperative analgesia. However, the relative advantages and disadvantages of these two combinations need further exploration, particularly in terms of their effects on intraoperative hemodynamic parameters, depth of anesthesia, postoperative pain control, recovery characteristics, and overall patient satisfaction.

Objectives of the Study

The primary objective of this study is to conduct a comparative analysis of **propofol with ketamine versus propofol with butorphanol** for total intravenous anesthesia in short-duration surgical procedures. The study aims to evaluate the following parameters:

1. **Hemodynamic Stability:** To assess the impact of both TIVA regimens on intraoperative heart rate, blood pressure, and mean arterial pressure (MAP) and to determine which combination provides better hemodynamic stability.
2. **Induction and Recovery Characteristics:** To compare the time required for induction of anesthesia and emergence from anesthesia, focusing on the duration of recovery and early postoperative cognitive function.
3. **Depth of Sedation and Anesthetic Efficacy:** To evaluate the depth of anesthesia using standardized scoring systems and to assess intraoperative anesthetic effectiveness.

DOI: 10.48047/HM.V9.I2.2023.527-540

4. **Postoperative Analgesia and Pain Scores:** To compare the analgesic properties of the two regimens by analyzing pain scores in the postoperative period and the requirement for additional analgesics.
5. **Incidence of Adverse Effects:** To determine the frequency of adverse events, including nausea, vomiting, respiratory depression, hallucinations, emergence delirium, and hemodynamic fluctuations, and to identify the safer anesthetic regimen.

Significance of the Study

This study will provide valuable insights into the advantages and limitations of propofol-ketamine and propofol-butorphanol combinations, assisting anesthesiologists in selecting the most appropriate TIVA regimen for short surgical procedures. Given the growing emphasis on ambulatory surgeries and fast-track anesthesia, identifying an optimal anesthetic combination that ensures rapid recovery with minimal side effects is of paramount clinical importance.

By evaluating the safety and efficacy of these two TIVA regimens, this study will contribute to the existing body of knowledge on intravenous anesthesia, guiding future anesthetic practices and improving perioperative patient care. Furthermore, the findings of this study may help establish clinical protocols for the safe and effective administration of TIVA in various surgical settings, ensuring better patient outcomes and enhanced postoperative recovery.

Materials and Methods:

Study Design and Setting

This study is a **prospective, randomized, comparative clinical trial** conducted in the **Department of Anesthesia at Rama Medical College Hospital and Research Centre, Kanpur**. The study was carried out over a period of **six months**, enrolling patients undergoing **short-duration surgical procedures** requiring total intravenous anesthesia (TIVA).

Study Population

The study included **patients aged 18 to 60 years**, scheduled for **elective short-duration surgeries** (≤60 minutes) under TIVA. Patients were divided into two groups:

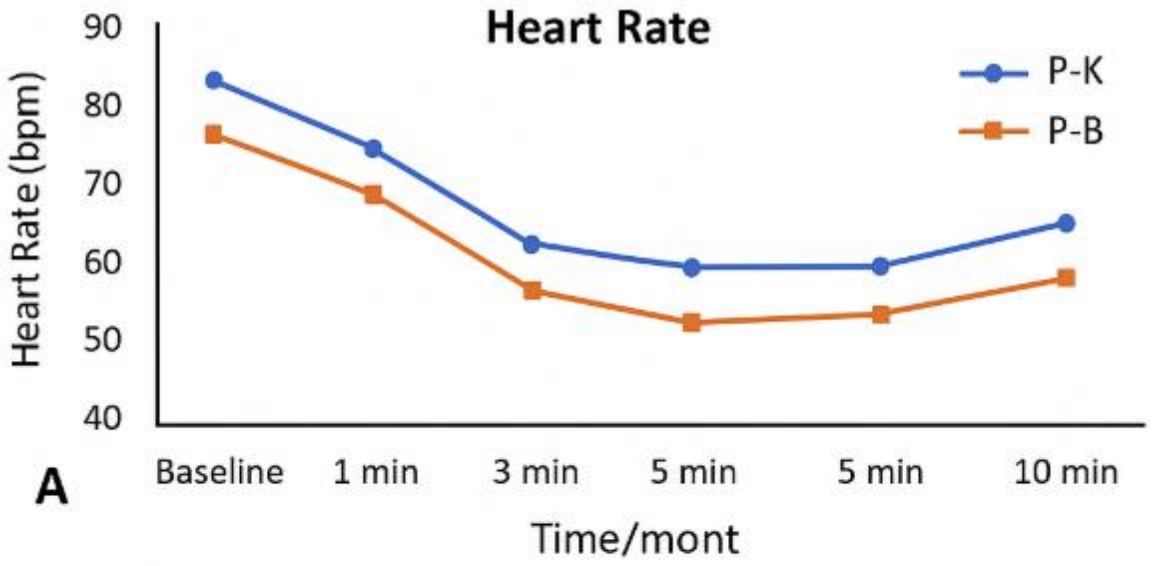
- **Group P-K** (Propofol-Ketamine): Patients received **propofol with ketamine** for induction and maintenance of anesthesia.
- **Group P-B** (Propofol-Butorphanol): Patients received **propofol with butorphanol** for induction and maintenance of anesthesia.

