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Acid-base Status and Electrolyte Changes During Propofol Based General Anesthesia in Patients Undergoing Septoplasty

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ABSTRACT

Propofol is a widely used hypnotic agent globally; however, it may have adverse effects on critical patient outcomes, potentially by interfering with the organ-protective properties of other interventions. Propofol anesthesia can lead to disruptions in metabolic balance. This research aims to examine alterations in acid-base and electrolyte levels during septoplasty surgery when propofol-based anesthesia is administered. In this prospective, observational cohort study, a total of 30 patients between the ages of 18 and 65 with an American Society of Anesthesia physical status I-II were included. Arterial blood samples were collected both before the administration of propofol and five minutes after propofol injection, with the purpose of evaluating the acid-base status and electrolyte parameters including sodium, chloride, calcium and potassium. No cases of acidosis or statistically significant alterations in electrolyte levels were observed in patients following the administration of propofol. Furthermore, none of the patients exhibited any adverse effects such as cardiac failure, rhabdomyolysis, severe metabolic acidosis, or renal failure attributable to propofol during the study. We suggest that the induction dose of propofol for general anesthesia does not lead to metabolic acidosis or electrolyte disturbances.

Keywords: Propofol, Arterial, Metabolic acidosis, Anesthesia, Acid-base balance, Potassium, Anion gap

INTRODUCTION

Propofol, known chemically as 2,6-diisopropylphenol, was originally developed by replacing a hydrogen atom at the 2 position of the chemical solvent 1,3-diisopropylbenzene with a hydroxy group [1]. Propofol possesses unique characteristics, including a rapid onset and elimination, short duration of action, quick recovery from anesthesia, a very low incidence of adverse effects, and no mutagenic or teratogenic effects [2]. These qualities collectively make propofol an ideal hypnotic agent. Given that more than 300 million surgeries and 13-20 million intensive care unit patients undergo mechanical ventilation each year worldwide, it is reasonable to estimate that hundreds of millions of patients receive some form of anesthesia and sedation with propofol annually [3, 4].

On the contrary, the debate regarding the pros and cons of intravenous (IV) anesthetic management for patients is ongoing. There is a growing body of evidence pointing to the potential harm associated with the use of propofol. Hypnotics, while undeniably valuable in specific scenarios, also come with inherent adverse effects. For instance, studies have indicated that the depth of anesthesia is inversely correlated with the outcomes of patients under general anesthesia [5–7]. Beyond this, propofol has been linked to the risk of accidental

microbial contamination [8,9]. It can also impede the organ-protective effects of various drugs and techniques, such as halogenated agents and remote ischemic preconditioning [10,11]. Furthermore, several meta-analyses have demonstrated increased mortality with total IV anesthesia compared to volatile anesthetic agents in cardiac surgery populations [2,12,13]. While a randomized trial discovered an elevated mortality rate among children undergoing sedation with propofol in pediatric intensive care units, there remain numerous reports of propofol use for long-term sedation in children [14].

Furthermore, lactic acidosis, which can have severe consequences, is an observed adverse effect associated with propofol infusion. It may serve as an early indicator of the potentially life-threatening propofol infusion syndrome (PRIS). PRIS is characterized by progressive myocardial failure accompanied by dysrhythmias, metabolic acidosis, hyperkalemia, lipemia, and indications of muscle cell damage [15]. This metabolic disturbance predominantly manifests in intensive care patients who have received prolonged infusions of high-dose propofol, occurring more frequently in cases of impaired oxygen delivery, sepsis, or severe head injuries [16]. Nevertheless, reports have also documented instances of this syndrome in surgical patients receiving propofol at lower doses. Several studies have documented cases of refractory metabolic acidosis and hyperkalemia in patients who were sedated with propofol [17,18]. This phenomenon can potentially be elucidated by the presence of intralipid in propofol, which may compromise hepatic lactate metabolism, resulting in the accumulation of lactate and subsequent acidosis. Moreover, systemic hemodynamic alterations during propofol anesthesia can influence blood flow and perfusion pressure, which can result in changes in electrolytes including sodium, potassium or chloride and changes in anion gap.

The aim of this prospective study was investigating the acid-base status profile and electrolyte changes in patients subjected to propofol-based general anesthesia, all the while maintaining all other components of conventional anesthetic protocols.

MATERIALS & METHODS

In this prospective, observational cohort study, a total of 30 patients were included following approval from the (Reference: 58/21) was obtained from Northern Cyprus Ministry of Health's Dr Burhan Nalbantoglu State Hospital Ethic Committee and obtaining written informed consent. The study included patients between the ages of 18 and 65 with an American Society of Anesthesia (ASA) physical status I and II who were undergoing septoplasty under general anesthesia. Patients who were excluded from the study encompassed those with renal failure, severe liver disease, ischemic heart disease, and a history of propofol allergy.

