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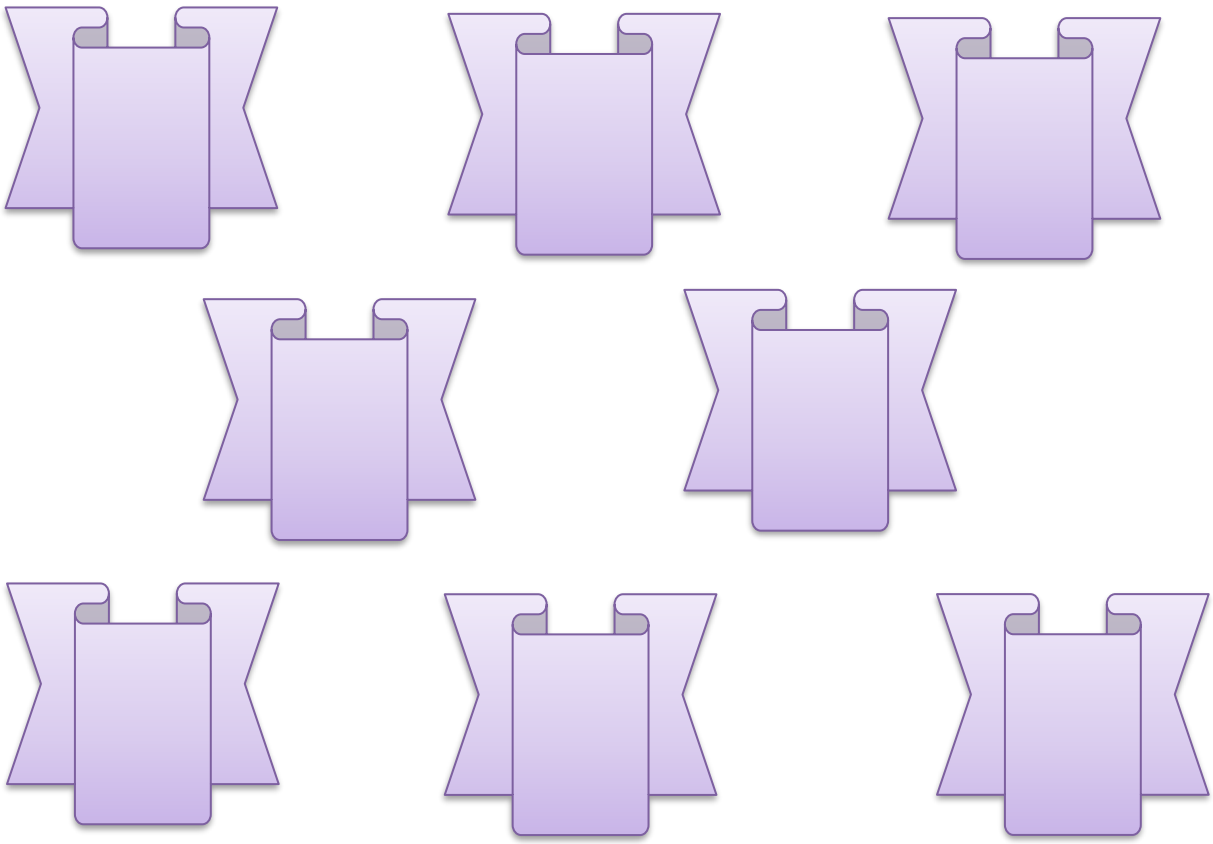

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Original Article

Role of Atropine in Attenuating the Side Effects of Propofol in Procedural Sedation in Anterior Shoulder Dislocation Reduction: A Randomized Controlled Trial

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ABSTRACT

Background: Propofol administration is associated with apnea, bradycardia, hypotension, and injection-site pain.

Aim of the work: To determine the impact of atropine in reducing the adverse effects of propofol used in procedural sedation for anterior shoulder dislocation [ASD] reduction.

Patients and Methods: This randomized, controlled, single-blind study was carried out on 50 patients aged from 18 to 60 years old, both sexes, undergoing ASD reduction. Patients were randomly assigned to two equal groups. Patients received 0.6 mg atropine in group 1 and saline in group 2 before propofol administration. Propofol 2 mg/kg and fentanyl 1 mcg/kg were utilized for sedation. Monitoring of heart rate [HR], and mean arterial pressure [MAP] were started just before the administration of atropine [T_0] and at a one-minute interval after induction for 15 minutes [T_1 -T_{15}]. The incidence of apnea was recorded after propofol administration.