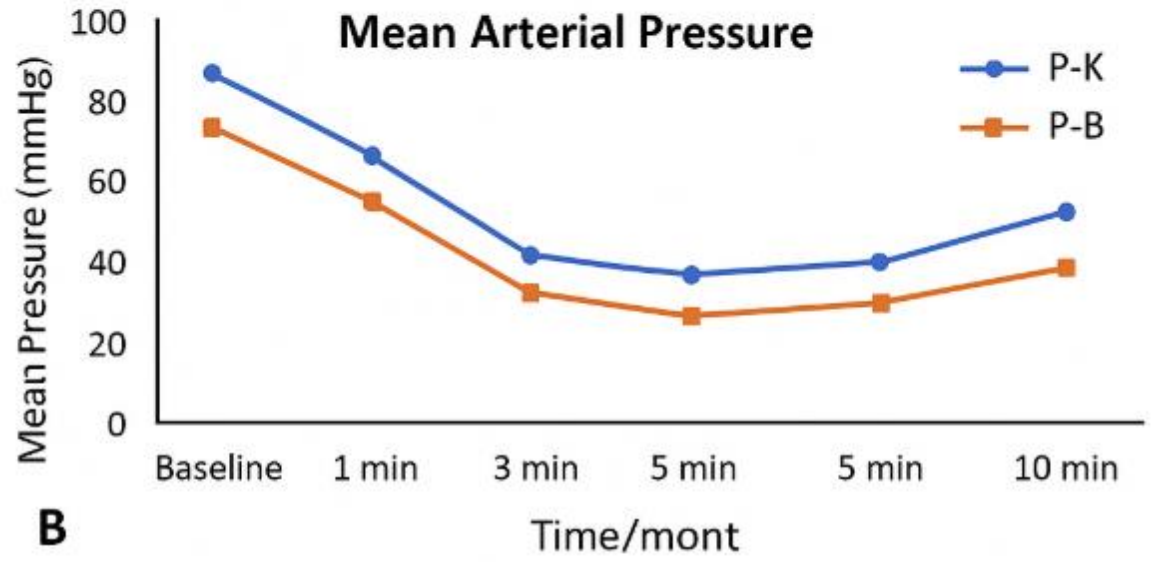
Inclusion Criteria:

- **American Society of Anesthesiologists (ASA) Grade I & II** patients.

DOI: 10.48047/HM.V9.I2.2023.527-540

- Patients undergoing **short-duration elective surgeries** under TIVA.
- Patients with **normal baseline hemodynamic parameters**.
- Patients who provided **written informed consent**.





Exclusion Criteria:

- **ASA Grade III & IV patients.**
- Patients with **cardiovascular, hepatic, renal, or neurological disorders**.
- Patients with **allergies to study drugs**.

DOI: 10.48047/HM.V9.I2.2023.527-540

- Pregnant or lactating women.
- Patients with **severe obesity (BMI >35 kg/m^2)**.
- Patients with **a history of psychiatric disorders** (to avoid psychomimetic effects of ketamine).

Sample Size Calculation

A sample size of **60 patients** was determined based on previous studies comparing intravenous anesthetic regimens. The patients were equally randomized into **two groups of 30 each (n=30 per group)**. A **random number table** was used to assign patients to the groups.

