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REPORTS OF ORIGINAL INVESTIGATIONS

Efficacy of a propofol bolus against placebo to prevent cough at emergence from general anesthesia with desflurane: a randomized controlled trial

Efficacité d'un bolus de propofol par rapport à un placebo pour prévenir la toux à l'émergence d'une anesthésie générale avec desflurane : une étude randomisée contrôlée

Marie-Félix Ouellet, MD, FRCPC · Alex Moore, MD, FRCPC · Stephan Williams, MD, PhD, FRCPC · François Girard, MD, FRCPC · Julie Desroches, PhD · Monique Ruel, RN · Pierre Beaulieu, MD, PhD, FRCA

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Abstract

Purpose *Emergence from anesthesia is a critical period and cough can result in adverse effects. Propofol inhibits airway reflexes and when infused it reduces cough more than inhalation anesthesia does. We evaluated the effect of a propofol bolus given at emergence on the incidence of coughing following a desflurane-based anesthesia.*

Methods *One hundred and fifty-four patients scheduled for elective surgery were prospectively randomized to propofol (0.5 mg·kg^{-1}) or normal saline (NS) administered at the end of the surgery at 1 minimum alveolar concentration (MAC) of desflurane. A "no touch" emergence technique was used until extubation. The primary outcome was the incidence of cough at the discontinuation of desflurane (T0) and reaching a MAC adjusted for age (MAC$_{age}$) of 0.15. Secondary outcomes included incidence and severity of cough until five minutes postextubation (T0–T5), time to extubation, nausea and vomiting, sedation, hemodynamic variations, postoperative hypoventilation, hypoxemia, and sore throat.*

Results *We could not draw inferences on the incidence of cough between T0 and MAC$_{age}$ of 0.15 because only 27/68 (40%) patients in the NS group and 13/73 (18%) patients in the propofol group regained consciousness before reaching a MAC$_{age}$ of 0.15. There were no significant differences between the groups in coughing incidence and severity between T0 and T5 (NS group, 57/68 [84%] vs propofol group, 70/73 [96%]). The mean time to extubation in the*

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M.-F. Ouellet, MD, FRCPC
Department of Anesthesiology, Hôpital de Granby, Granby, QC, Canada

Department of Anesthesiology, Faculty of Medicine, Université de Sherbrooke, Sherbrooke, QC, Canada

A. Moore, MD, FRCPC · S. Williams, MD, PhD, FRCPC · F. Girard, MD, FRCPC
Department of Anesthesiology, CHUM, Montreal, QC, Canada

Department of Anesthesiology and Pain Medicine, Faculty of Medicine, Université de Montréal, Montreal, QC, Canada

J. Desroches, PhD · M. Ruel, RN
Department of Anesthesiology, CHUM, Montreal, QC, Canada

P. Beaulieu, MD, PhD, FRCA (✉)
Department of Anesthesiology, CHUM, Montreal, QC, Canada
e-mail: pierre.beaulieu@umontreal.ca

Department of Anesthesiology and Pain Medicine, Faculty of Medicine, Université de Montréal, Montreal, QC, Canada

Department of Pharmacology & Physiology, Faculty of Medicine, Université de Montréal, Montreal, QC, Canada

propofol group was prolonged by 3 min 27 sec (95% confidence interval, 1 min 7 sec to 4 min 47 sec; P < 0.001) and more vasopressors were used at emergence (P = 0.02). The incidence of respiratory complications, nausea and vomiting, agitation, and sedation were not different between groups.

Conclusion *In the present trial, a propofol bolus administered at emergence did not reduce the incidence of cough occurring between T0 and T5 following a desflurane-based general anesthesia compared with placebo.*

Trial registration *ClinicalTrials.gov (NCT02932397); registered 13 October 2016.*

Résumé

Objectif *L'émergence de l'anesthésie est une période critique et la toux peut entraîner des effets indésirables. Le propofol inhibe les réflexes des voies aériennes et, lorsqu'il est perfusé, il est plus efficace pour réduire la toux que l'anesthésie inhalée. Nous avons évalué l'effet d'un bolus de propofol administré à l'émergence sur l'incidence de toux après une anesthésie à base de desflurane.*