Results: The incidence of apnea was significantly lower with atropine compared to the control group [8% vs. 44%, P=0.004]. HR was significantly higher from T1 to T15 in group 1 compared to group 2 [P <0.05]. MAP was significantly higher from T5 to T15 group 1 than in group 2 [P <0.05]. Hypotension [MAP<65mmHg] and bradycardia [HR<60 beats/min] were insignificantly different between both groups. Allergies did not occur in both groups.

Conclusion: In ASD reduction, atropine attenuates the negative effects of propofol by reducing the incidence of apnea and avoiding the decrease in HR and MAP.

Keywords: Propofol; Atropine; Sedation; Apnea; Anterior Shoulder Dislocation.

INTRODUCTION

Anterior shoulder dislocation [ASD] reduction is a frequent emergency department [EDs] condition. Most of these dislocations are caused by trauma, whereas the rest occur spontaneously [1]. Most ASD reductions are done using procedural sedation and analgesia [PSA] [2].

Propofol is a potent, short-acting sedative and anesthetic involved in several situations requiring short procedural sedation. It has more rapid and deeper sedation, intense muscle relaxation, and faster recovery time over midazolam, enabling shoulder reduction [3]. Propofol is increasingly given to patients for painful procedures and situations requiring anxiolysis or immobilization [4].

However, propofol has drawbacks, such as the possibility of profound sedation, apnea, dose-dependent hypotension, bradycardia, and pain with injection [5].

Fentanyl and propofol have a depressant effect on the heart rate [HR], which can be reversed with atropine. This reversal not only reduces bradycardia and promotes the desired increase in arterial blood pressure, but it also increases cardiac index and tissue oxygenation [6].

There is a lack of publications demonstrating the role of atropine in preventing apnea and the undesirable hemodynamic effects of propofol.

The aim of the work was to determine the consequence of atropine administration in attenuating the adverse events of propofol used in procedural sedation in ASD reduction.

PATIENTS AND METHODS

This randomized controlled single-blind trial was conducted on 50 cases aged from 18 to 65 years old, both sexes and American Society of Anesthesiologists [ASA] I and II undergoing ASD reduction at Tanta and Kafr-Elsheikh University Hospitals, Egypt, from January 2023 to May 2023.

Approval from the Ethical Committee was obtained from Tanta University Hospitals [Approval code: 36148/12/22] before the start of the trial. Each patient gave written informed consent before enrolling in the trial.

Exclusion criteria were contraindications of atropine, ischemic heart disease, tachya-rrhythmias, Mallampati grade III and IV, body mass index [BMI] > 35, and anticipated difficult airway.

Randomization was accomplished using opaque, sealed envelopes and a computer-generated number. Before shifting to the operation theatre, cases were randomly assigned into two groups [25 in each]; group 1 [injected with 0.6 mg atropine] and group 2 [injected with saline only]. Patients will be blinded to the study intervention.

Patients were exposed to complete history taking, general examination, and routine laboratory investigations.

On admission to the operation theatre, the patient was connected to ECG, non-invasive blood pressure, and pulse oximeter. 20G cannula was inserted into the peripheral vein of the other upper limb. Then, a crystalloid solution infusion was infused. Just before induction, patients in group 1 received 0.6 mg atropine diluted in saline [10ml], and patients in group 2 received saline only [10ml].

Ten liters of 100% O_2 through a facemask were administered to oxygenate the patients. Propofol 2 mg/kg and fentanyl 1 mcg/kg were utilized to produce sedation.

HR and mean arterial pressure [MAP] were documented before injection [T_0] and every minute following induction until 15 minutes [T_1 -T_{15}]. Apnea [no detectable expired CO_2 for > 20 seconds and was managed by mask-assisted ventilation if SpO_2 <90% lasted for 30 seconds], hypotension [MAP < 65 mm Hg and was treated by ephedrine 5 mg IV and/or saline 0.9% IVI], bradycardia [HR < 60 beats/min and was treated by atropine 0.6 mg IV], and allergies were documented after propofol administration.

The primary outcome was the incidence of apnea. The secondary outcomes were changes in HR and MAP and incidence of complications including hypotension, bradycardia, and allergy.