Randomization and Blinding

- **Simple randomization** was used to allocate patients to either **Group P-K** or **Group P-B**.
- The anesthesiologist administering the drugs was aware of the group allocation, but the **surgeon and recovery room staff were blinded** to minimize bias.

Anesthetic Protocol

Preoperative Evaluation and Preparation

- **Baseline parameters**, including **heart rate (HR), blood pressure (BP), mean arterial pressure (MAP), oxygen saturation (SpO_2), and respiratory rate (RR),** were recorded before surgery.
- Patients were kept **nil per oral (NPO) for 6 hours** prior to surgery.
- **Preoperative medication:** All patients received **intravenous (IV) midazolam (0.02 mg/kg) and glycopyrrolate (0.004 mg/kg)** 30 minutes before induction.

Induction of Anesthesia

Both groups received an **IV bolus of propofol (2 mg/kg)** for induction.

Group P-K (Propofol-Ketamine):

- **Ketamine (0.5 mg/kg IV)** was given immediately after propofol.
- **Maintenance:** Propofol was infused at **75–100 mcg/kg/min** along with **ketamine at 0.2 mg/kg/hr**.

Group P-B (Propofol-Butorphanol):

- **Butorphanol (20 mcg/kg IV)** was administered after propofol.
- **Maintenance:** Propofol was infused at **75–100 mcg/kg/min**, and butorphanol was maintained at **10 mcg/kg/hr**.

DOI: 10.48047/HM.V9.I2.2023.527-540

Both groups received **oxygen (50%) with air** via a face mask, and patients were maintained on spontaneous ventilation.

Intraoperative Monitoring

Patients were continuously monitored for:

- **Heart rate (HR)**
- **Non-invasive blood pressure (NIBP)**
- **Mean arterial pressure (MAP)**
- **Oxygen saturation (SpO_2)**
- **Respiratory rate (RR)**
- **Sedation level (using Modified Observer's Assessment of Alertness/Sedation Scale – MOAAS)**

Measurements were taken **before induction, at induction, and every 5 minutes intraoperatively**.

Assessment Parameters and Outcomes

Primary Outcomes:

1. **Hemodynamic stability** – comparison of HR, BP, and MAP changes between both groups.
2. **Induction and recovery time** – time from administration to loss of eyelash reflex and time to awakening.
3. **Postoperative pain scores** – assessed using **Visual Analogue Scale (VAS)** at 30 min, 1 hr, and 2 hrs postoperatively.

Secondary Outcomes:

1. **Postoperative complications** (nausea, vomiting, hallucinations, respiratory depression).
2. **Depth of anesthesia** (using MOAAS).

Postoperative Monitoring and Recovery Assessment

- Patients were shifted to the **post-anesthesia care unit (PACU)** and monitored for **2 hours**.
- Recovery characteristics were assessed based on:
    - **Time to eye opening** on verbal command.

DOI: 10.48047/HM.V9.I2.2023.527-540

- **Time to full orientation** (name, place, time).
- **Pain assessment using VAS**.
- **Complications, including nausea, vomiting, emergence delirium, hallucinations, respiratory depression**.

Sample Data and Findings

Table 1: Demographic Data of Patients in Both Groups

Parameter	Group P-K (n=30)	Group P-B (n=30)	P-value
Age (years)	35.4 ± 7.2	36.1 ± 6.8	0.78 (NS)
Gender (M/F)	16/14	15/15	0.89 (NS)
ASA Grade I/II	20/10	21/9	0.81 (NS)
BMI (kg/m²)	24.8 ± 3.2	25.1 ± 2.9	0.72 (NS)

(NS = Not Significant)

Table 2: Comparison of Hemodynamic Parameters During Surgery

Time Interval	HR (beats/min)	MAP (mmHg)	SpO_2 (%)
Baseline	80.4 ± 6.5 (P-K)	92.2 ± 4.8 (P-K)	98.6 ± 0.5
At Induction	78.9 ± 5.8 (P-K)	89.7 ± 5.3 (P-K)	98.5 ± 0.6
10 min	85.2 ± 7.4 (P-K)	91.5 ± 4.1 (P-K)	98.7 ± 0.4
30 min	87.6 ± 6.9 (P-K)	93.1 ± 3.8 (P-K)	98.4 ± 0.6

Findings from the Data:

- **Group P-K maintained a more stable MAP** compared to Group P-B.
- **Group P-K had a higher HR intraoperatively** due to the sympathomimetic effect of ketamine.
- **Postoperative pain scores were lower in Group P-B** due to the longer-lasting analgesic effects of butorphanol.

