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Original Article

Effect of Intravenous Aminophylline on Recovery Acceleration from General Anesthesia in Laparotomy Patients: A Bispectral Index Evaluation

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Abstract

Background: Postoperative recovery is a critical aspect of surgical care, particularly following general anesthesia. This study explores the impact of intravenous aminophylline on accelerating recovery in laparotomy patients, utilizing the Bispectral Index (BIS) for precise monitoring. **Methods:** This study was designed as a randomized, double-blind, controlled trial conducted between June and September 2018. The population included patients scheduled for elective laparotomy under general anesthesia with isoflurane inhalation. A total of 46 participants were randomly assigned to one of two groups: the intervention group, which received intravenous aminophylline, and the control group, which received 0.9% NaCl as a placebo. Recovery time was measured from the point of drug administration (T0) using the Bispectral Index (BIS). Statistical analysis included Fisher's exact test to assess normality and the Mann-Whitney test to determine differences between the groups. **Results:** The research involved 46 participants, evenly distributed into two cohorts. In the aminophylline cohort, the average time to recover was 10.48 minutes, whilst in the NaCl cohort, it was 15.48 minutes. A notable statistical difference was detected between the two cohorts ($p < 0.05$). Aminophylline demonstrated a significant ability to accelerate recovery time in comparison to NaCl, effectively shortening the recovery period by roughly 50%. **Conclusion:** Intravenous aminophylline significantly accelerated recovery from general anesthesia in laparotomy patients, as assessed by the Bispectral Index. Its superior efficacy compared to 0.9% NaCl highlights its potential as a valuable intervention in postoperative care.

Keywords: Aminophylline; General anesthesia; Bispectral Index (BIS); Postoperative recovery

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INTRODUCTION

Surgery is a medical procedure performed to diagnose or treat diseases, injuries, or deformities. According to the World Health Organization (WHO), the number of surgical procedures has risen significantly over recent years, reflecting advancements in medical technology and growing accessibility to surgical care.[1] Among these procedures, laparotomy—a major surgical intervention—requires an incision in the abdominal wall to address conditions such as hemorrhage, perforation, cancer, or obstruction. It is commonly performed for digestive and uterine conditions, including appendicitis, gastric or colon cancer, and intestinal obstruction.[2]

General anesthesia is widely employed in laparotomy procedures to induce a reversible state of unconsciousness, analgesia, amnesia, and muscle relaxation, ensuring patient comfort and surgical precision.[3] Anesthesia can be administered intravenously (e.g., barbiturates, propofol) or via inhalation (e.g., isoflurane, desflurane), with recovery

from inhalational agents primarily dependent on pulmonary elimination. Factors influencing recovery include alveolar ventilation, the blood-gas partition coefficient, and the minimum alveolar concentration required for awakening (MACawake).[4]

Pharmacological interventions, such as aminophylline, have demonstrated potential in improving postoperative recovery. Aminophylline has been shown to accelerate recovery from anesthesia by reducing the depth and duration of sedation induced by agents like barbiturates, diazepam, midazolam, and propofol.[2,3]Additionally, it has proven effective in mitigating bronchospasm in neonates, reducing postoperative apnea, and managing asthma exacerbations in pediatric patients unresponsive to first-line therapies.[1,5] Importantly, aminophylline has been identified as a potential propofol antagonist, capable of reversing prolonged sedation without significant adverse effects.[4,5]

The Bispectral Index (BIS), an electroencephalogram-based monitoring tool, provides a reliable method for assessing the depth of anesthesia and the hypnotic effects of anesthetic agents. It plays a crucial role in optimizing sedative drug dosages and ensuring precise anesthesia management.[6]

This study aims to evaluate the effect of intravenous aminophylline on accelerating recovery from general anesthesia in laparotomy patients. By utilizing the BIS for monitoring, this research seeks to provide insights into the clinical efficacy of aminophylline in improving postoperative recovery quality and reducing sedation duration, thereby contributing to enhanced patient outcomes in surgical care.

MATERIALS AND METHODS

This study was a randomised, double-blind, controlled clinical trial conducted to evaluate the effect of intravenous aminophylline on recovery time from general anaesthesia using isoflurane inhalation. Recovery was assessed utilising the Bispectral Index (BIS) at a tertiary hospital in the Philippines. The research commenced following ethical clearance from the Health Research Ethics Committee and approval from the hospital administration, with data collection continuing until the required sample size was achieved.

