

# Subhypnotic dose of propofol as a therapeutic modality for postextubation spasm and cough

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## Objectives

To evaluate the effect of injection of a subhypnotic dose of propofol on postextubation laryngospasm and cough following both total intravenous anesthesia (TIVA) and general inhalational anesthesia.

## Patients and methods

The study included 120 patients divided randomly into two equal groups: the inhalation group and the TIVA group. The inhalation group was assigned to receive inhalational anesthesia with no propofol for either induction or before extubation, and the TIVA group was assigned to receive TIVA. After extubation, the frequency and severity of laryngospasm and cough within 2 min after extubation were recorded. All patients who developed postextubation manifestations received positive pressure ventilation (PPV) using a face mask, and if the condition persisted a subhypnotic dose of propofol (0.8 mg/kg) was given in conjunction with PPV.

## Results

Seventy-three (60.8%) patients developed postextubation cough: 31 patients (51.7%) in the TIVA group and 42 patients (70%) in the inhalation group, with significantly higher frequency of occurrence and higher severity scores of cough in the inhalation group compared with the TIVA group. Sixty-one (50.8%) patients developed postextubation laryngospasm: 24 patients (40%) in the TIVA group and 37 patients (61.7%) in the inhalation group, with significantly higher frequency of occurrence and severity of laryngospasm in the inhalation group. PPV alone allowed relief of postextubation manifestations in 43 of 49 patients; propofol subhypnotic dose in conjunction with PPV relieved laryngospasm and cough in 21 patients; nine patients required a second propofol dose, whereas two patients required reintubation and oxygenation and were readministered a third dose of propofol before reextubation, which was conducted safely with significantly higher need for the subhypnotic dose of propofol with inhalational anesthesia compared with TIVA.

## Conclusion

Propofol-based TIVA could minimize but not prevent postextubation cough and laryngospasm compared with balanced inhalational anesthesia. Subhypnotic dose of propofol (0.8 mg/kg) could be used as an adjunct to PPV as a therapeutic modality for spasm and cough, with a success rate of 93.3% for laryngospasm relief.

## Keywords:

cough, laryngospasm, postextubation, propofol, subhypnotic dose

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## Introduction

Emergence from anesthesia and extubation induce variant physiological responses including unwanted circulatory and airway reflexes resulting in hypercirculatory manifestations in the form of tachycardia and hypertension and cough, laryngospasm, and bronchospasm. These events may predispose or induce multiple complications either in the operative site or elsewhere in the body [1].

Multiple trials were conducted to minimize or ameliorate the frequency of extubation-related events; however, the outcomes were discrepant. Andrzejowski and Francis [2]

found no difference in the degree of coughing or the hemodynamic response to tracheal extubation after either saline or 2% lidocaine was injected into the appropriate lumen of the tracheal tube. The results obtained by Minogue *et al.* [3] supported the use of endotracheal lidocaine before intubation in patients undergoing general anesthesia for surgery of less than 2 h duration in cases in which coughing on emergence is undesirable. Guler *et al.* [4] suggested that a single-dose bolus injection of dexmedetomidine before tracheal extubation attenuates airway circulatory reflexes during extubation. Yörükoğlu *et al.* [5] found that prone extubation offers less cough and breath holding and continuation of monitoring compared with supine emergence after spine surgery.



Propofol has gained widespread popularity as an induction agent because of the ease and reliability of its use, together with its short duration of action and minimal hangover effect. Such properties allow propofol to be used in short-term surgeries; however, 1-day surgeries and outpatient surgical procedures require early and easy recovery and the general practice of using volatile anesthetics; however, the after effects on emergence still represent a dilemma for anesthetists [6].

The present comparative study aimed to evaluate the effect of injection of a subhypnotic dose of propofol on postextubation laryngospasm and cough following both propofol-based total intravenous anesthesia (TIVA) and balanced general inhalational anesthesia.