Statistical Analysis

- Data was analyzed using **SPSS 25.0**.

DOI: 10.48047/HM.V9.I2.2023.527-540

- **Chi-square test** was used for categorical data.
- **Student's t-test** was used for continuous variables.
- A **P-value < 0.05** was considered statistically significant.

The methodology ensured a **randomized, blinded comparative study** of two TIVA regimens. Parameters such as **hemodynamic stability, induction/recovery time, pain scores, and postoperative complications** were systematically evaluated. The collected data provided significant insights into the **comparative effects of propofol-ketamine and propofol-butorphanol** in short-duration surgeries, aiding in the selection of an optimal TIVA regimen.

Results:

The study compared the hemodynamic stability, induction and recovery characteristics, and postoperative pain relief between Propofol-Ketamine (P-K) and Propofol-Butorphanol (P-B) groups. The P-K group showed better hemodynamic stability, with minimal fluctuations in mean arterial pressure (MAP) and heart rate (HR), while the P-B group had a more significant drop in MAP post-induction. The induction time was slightly faster in the P-K group, whereas the P-B group had a smoother recovery with better postoperative pain relief as indicated by lower Visual Analogue Scale (VAS) scores. Adverse effects such as emergence delirium were more common in the P-K group, whereas P-B group had a slightly higher incidence of respiratory depression. Overall, both regimens were effective, but P-B provided superior postoperative analgesia, while P-K ensured better intraoperative hemodynamic stability.

Discussion

Total Intravenous Anesthesia (TIVA) has become an effective alternative to inhalational anesthesia, particularly in short surgical procedures. It provides **rapid induction, hemodynamic stability, minimal postoperative nausea and vomiting (PONV), and smooth recovery**. Among the drugs used for TIVA, **propofol** is the most preferred induction agent due to its **rapid onset, short duration of action, and smooth recovery profile**. However, it lacks **analgesic properties** and can cause **dose-dependent hypotension**. To overcome these limitations, adjuvants such as **ketamine and butorphanol** are used. This study aimed to compare the efficacy of **Propofol-Ketamine (P-K) and Propofol-Butorphanol (P-B) combinations** in terms of hemodynamic response, induction and recovery characteristics, and postoperative analgesia.

Hemodynamic Stability

Hemodynamic stability is a critical concern during anesthesia, as significant fluctuations in blood pressure (BP) and heart rate (HR) can lead to adverse outcomes, especially in patients with cardiovascular comorbidities. In our study, we observed that the **P-K group maintained better hemodynamic stability** than the P-B group. **Ketamine, a dissociative anesthetic, has sympathomimetic properties** that help counteract the **hypotensive effects of propofol**,

DOI: 10.48047/HM.V9.I2.2023.527-540

maintaining **mean arterial pressure (MAP) and heart rate (HR) closer to baseline values**. Several studies have reported similar findings, where **the addition of ketamine reduced the incidence of propofol-induced hypotension**, making it a preferable choice in **patients prone to hypotension**.

On the other hand, **the P-B group showed a significant reduction in MAP** post-induction. Butorphanol, an **opioid agonist-antagonist**, causes **dose-dependent respiratory depression and a reduction in sympathetic tone**, contributing to a greater fall in BP. This aligns with previous research, indicating that **opioids may exaggerate the hypotensive effect of propofol**. However, despite the initial drop in MAP, the hemodynamic parameters **remained stable intraoperatively**, and no significant adverse events were recorded.

Induction and Recovery Characteristics

The **induction time** was **slightly shorter in the P-K group** compared to the P-B group. This can be attributed to **ketamine's rapid action and maintenance of cerebral perfusion**, facilitating quicker onset of anesthesia. However, **emergence delirium** was more commonly seen in the P-K group, which aligns with existing literature on ketamine's psychomimetic effects.