Sample size calculations: The sample size calculation was performed using G. power 3.1.9.2 [Universitat Kiel, Germany]. The incidence of apnea [the primary outcome] was 42 % with propofol according to a previous study [7] and expected to be 10% with

administration of atropine. Based on 0.05 α error, 80% power of the study, group ratio 1:1 and two added cases to overcome dropout, 25 patients were allocated to each group.

Statistical analysis: SPSS v26 [IBM Inc., Chicago, IL, USA] was used for statistical analysis. Quantitative data were provided as mean and standard deviation [SD] and compared using an unpaired Student t-test. Qualitative variables were provided as frequency and percentage and compared using the Chi-square or Fisher's exact test. A two-tailed P value less than or equal to 0.05 was deemed statistically significant.

RESULTS

In the current study, the eligibility of 71 cases was evaluated; 16 cases did not match the inclusion criteria, and 5 cases refused participation in the research. The remaining cases were assigned to two groups [25 cases each] in a random and parallel manner. All cases were followed up and statistically analyzed [figure 1].

Demographic data and duration of surgery showed no significant differences between the two groups [table 1].

HR measurements were insignificantly different at T_0 between both groups and were significantly higher from T_1 to T_{15} in group 1 compared to group 2 [P value<0.05] [figure 2].

MAP measurements were insignificantly different at T_0 to T_4 between both groups and were significantly higher from T_5 to T_{15} in cases in group 1 compared to cases in group 2 [P value<0.05] [figure 3].

Group 1 had a significantly lower incidence of apnea than group 2 [2 [8%] vs. 11 [44%], P value=0.004]. The hazardous ratio of apnea was 0.18 times [95% confidence interval 0.04-0.74] in group 1 compared to group 2 [figure 4].

Hypotension and bradycardia did not vary significantly between the two groups. None of the patients in either group developed allergies [table 2].