Monitoring during the surgical procedure included electrocardiograms, pulse oximetry, capnography, and noninvasive blood pressure measurements. The patients were preoxygenated (4 lt/min) when lying on a supine position. Upon establishing IV access, a cannula was inserted into the radial artery for sampling of blood gas measurement. Immediately before the anesthesia induction, an artery sample for analysis of blood gas was obtained and this time was defined as T0. After the anesthesia was induced with propofol (2-3 mg/kg IV), we collected 1 mL of arterial blood samples from each patient, this time was defined as T1. Anesthesia induction followed by fentanyl (2 μg/kg IV) and rocuronium (0.6 mg/kg IV) before performing laryngoscopy and tracheal intubation. The maintenance of anesthesia was accomplished with sevoflurane at a concentration of 1.5-2 minimum alveolar concentrations. During the surgery, patients were provided with a mixture of 50% air and oxygen. At the end of the operation, any residual neuromuscular blockade was reversed through the administration of neostigmine (0.04 mg/kg IV) and atropine (0.02 mg/kg IV).

Arterial blood gas parameters including pH osmolarity uncorrected for temperature was measured with a blood gas analyzer (ABL 825, Radiometer Medical A/S, Copenhagen, Denmark). Standard serum bicarbonate concentration was analyzed using the classical Henderson-Hasselbalch equation and the Siggaard-Andersen nomogram. The normal anion gap is dependent on serum phosphate and albumin concentrations, typically falling within the range of 4 to 12 mmol/L. An increased or normal anion gap metabolic acidosis is usually a result of an excess of acid or a decrease in base. Conversely, a reduced anion gap is most commonly attributed to a reduced albumin concentration, given that albumin is the primary unmeasured anion. The primary application of the anion gap is the classification of cases involving metabolic acidosis, a condition characterized by lower-than-normal blood pH. This classification distinguishes between cases with and without unmeasured anions in the plasma. The anion gap formula is: $(Na^+ + K^+) – (Cl^- + HCO3^-) = \text{Anion Gap}$ [19].

STATİSTİCAL ANALYSİS

Sample size calculations were conducted using G*Power software version 3.1.9.7 from Heinrich-Heine-Universität, Düsseldorf, Germany. Considering the anion-gap changes as the primary outcome, we determined that a sample size of 36 patients was necessary to detect a 20% difference with a significance level (α) of 0.05 and a power of 80%. Considering a 15% dropout probability, we included 42 patients in the study group. Data analysis was carried out using the SPSS version 23.0 statistical software (IBM Corporation, Armonk, NY). Continuous quantitative data with a normal distribution were presented as numbers, mean ± standard deviation, and interquartile range. The normality of the data distribution was assessed with a Kolmogorov–Smirnov test. For parametric data involving repeated measurements, the paired sample test was employed for statistical evaluation. Statistical significance was considered for p-values less than 0.05.

RESULT

In this research, a total of 42 patients who were scheduled for elective surgery under propofol based general anesthesia were included. The mean age of the patients was 41.33±7.84 years. The proportion of females and males was 47.6% (20/42) and 52.4% (22/42), respectively. The average body mass index (BMI) was 26±4.2, and the average hemoglobin was 13.89±2.1 g/dL. The demographic characteristics of these patients are provided in Table 1.

Table 1: Baseline characteristics

	All Patients (n=42)
Age (yr)	41.33±7.84
Sex Female Male	 20 (47.6%) 22 (52.4%)
BMI (kg/m^2)	26±4.2
ASA Status (I/II)	25/17
Hemoglobin	13.89±2.1
Hematocrit	41.93±5.58
MCV	84.44±7.64
LYMPH	7.41±2.92
Platelet	2.23±0.79
Albumin	4.59±0.36
Creatinine	0.76±0.22
AST ALT	27.33±10.41 25.73±10.75

The values are presented as mean ± standard deviation, median (minimum-maximum) and numbers of patients.

When examining the arterial blood gas parameters between T0 and T1, no significant differences were present in electrolyte parameters including sodium, potassium, chloride and calcium (Table 2). There was no statistically significant

difference between the T0 and T1 time points in pH, anion gap and osmolarity (Table 2).

Table 2: The differences of blood gas parameters in comparison to preoperative value.

	T0	T1	p
Na	146.81±3.79	147.10±4.05	0.735
K	4.28±0.92	4.36±0.87	0.683
Ca	1.14±0.76	1.16±0.78	0.905
Cl	107.98±2.76	108.01±3.39	0.964
pH	7.41±0.03	7.40±0.05	0.269
Glucose	97.10±17.56	100.48±19.16	0.401
Urea	14.21±5.33	14.53±5.16	0.780
Osmolarity	304.91±7.86	304.96±8.40	0.977
Anion gap	4.80±1.41	4.90±1.31	0.737

Values are presented as numbers or mean ± standard deviation. Statistically significant at the $p < 0.05$ level.