The study population comprised all patients scheduled for elective abdominal laparotomy under general anaesthesia with isoflurane inhalation. Patients aged 19–60 years, classified as ASA (American Society of Anesthesiologists) physical status I or II, and willing to provide written informed consent were included in the study. Patients were excluded if they had a history of aminophylline use within 4–5 days prior to surgery or a history of cardiac arrhythmia or seizures. Dropout criteria encompassed life-threatening emergencies involving the heart, lungs, or brain subsequent to aminophylline administration or allergic reactions such as anaphylactic shock.

Participants were randomly assigned to two groups utilising block randomisation. The intervention group received intravenous aminophylline at a dose of 3 mg/kg body weight, diluted in 20 mL of aquabidest and administered over 10 minutes using a syringe pump. The control group received an equivalent volume of intravenous normal saline (0.9% NaCl) administered in the same manner. The allocation of drugs was blinded to both the participants and the researchers, with preparation handled by a separate investigator.

Patients were prepared preoperatively, and baseline data were recorded. In the operating room, standard monitoring equipment was applied, including electrocardiography (ECG), blood pressure, heart rate, respiratory rate, and oxygen saturation. General anaesthesia was induced using fentanyl (2 mcg/kg), midazolam (0.05 mg/kg), propofol (2 mg/kg), and rocuronium (1 mg/kg), with maintenance achieved using isoflurane (0.5–1.5 vol%) and additional doses of rocuronium as required. At the conclusion of the surgery, isoflurane was discontinued, and reversal agents (neostigmine and atropine) were administered. The allocated study drug was subsequently administered intravenously over 10 minutes.

Recovery was monitored utilising BIS values, which were recorded at the commencement of drug administration (T0) and at 5-minute intervals (T1–T6) until recovery was

achieved, defined as a BIS value greater than 90. Data collection ceased once this criterion was met. Patients were subsequently observed in the recovery room before being transferred to the ward.

Data were verified for completeness, coded, and entered a master table using SPSS software for analysis. Numerical data were expressed as mean ± standard deviation (SD), while categorical data were presented as frequencies and percentages. Normality of numerical data was assessed using Fisher's exact test, and the Mann-Whitney test was employed to evaluate differences between groups. A p-value of less than 0.05 was considered statistically significant, with a confidence interval of 95%.

RESULTS

This study was conducted from July to September 2018 at the Central Surgical Installation of a tertiary hospital in the Philippines using a double-blind randomized sampling method. The study involved 46 participants equally divided into two groups: the aminophylline group and the NaCl 0.9% group. Participants were homogeneously distributed across demographic characteristics, including age, gender, and ASA classification, as confirmed by statistical analysis ($p > 0.05$).

Regarding age distribution, participants aged 19–32 years were absent in the aminophylline group (0%) but constituted 21.8% of the NaCl 0.9% group. In the 33–46 age group, 47.8% of participants were in the aminophylline group compared to 39.1% in the NaCl 0.9% group. For participants aged 47–60 years, 52.2% were in the aminophylline group and 39.1% in the NaCl 0.9% group. Gender distribution showed 34.7% male and 65.3% female participants in the aminophylline group, compared to 39.1% male and 60.9% female in the NaCl 0.9% group. For ASA classification, the aminophylline group included 43.4% of participants classified as ASA I and 56.6% as ASA II, while the NaCl 0.9% group had 60.8% ASA I and 39.2% ASA II. Statistical analyses revealed no significant differences in these demographic variables between the two groups.

Table 1. Demographic Characteristics of Participants

Characteristic	Aminophylline n (%)	NaCl 0.9% n (%)	Total n (%)	p-value
Age (years)				
19–32	0 (0%)	5 (21.8%)	5 (10.9%)	0.782
33–46	11 (47.8%)	9 (39.1%)	20 (43.5%)	
47–60	12 (52.2%)	9 (39.1%)	21 (45.6%)	
Gender				
Male	8 (34.7%)	9 (39.1%)	17 (36.9%)	0.596
Female	15 (65.3%)	14 (60.9%)	29 (63.1%)	
ASA Classification				
ASA I	10 (43.4%)	14 (60.8%)	24 (52.1%)	0.488
ASA II	13 (56.6%)	9 (39.2%)	22 (47.9%)	

Analysis of recovery times demonstrated that aminophylline significantly accelerated recovery from general anesthesia compared to NaCl 0.9% ($p < 0.05$). At T0, the mean BIS value was 69.61% in the aminophylline group and 63.26% in the NaCl 0.9% group, with a significant difference ($p < 0.05$). Similarly, at T1, the aminophylline group had a mean BIS value of 81.91% compared to 73.04% in the NaCl 0.9% group, and at T2, the mean BIS values were 90.30% and 82.04%, respectively. Significant differences in BIS values were observed across all measured time points (T0–T4), indicating faster recovery in the aminophylline group.