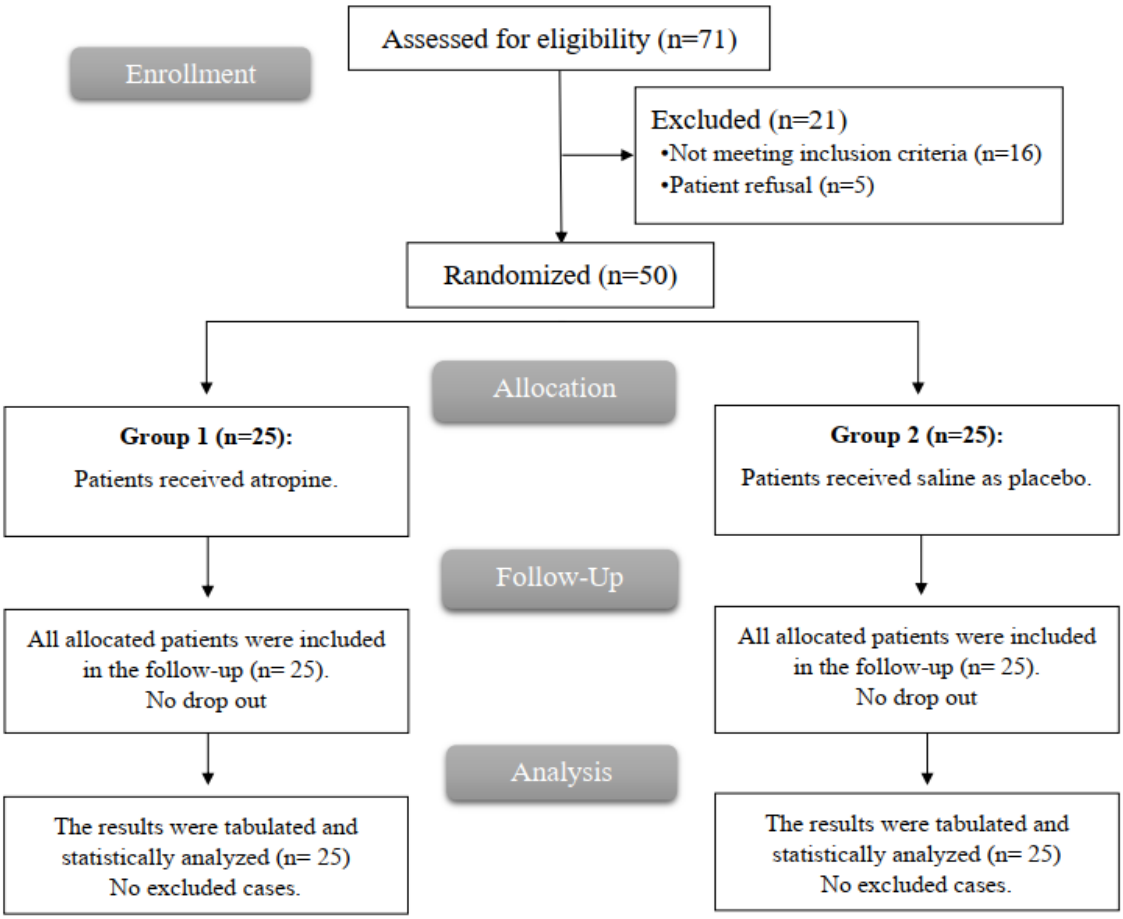

Figure [1]: CONSORT flowchart of the enrolled patients

Table [1]: Demographic data and duration of surgery of the studied groups

		Group 1 [n=25]	Group 2 [n=25]	P value
Age [years]		41.8 ± 11.64	39.72 ± 10.46	0.510
Sex	**Male**	17 [68%]	14 [56%]	0.382
	Female	8 [32%]	11 [44%]	
Weight [kg]		70.96 ± 9.57	73.56 ± 9.33	0.336
Height [m]		1.69 ± 0.06	1.7 ± 0.07	0.486
BMI [kg/m^2]		25.08 ± 4.2	25.68 ± 4.59	0.637
ASA physical status	**I**	16 [64%]	17 [68%]	0.765
	II	9 [36%]	8 [32%]	
Duration of surgery [min]		6.8 ± 2.45	7.2 ± 2.53	0.573

Data are presented as mean ± SD or frequency [%], BMI: Body Mass Index, ASA: American Society of Anesthesiologists.

Table [2]: Complications in the studied groups

	Group 1 [n=25]	Group 2 [n=25]	P value
Hypotension	2 [8%]	5 [20%]	0.417
Bradycardia	0 [0%]	2 [8%]	0.49
Allergy	0 [0%]	0 [0%]	---

Data are presented as frequency [%].