### Patients and methods

The study was conducted at the Anesthesia Department, Benha University Hospital, and included 120 patients assigned for various major abdominal surgeries. After obtaining written informed consent the patients were divided randomly, using sealed envelopes, into two equal groups: the control group ( $n = 60$ ) was assigned to receive inhalational anesthesia with no propofol for either induction or before extubation and group B ( $n = 60$ ) was assigned to receive TIVA.

Patients with a history of bronchial asthma, allergy especially to any of the used medications, and those who had chest, cardiovascular, or upper respiratory tract diseases were not enrolled in the study, nor were smokers and obese patients with BMI greater than  $35 \text{ kg/m}^2$ .

For patients assigned to receive inhalational anesthesia, anesthesia was induced with thiopental ( $3\text{--}5 \text{ mg/kg}$ ), fentanyl ( $2\text{--}3 \mu\text{g/kg}$ ), and rocuronium ( $0.5 \text{ mg/kg}$ ). Balanced anesthesia was continued with isoflurane, fentanyl, and rocuronium adapted to the patient's physiological reaction to surgical stimuli. After tracheal intubation using an endotracheal tube of 7.5 mm inside diameter for women and 8.5 mm for men, the lungs were ventilated with 50%  $\text{O}_2$  in air. Ventilation was controlled with a tidal volume of  $8\text{--}10 \text{ ml/kg}$ , and the ventilatory rate was adjusted to maintain an arterial partial pressure of carbon dioxide of  $32\text{--}42 \text{ mmHg}$ .

For patients assigned to receive TIVA, anesthesia was induced with  $2.5 \text{ mg/kg}$  of propofol,  $2\text{--}3 \mu\text{g/kg}$  of fentanyl, and  $0.6 \text{ mg/kg}$  of rocuronium; after the patient fell asleep fentanyl ( $1\text{--}2 \mu\text{g/kg/h}$ ) and propofol ( $100\text{--}200 \mu\text{g/kg/h}$ ) were given as a continuous intravenous infusion.

Patients were continuously monitored using noninvasive monitors for heart rate, blood pressure, respiratory rate, and  $\text{SpO}_2$ . After completion of the surgical procedure, the maintenance anesthetic agents were discontinued. Reversal of muscle relaxant was performed using neostigmine ( $0.04\text{--}0.08 \text{ mg/kg}$ ) and atropine ( $0.01\text{--}0.02 \text{ mg/kg}$ ). Thereafter, after resumption of regular spontaneous ventilation, the endotracheal secretion was aspirated and removed, and the trachea was extubated while applying

suction through the tube when patients opened their eyes, lifted their head, or attempted self-extubation.

After extubation, when normal breathing was assured, the frequency and severity of laryngospasm and cough responses within 2 min after extubation were recorded and graded as follows: grade 0, no symptoms; grade 1, when stridor was heard; grade 2, if spontaneous respiratory effort was evident with suspicion of tracheal stenosis, but  $\text{SpO}_2$  was at least 90%; and grade 3, if  $\text{SpO}_2$  was less than or equal to 85% or if there was evident cyanosis [7]. The severity of coughing after extubation was determined as follows: grade 0, no cough; grade 1, only one episode of cough; grade 2, two episodes of cough or repeated slight coughs; and grade 3, if there was repeated or severe cough [3]. All patients who developed extubation response received positive pressure ventilation (PPV) using a face mask, and if the condition persisted a subhypnotic dose of propofol ( $0.8 \text{ mg/kg}$ ) was given in conjunction with PPV.

### Statistical analysis

Data are presented as mean  $\pm$  SD, range, numbers, and percentages and were analyzed using Wilcoxon's ranked test for unrelated data (Z test) and the  $\chi^2$ -test. Statistical analysis was conducted using SPSS program version 15 (2006) (SPSS Inc., Chicago, Illinois, USA) and  $P$  value less than 0.05 was considered significant.

### Results

The study included 85 men and 35 women with a mean age of  $34.9 \pm 5.4$  years (range: 27–56 years). Ninety-three patients were American Society of Anesthesiologists (ASA) I and 27 patients were ASA II. There was nonsignificant ( $P > 0.05$ ) difference between the studied groups as regards age, sex, ASA, and BMI (Table 1).