The mean recovery time in the aminophylline group was 10.48 minutes, significantly shorter than the 15.48 minutes observed in the NaCl 0.9% group ($p < 0.05$). At T2, 60.8%

of participants in the aminophylline group had recovered, compared to 17.4% in the NaCl 0.9% group. By T3, 26.1% of aminophylline participants had recovered compared to 13.1% in the NaCl 0.9% group. At T4, 13.1% of participants in the aminophylline group achieved recovery, while 69.5% of participants in the NaCl 0.9% group reached this milestone. In summary, the aminophylline group exhibited a faster recovery trajectory, as indicated by higher BIS values and shorter recovery times. These results highlight the efficacy of intravenous aminophylline in accelerating recovery from general anesthesia compared to NaCl 0.9%.

Table 2. Effect of Treatment on Recovery Time

Time Point	Group	Mean BIS (%)	N	Standard Deviation	p-value
T0	Aminophylline	69.61	23	6.57	0.000
	NaCl 0.9%	63.26	23	5.95	
T1	Aminophylline	81.91	23	6.73	0.000
	NaCl 0.9%	73.04	23	6.28	
T2	Aminophylline	90.30	23	7.14	0.000
	NaCl 0.9%	82.04	23	7.01	
T3	Aminophylline	93.56	23	5.36	0.000
	NaCl 0.9%	88.84	23	4.09	
T4	Aminophylline	97.90	23	2.83	0.000
	NaCl 0.9%	96.93	23	1.67	
Mean Recovery Time	Aminophylline	10.48 minutes	23	-	0.000
	NaCl 0.9%	15.48 minutes	23	-	

DISCUSSION

This study aimed to evaluate the effects of intravenous aminophylline (3 mg/kg) on recovery time after general anesthesia with isoflurane inhalation in laparotomy surgery patients. Recovery was assessed using the Bispectral Index (BIS) at a tertiary hospital in the Philippines. A total of 46 patients who met the inclusion criteria were divided into two groups: one receiving aminophylline and the other receiving 0.9% NaCl (normal saline).

Demographic analysis showed no significant differences between groups in terms of sex, age, or ASA physical status, minimizing potential bias and ensuring the reliability of the findings. The results demonstrated that aminophylline significantly shortened recovery time compared to 0.9% NaCl ($p < 0.05$). The mean recovery time in the aminophylline group was 10.48 minutes, nearly half of the 15.48 minutes observed in the NaCl group. These findings align with previous studies showing aminophylline's ability to counteract the sedative effects of anesthetic agents, such as benzodiazepines and propofol, and accelerate recovery even under their influence.[7,8]

Aminophylline acts as an adenosine receptor antagonist, inhibiting central nervous system neuromodulation. Adenosine plays a role in promoting sleep, with receptor subtypes A1 and A2A involved in sedation. By blocking these receptors, aminophylline reduces sedation depth, increases BIS values, and facilitates faster recovery. This mechanism explains its effectiveness in reducing recovery time and achieving BIS ≥ 90 more quickly compared to control groups.[9,10]

No significant adverse effects were observed following intravenous aminophylline administration in this study. This supports its safety and clinical utility for expediting recovery in patients under general anesthesia. The findings of this study are consistent with previous research. For example, studies have shown that aminophylline administration reduces extubation time and accelerates BIS recovery to ≥ 90, with a faster recovery rate

in groups receiving aminophylline compared to controls.[11,12] These results further underscore aminophylline's potential as an effective pharmacological intervention for improving postoperative recovery.

CONCLUSION

Intravenous aminophylline significantly accelerated recovery from general anesthesia in lapa-rotomy patients, as assessed by the Bispectral Index. Its superior efficacy compared to 0.9% NaCl highlights its potential as a valuable intervention in postoperative care.

Abbreviations: BIS, Bispectral Index; NaCl, Sodium Chloride; ASA, American Society of Anesthesiologists; MACawake, Minimum Alveolar Concentration for Awakening; CNS, Central Nervous System; A1, Adenosine Receptor Subtype 1; A2A, Adenosine Receptor Subtype 2A.

Supplementary Materials: The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions: S.B. conceptualized the study design, conducted data collection, and performed statistical analysis. H.S.K. critically reviewed and revised the manuscript, interpreted the data, and contributed to writing the final draft. All authors have read and approved the final manuscript.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available from the corresponding author upon reasonable request.

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Conflicts of Interest: The authors declare no conflicts of interest.

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