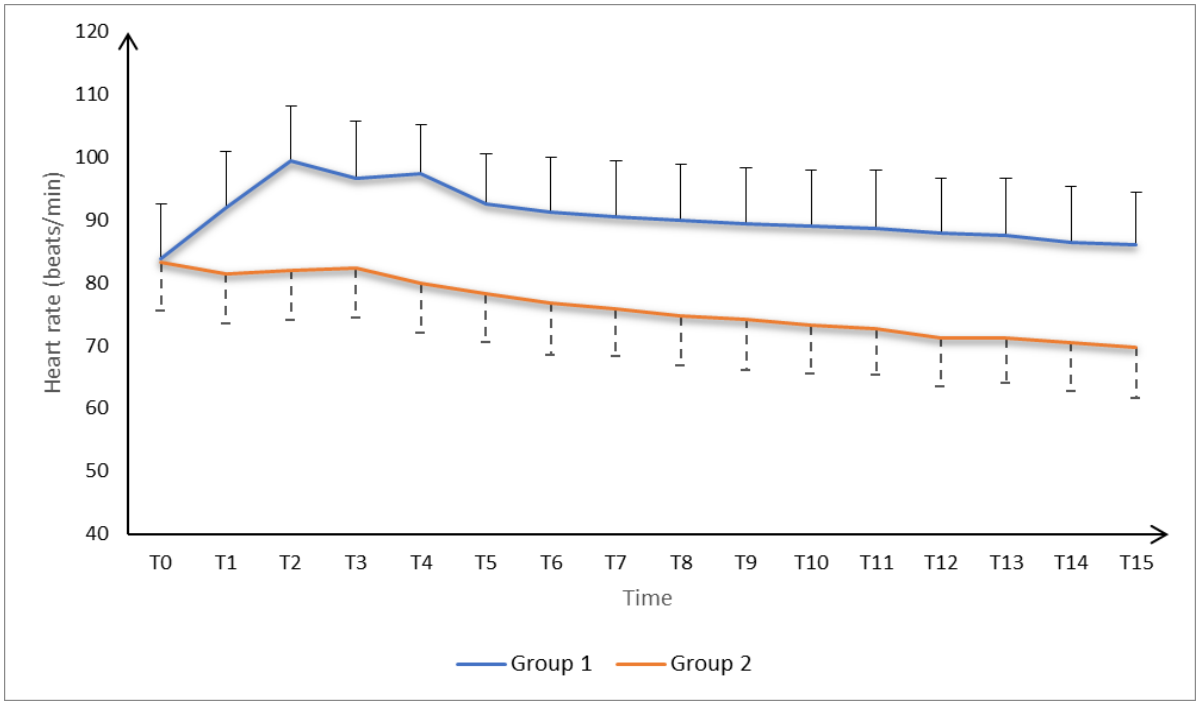

Figure [2]: Heart rate measurements of the studied groups

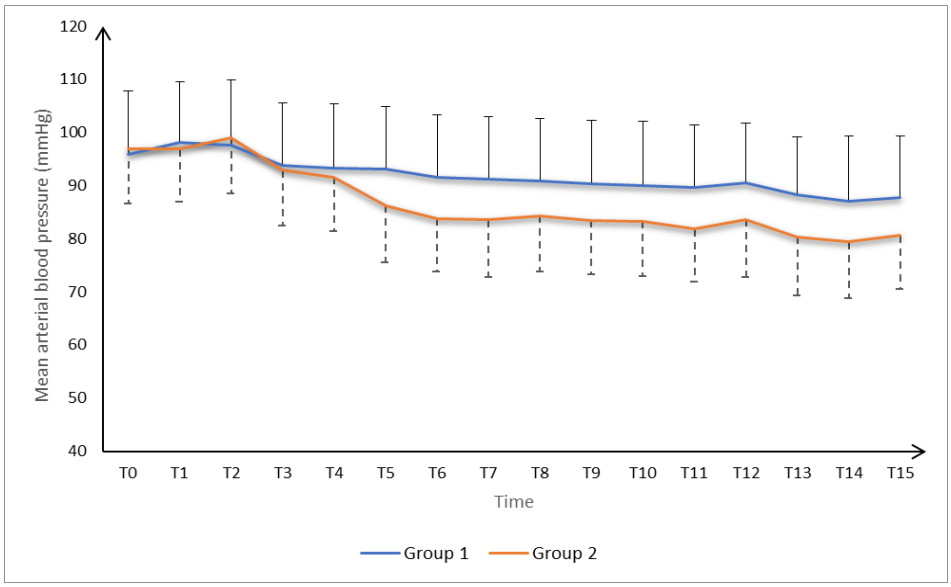

Figure [3]: Mean arterial blood pressure measurements of the studied groups

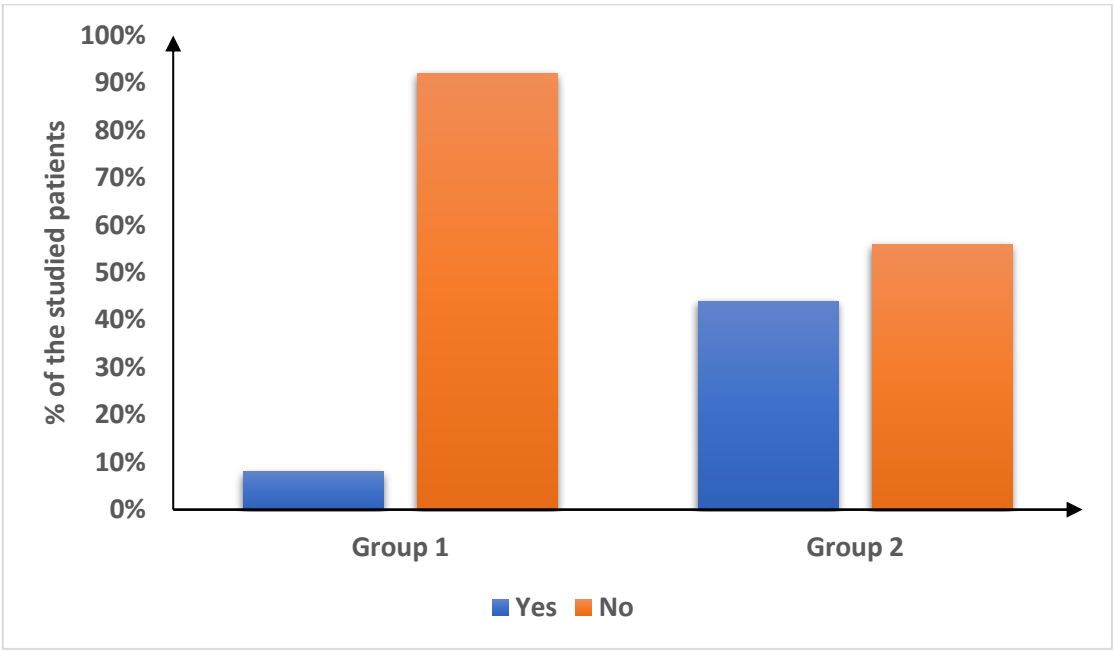

Figure [4]: The incidence of apnea in studied groups

DISCUSSION

ASD reduction may necessitate deep sedation and muscle relaxation to alleviate the accompanying pain and spasms [8]. Propofol is increasingly utilized in EDs for painful operations and patients requiring anxiolysis or immobilization, such as ASD [4]. Propofol enhances the inhibitory neurotransmitter gamma-aminobutyric acid [GABA] at GABA receptors [9]. Hence GABA exhibits a high ACE inhibitory activity that leads to hypotension. CNS-controlled chronotropic effects on the heart by GABA enhance the vagal tonus and consequently affect HR [10]. As a result of the propofol effect on GABA, propofol frequently causes unwanted bradycardia and hypotension, which raises concerns about tissue oxygenation [11].

Meng *et al.* [7] found that propofol was associated with apnea, hypotension, and sinus bradycardia in 42%, 88%, and 10% of patients undergoing gastroscopy, respectively. **Li *et al.*** [12] demonstrated that propofol 2 mg/kg significantly increases systolic and diastolic hypotension frequencies. Also, our result was supported by **Kim *et al.*** [13] study in which MAP was decreased in 12.6% of patients infused with 3.54 mg/kg/h propofol before elective hand surgeries.

In our study, hypotension and bradycardia were insignificantly different between the two groups due to the administration of atropine. In accordance with our study, hypotension and bradycardia occurred in 15.6% and 19% of patients after propofol sedation in patients who underwent colonoscopy, respectively [13]. Besides, the incidence of hypotension during induction with propofol was high [44%] in patients undergoing gastrointestinal endoscopy [14]. **Xiao *et al.*** [15] concluded that MAP and HR values significantly decreased after using propofol in gastroscopy sedation.

Our results showed that HR and MAP were significantly higher in group 1 than in group 2 after propofol administration.