Seventy-three (60.8%) patients developed postextubation cough: 31 patients (51.7%) in the TIVA group and 42 patients (70%) in the control group, with significantly higher frequency of postextubation cough in the control versus the TIVA group ( $\chi^2 = 3.797$ ,  $P < 0.05$ ). Forty-nine patients (40.8%) developed grade 1 cough; 16 patients (13.3%) developed grade 2 cough; and eight patients (6.7%) developed grade 3 cough with significantly higher frequency of higher cough grades in the control group versus the TIVA group ( $\chi^2 = 3.276$ ,  $P < 0.05$ ) (Table 2 Fig. 1).

Sixty-one (50.8%) patients developed postextubation laryngospasm: 24 patients (40%) in the TIVA group and 37 patients (61.7%) in the control group, with significantly higher frequency of extubation events in the control versus TIVA group ( $\chi^2 = 6.834$ ,  $P < 0.01$ ). Forty-three patients (35.8%) developed grade 1 spasm, 13 patients (10.8%) developed grade 2 spasm, and five patients (4.2%) developed grade 3 spasm, with significantly higher frequency of higher spasm grades in the control group versus the TIVA group ( $\chi^2 = 3.181$ ,  $P < 0.05$ ) (Table 3 Fig. 2).



Table 1 Patients' enrollment data

	TIVA group	Inhalational group	Total
Age (years)	37 ± 6.6 (29–55)	34.9 ± 5.4 (27–55)	35.9 ± 6.1 (27–56)
Sex			
Males	42 (70%)	43 (71.7%)	85 (70.8%)
Females	18 (30%)	17 (28.3%)	35 (29.2%)
ASA grade			
ASA I	47 (78.3%)	46 (76.7%)	93 (77.5%)
ASA II	13 (21.7%)	14 (23.3%)	27 (22.5%)
BMI data			
Weight (kg)	86.7 ± 6.4 (78–94)	84.4 ± 3.6 (83–95)	85.6 ± 5.3 (78–95)
Height (cm)	165.3 ± 5.5 (158–180)	165.6 ± 4.3 (158–176)	165.4 ± 4.9 (158–180)
BMI (kg/m <sup>2</sup> )	31.5 ± 2.1 (26.8–33.8)	31 ± 2.2 (25.6–34.1)	31.2 ± 2.1 (25.6–34.1)

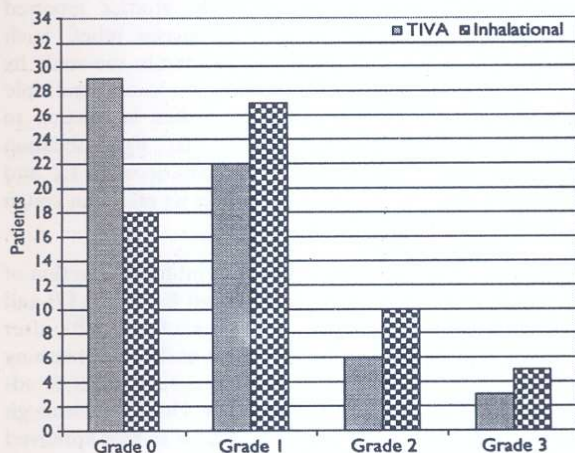
Data are presented as mean ± SD and numbers; ranges and percentages are in parentheses. ASA, American Society of Anesthesiologists; TIVA, total intravenous anesthesia.

Table 2 Patients' distribution according to severity of postextubation cough

	TIVA group	Inhalational group	Total
Grade 0	29 (48.3%)	18 (30%)	47 (39.2%)
Grade 1	22 (36.7%)	27 (45%)	49 (40.8%)
Grade 2	6 (10%)	10 (16.7%)	16 (13.3%)
Grade 3	3 (5%)	5 (8.3%)	8 (6.7%)
Statistical analysis	$\chi^2 = 3.276, P < 0.05$		

Data are presented as numbers; percentages are in parentheses.