During the procedure, no notable complications such as hypotension or bradycardia were noted. Although a few patients did experience temporary discomfort and pain at the injection site immediately after the injection, there were no occurrences requiring additional medical attention. Patients who did encounter these issues did not display any enduring abnormalities and were discharged after a short period of bed rest.

DISCUSSION

In this study, we investigated acid-base status profile and electrolyte changes under propofol-based anesthesia in patients with ASAI-II during septoplasty surgery. The acidosis or statistically significant electrolyte changes were not encountered in patients after propofol injection. The adverse effects of propofol including cardiac failure, rhabdomyolysis, severe metabolic acidosis and renal failure were observed in any of the patients.

Propofol, characterized as a short-acting hypnotic agent with economically viable attributes and a tolerable hemodynamic profile, holds significance in clinical practice. On a global scale, a substantial number of patients, estimated at approximately 300 million, undergo surgical procedures [2-4]. Given that these individuals are administered hypnotic agents including propofol during, even minor advantageous or detrimental effects of these medications could potentially manifest as significant health concerns.

The adverse impact of propofol on patient survival cannot be attributed to immediate or acute reactions, such as allergic responses. Existing literature has outlined four potential mechanisms that might elucidate the side effects of propofol on survival. First, propofol may induce PRIS characterized by metabolic acidosis, rhabdomyolysis, hyperlipidemia, and hepatomegaly [20]. Notably, high-dosage (>4 mg/kg/h) and prolonged (>48 h) administration are recognized risk factors. Despite its well-established nature, recent reports of propofol infusion syndrome persist in intensive care settings [21]. Second, propofol's lipophilic nature can heighten the risk of infection, as it supports bacterial growth at room temperature [22]. This has been substantiated by 58 documented instances of propofol-related infection outbreaks between 1989 and 2014 [23]. Even though ethylenediamine tetraacetic acid-containing propofol was introduced around 2000 to inhibit bacterial growth and advancements have been made in preparation and administration techniques to reduce contamination risks, the potential for bacterial growth remains [24-25]. Third, propofol may inhibit the protective properties of other interventions designed to safeguard organs (e.g., volatile organ protection, remote ischemic preconditioning [26]. Fourth, propofol can induce hemodynamic instability by promoting vasodilation and diminishing myocardial contractility [27]. Even brief episodes of hypotension have been associated with

increased mortality, suggesting that hemodynamic impairment could contribute to the elevated mortality rates [28].

In this present study, none of the patients experienced changes in acid-base and electrolyte parameters. In all of our patients, the postoperative course was uneventful, and common causes of lactic acidosis, including hypothermia, prolonged hemodynamic disturbances, or hypoxemia, were systematically ruled out. While it has been demonstrated that metabolic acidosis can potentially harm neurons, the clinical consequences of these observations in terms of perioperative morbidity and mortality are actually not known. However, lactic acidosis could also serve as an early indicator of PRIS. This syndrome, rarely reported during surgical anesthesia in adults, is triggered by propofol in association with catecholamines and steroids, impairing free fatty acid utilization and mitochondrial activity in muscles and the heart [29-30]. Factors contributing to PRIS include a young age, high-rate and prolonged propofol infusions, an imbalance between energy demand and supply, systemic inflammation and sepsis, as well as neurological illnesses [31]. Nevertheless, as already reported by Cravens et al., the incidence of metabolic acidosis is likely underestimated during surgical anesthesia [32]. While propofol has several potential advantages when used general anesthesia, as already mentioned, it would be reasonable to monitor the acid-base status during and after propofol-based anesthesia and, if moderate or severe acidosis occurs, to consider switching to another hypnotic agent, especially in patients experiencing muscle or heart insults.

This present study had some limitations that needed to be reported. Firsty, only the ASA I-II patients were included in this present study. Considering that ASA III and IV patients with comorbidities are prone to hemodynamic and electrolyte disturbance. Therefore, further studies are needed to investigate the effect of propofol injection on acide-base profile and electrolytes. Second, blood samples were obtained only after 5 minutes of propofol injection. Evaluating repeated blood samples could affect the results of this study. Third, we did not evaluate the effect of slower or faster injection of propofol. If a relatively rapid induction of anesthesia is required, it could. Lastly, only adult patients were included. Further studies are needed to compensate for these limitations.

CONCLUSION

In conclusion, this study suggests that propofol-based anaesthesia during uncomplicated septoplasty surgery does not lead to acid-base and electrolyte changes. No instances of cardiac failure, rhabdomyolysis, severe metabolic acidosis, or renal failure were documented in any of the patients as a result of propofol use. Prospective randomized controlled trials are needed to definitively establish the validity of these results.

Declaration by Authors

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