Atropine may counteract the electrophysiological cardiac effects of propofol. Atropine was administered to decrease parasympathetic activation, avoiding bradycardia by inhibiting the muscarinic activities of acetylcholine on smooth muscles and tissues innervated by postganglionic cholinergic neurons [16]. The exact mechanism of atropine in reducing the incidence of apnea has not been clarified yet.

In line with our results, **Raymond *et al.*** [17] observed that HR at 1 min after induction with 2–3 mg/kg propofol [control group] decreased by 10 beats/min and increased by 10 beats/min after administration of 0.01 mg/kg of atropine [the study group].

Significant decreases in MAP and HR were observed after the induction of anesthesia in the saline group compared to the atropine group during the induction of anesthesia, as shown by **Poterman *et al.*** [18].

In this trial, the incidence of apnea was significantly lower with atropine. Allergies didn't occur in any patient in both groups. In **Taylor *et al.*** [4], 23 % of patients in the propofol group had respiratory depression that was characterized by reduced rate and/or decreased PaO_2 and/or partial obstruction, which support the propofol-induced respiratory problem.

In propofol ambulatory anesthesia for surgical abortion, the experimental group had a significantly higher apnoea rate due to propofol that need side stream capnography monitoring [19]. In a previous study, the incidence of airway obstruction was 53.6 % of patients who received propofol that monitored anesthesia care [20].

To our best knowledge, this trial is the first one to focus on the effect of giving atropine to patients whose anesthesia induced with propofol, to overcome the undesirable cardiovascular and respiratory effects of propofol.

This trial was limited by the relatively small sample size, which may contribute to insignificant results of secondary outcomes. We recommend applying our study design and methodology in a multicentral setting with a larger sample size and different doses, volumes, and infusion rates for interventional drugs.

Conclusions: Atropine administration with propofol is highly recommended to attenuate the negative effects of propofol in ASD reduction by avoiding the decrease in HR and MAP and reducing the incidence of apnea.

Acknowledgement: There are none to be declared.

Conflict of interests: None to be declared**.**

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