Figure 1



Patients' distribution according to cough severity grades. TIVA, total intravenous anesthesia.

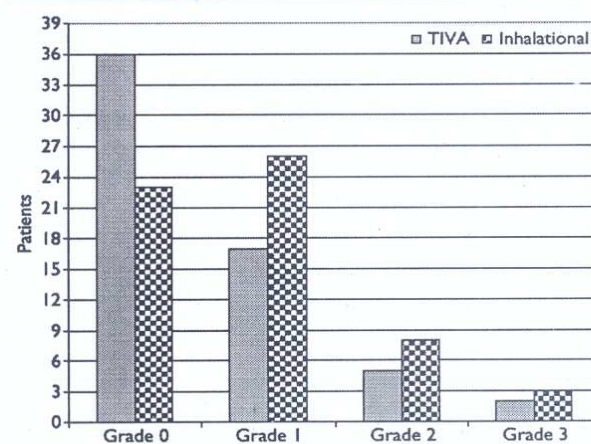
Table 3 Patients' distribution according to severity of postextubation laryngospasm

	TIVA group	Control group	Total
Grade 0	36 (60%)	23 (38.3%)	59 (49.2%)
Grade 1	17 (28.3%)	25 (43.4%)	43 (35.8%)
Grade 2	5 (8.3%)	8 (13.3%)	13 (10.8%)
Grade 3	2 (3.4%)	3 (5%)	5 (4.2%)
Statistical analysis	$\chi^2 = 3.181, P < 0.05$		

Data are presented as numbers; percentages are in parentheses.

PPV allowed relief of grade 1 postextubation manifestations in 43 of 49 patients (87.7%) without the need for propofol injection. For the remaining 30 patients who had

Figure 2



Patients' distribution according to spasm severity grades. TIVA, total intravenous anesthesia.

resistant cough episodes, administration of the subhypnotic dose of propofol in conjunction with PPV relieved spasm and cough in 21 patients (70%). The remaining nine patients required a second dose of propofol, which relieved cough and spasm in seven patients, whereas the remaining two patients required reintubation and oxygenation; reextubation was tried once more after an additional dose of propofol before reextubation, which was conducted safely without complications (Table 4).

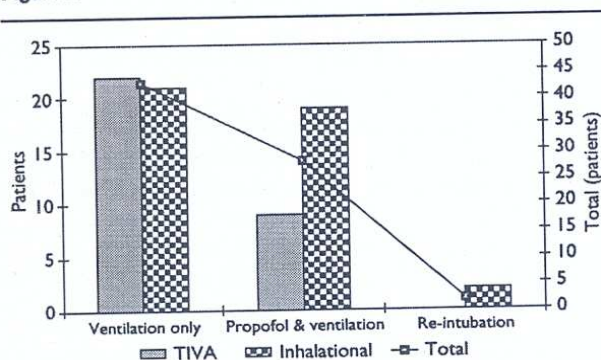
Of the 31 patients in the TIVA group who had postextubation cough and laryngospasm, 22 (71%) responded to PPV, seven (22.5%) received one dose of propofol, and two (6.5%) received it twice. On the contrary, of the 42 patients in the inhalation group who had postextubation cough and laryngospasm, 21 (50%) responded to PPV, 14 (33.3%) received one dose of propofol, five (11.9%) received it twice, and the other two patients (4.8%) required reintubation and received the third propofol subhypnotic dose (Fig. 3). There was significantly higher frequency for the subhypnotic dose of propofol with inhalational anesthesia compared with TIVA ( $\chi^2 = 5.625, P < 0.05$ ).



**Table 4 Patients' distribution according to management policy for postextubation cough and laryngospasm**

Line of management	Data
No therapy	47 (39.2%)
Positive pressure ventilation	43 (35.8%)
Subhypnotic dose of propofol	
Once	21 (17.5%)
Twice	7 (5.8%)
Thrice	2 (1.7%)

Data are presented as numbers; percentages are in parentheses.