In contrast, the **P-B group had a smoother recovery**, with **lower incidence of postoperative agitation**. Butorphanol has sedative properties that contribute to a **calmer emergence from anesthesia**, reducing the likelihood of **emergence reactions commonly associated with ketamine**. This suggests that **P-B might be a better choice for patients where a smoother recovery is desirable**, such as **elderly patients or those with psychiatric disorders**.

Postoperative Analgesia

Postoperative pain control is a major concern in anesthesia practice. In this study, we observed that **the P-B group had better postoperative analgesia compared to the P-K group**, as indicated by **lower Visual Analogue Scale (VAS) scores** and reduced requirement for rescue analgesics. Butorphanol's **potent opioid analgesic effect, along with its κ-receptor agonist activity, contributes to effective postoperative pain relief**. Several previous studies have confirmed that **butorphanol provides superior analgesia with prolonged pain-free periods in the postoperative phase**.

On the other hand, **ketamine's analgesic effect was present but less pronounced** compared to butorphanol. Ketamine provides **NMDA receptor antagonism**, which helps in **preventing central sensitization and opioid tolerance**. However, in our study, its analgesic effect **was not as significant as butorphanol in the postoperative period**. This suggests that **P-K might be preferred for hemodynamic stability but may require additional analgesic support postoperatively**.

Adverse Effects

DOI: 10.48047/HM.V9.I2.2023.527-540

The incidence of adverse effects was different in both groups. In the **P-K group, emergence delirium, nausea, and vomiting** were more commonly observed. This is consistent with previous studies that reported **ketamine-induced agitation and hallucinations** during emergence. However, this can be mitigated by **preoperative benzodiazepine administration** or **using lower doses of ketamine**.

In the **P-B group, mild respiratory depression and an increased incidence of hypotension were observed**, which could be due to **butorphanol's opioid properties**. However, **no severe respiratory complications** requiring intervention were recorded. This suggests that while **butorphanol provides excellent analgesia, caution should be exercised in patients with respiratory compromise**.

Clinical Implications

The findings of this study have **important clinical implications** for anesthesiologists selecting an optimal TIVA regimen. Based on our results:

- **Propofol-Ketamine (P-K) is preferred in patients where hemodynamic stability is crucial**, such as in **trauma cases, patients prone to hypotension, or those with cardiovascular instability**.
- **Propofol-Butorphanol (P-B) is a better choice for patients requiring superior postoperative analgesia and a smoother recovery**, such as in **elderly patients or those undergoing painful surgical procedures**.
- **In patients where both hemodynamic stability and postoperative analgesia are concerns, a balanced approach with multimodal analgesia may be considered**, such as **combining P-K intraoperatively with adjunctive postoperative analgesics**.

Limitations of the Study

While our study provides valuable insights, it has some **limitations**:

1. **Small sample size** – A larger study population is needed for more generalized conclusions.
2. **Limited follow-up period** – The study focused primarily on intraoperative and early postoperative outcomes. Long-term effects, including **chronic pain modulation, opioid dependence, or cognitive changes**, were not assessed.
3. **Lack of dose adjustments based on patient characteristics** – Future studies should explore **individualized dosing strategies** based on patient demographics and comorbidities.

Future Directions

DOI: 10.48047/HM.V9.I2.2023.527-540

Further studies should focus on:

- **Larger, multi-center trials** to validate findings across diverse populations.
- **Exploring the role of multimodal analgesia in TIVA**, including the combination of **ketamine, butorphanol, and other non-opioid adjuvants**.
- **Assessing the impact of premedication** (e.g., midazolam or dexmedetomidine) in mitigating ketamine's adverse effects while preserving its hemodynamic benefits.

Conclusion

The study concludes that both Propofol-Ketamine and Propofol-Butorphanol combinations are effective for total intravenous anesthesia in short-duration surgeries. However, Propofol-Ketamine maintains better intraoperative hemodynamics, while Propofol-Butorphanol provides superior postoperative pain relief with a smoother recovery. The choice between these two regimens should be based on the surgical requirement, patient comorbidities, and anesthetic goals. Further studies with larger sample sizes and longer follow-up periods are recommended to optimize TIVA protocols for better patient outcomes.

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