**Figure 3**

Distribution of patients who developed spasm and cough according to therapeutic modality. TIVA, total intravenous anesthesia.

## Discussion

The applied policy for management of postextubation spasm and cough using PPV alone or in conjunction with a subhypnotic dose of propofol allowed relief from these manifestations in 60.8% of patients, and only two patients required reintubation.

These data are in line with those of multiple previous studies that tried propofol for relief of postextubation spasm and cough. Afshan *et al.* [8] found that a small dose of propofol (0.8 mg/kg body weight) was a useful drug for relieving laryngeal spasm in most children (76.9%) following the removal of Laryngeal Mask Airway. Sheridan *et al.* [9] tried short-term propofol infusions in 11 critically ill children maintained on morphine and midazolam infusions; nine children (82%) were successfully extubated on the first attempt, whereas two children required reintubation for postextubation stridor after extubation but were successfully extubated the next day again using the same propofol technique.

Hans *et al.* [10] compared the effect of propofol and sevoflurane for maintenance of anesthesia on emergence from anesthesia and extubation and reported that severe coughing at the time of tracheal extubation was significantly higher with sevoflurane.

Teng *et al.* [11] retrospectively reviewed 11 patients admitted to the Cardiac Intensive Care Unit who required mechanical ventilation and received a continuous

infusion of propofol as a bridge to extubation; all patients were successfully extubated. Pak *et al.* [12] compared the effect of a small dose of propofol or ketamine administered at the end of sevoflurane anesthesia on the incidence or severity of coughing in children undergoing a minimal invasive operation. They found that incidence of emergence without coughing was significantly higher with propofol than with ketamine and placebo and concluded that addition of 0.25 mg/kg propofol decreased the incidence of coughing after general anesthesia with sevoflurane in children undergoing nonpainful procedures.

The beneficial effect of propofol, irrespective of being used as a part of TIVA or given as a therapeutic line on occurrence of spasm and cough, could be attributed to the fact that propofol is known as a dose-dependent potent inhibitor of airway reflexes in hypnotic concentrations [13,14]. In addition, propofol is considered to effectively suppress *N*-methyl-D-aspartate receptors and block the ascending pathway from the trachea [15]; thus, occurrence of cough after stoppage of TIVA infusion could be attributed to the diminishing effect of propofol on laryngeal responses.

As regards the dose of propofol to be used, Brown *et al.* [16] used propofol at a dose of 0.5 mg/kg, and both Batra *et al.* [7] and Afshan *et al.* [8], as well as the current study, used 0.8 mg/kg; all of these studies reported comparable figures of success of spasm relief. Such outcome coincided with the results seen in the study by Guglielminotti *et al.* [17], who evaluated multiple propofol concentrations on cough reflex in relation to level of sedation and reported that light sedation was observed with propofol concentrations of 1.2 and 0.9 mg/ml without adversely affecting its effect on cough reflexes.

One point of debate was about the timing of injection of the subhypnotic dose of propofol. Both Batra *et al.* [7] and Pak *et al.* [12] performed tracheal extubation 60 s after administration of propofol when the child was breathing regularly and reacting to the tracheal tube so as to administer it in a prophylactic manner. However, although the current study used the dose similar to that approved by Batra *et al.* [7], which is 0.8 mg/kg, given the failure of PPV to relieve the spasm, it was used on therapeutic basis. This method of administration led to relief in 41 of the 44 patients with cough and spasm resistant to ventilation alone; even the remaining three patients who required reintubation were easily and safely extubated using the same dose as prophylactics, indicating the success of both timings for administration of the assigned dose of propofol.

Thus, it could be concluded that propofol-based TIVA could minimize but not prevent postextubation cough and laryngospasm in comparison with balanced inhalational anesthesia. Subhypnotic dose of propofol (0.8 mg/kg) could be used as an adjunct to PPV as a therapeutic modality for laryngospasm and cough with a success-rate of 93.3% of spasm relief.



## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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