Méthode *Cent cinquante-quatre patients devant bénéficier d'une chirurgie non urgente ont été randomisés prospectivement à recevoir du propofol (0,5 mg·kg^{-1}) ou une solution physiologique de sérum salé (NS) administrée à la fin de la chirurgie lorsque la concentration alvéolaire minimale (MAC) de desflurane était de 1. Une technique d'émergence « sans contact » a été utilisée jusqu'à l'extubation. Le critère d'évaluation principal était l'incidence de toux à l'arrêt du desflurane (T0) et à l'atteinte d'une MAC ajustée en fonction de l'âge (MAC$_{âge}$) de 0,15. Les critères d'évaluation secondaires comprenaient l'incidence et la gravité de la toux jusqu'à cinq minutes après l'extubation (T0-T5), le délai d'extubation, les nausées et vomissements, la sédation, les variations hémodynamiques, l'hypoventilation postopératoire, l'hypoxémie et les maux de gorge.*

Résultats *Nous n'avons pas pu tirer de conclusions sur l'incidence de toux entre T0 et à une MAC$_{âge}$ de 0,15 parce que seulement 27/68 (40 %) patients du groupe NS et 13/73 (18 %) patients du groupe propofol ont repris conscience avant d'atteindre une MAC$_{âge}$ de 0,15. Il n'y avait aucune différence significative entre les groupes dans l'incidence et la gravité de la toux entre T0 et T5 (groupe NS, 57/68 [84 %] vs groupe propofol, 70/73 [96 %]). Le temps moyen d'extubation dans le groupe propofol a été prolongé de 3 min 27 sec (intervalle de confiance à 95 %, 1 min 7 sec à 4 min 47 sec; P < 0,001) et une plus grande quantité de vasopresseurs a été utilisée à l'émergence (P = 0,02). L'incidence de complications respiratoires, de nausées et vomissements, d'agitation, et de sédation n'était pas différente entre les groupes.*

Conclusion *Dans la présente étude, un bolus de propofol administré à l'émergence n'a pas réduit l'incidence de toux survenant entre T0 et T5 après une anesthésie générale à base de desflurane par rapport au placebo.*

Enregistrement de l'étude *ClinicalTrials.gov (NCT02932397); enregistrée le 13 octobre 2016.*

Keywords cough · desflurane · emergence · propofol

During general anesthesia, emergence is a critical period[1] where cough can result in adverse effects such as tachycardia, hypertension, neck hematoma, wound dehiscence after laparotomy, and intracerebral hemorrhage after neurosurgery.[2,3] Furthermore, coughing during emergence from general anesthesia affects 40–76% of intubated patients.[4] Therefore, it is important to perform a smooth emergence to reduce coughing and to avoid these complications. Several drugs have been used to reduce cough at emergence, including dexmedetomidine, remifentanil, and lidocaine.[4–6] Propofol inhibits airway reflexes,[7] and total intravenous anesthesia (TIVA) reduces cough more than inhalation anesthesia does.[8–10] Nevertheless, the effect of a propofol bolus on the prevention of cough during emergence from a desflurane-based general anesthesia has never been evaluated.

We hypothesized that giving a propofol bolus at emergence from a desflurane-based general anesthesia would decrease the incidence of cough.

Methods

We conducted a randomized, placebo-controlled, double-blind clinical trial. Between November 2016 and October 2017, at the Centre Hospitalier de l'Université de Montréal (Montreal, QC, Canada), following local Research Ethics Board approval, 154 patients with an American Society of Anesthesiologists (ASA) Physical Status of I–III and age of 18–80 yr who were scheduled for an elective surgery with orotracheal intubation consented to be randomized to either the propofol or the control group. Ethnicity was identified by the research nurse/assistant when communicating with the patient preoperatively to fill in the case report form. The classification was designed by the investigators and divided into five categories (Caucasian, Black, Asian, American Indian, and other).

The trial was registered at ClinicalTrials.gov (NCT02932397) on 13 October 2016. Exclusion criteria included patients scheduled for ear, nose, and throat surgery, thoracic surgery, and neurosurgery; patients with tracheostomy; contraindication to propofol; history of asthma or chronic bronchitis; symptoms of upper airway

infection at the preoperative visit; history of difficult intubation (Cormack-Lehane grade 3 or 4 view); coagulation disorder; unsecured cerebral aneurysm; cognitive decline diagnosed before the operation; severe cardiovascular disease; pregnancy; breastfeeding; hearing problems; and language barrier (inability to speak French or English).

The primary objective of this study was to evaluate the effect of propofol administered as an *iv* bolus on the incidence of cough during emergence from a desflurane-based general anesthesia in intubated patients. Secondary objectives included the severity of cough, time to extubation, postoperative sedation, incidence of hypoventilation/hypoxia, changes in blood pressure and heart rate following the randomized drug administration, patient agitation at emergence, incidence of postoperative nausea and vomiting (PONV), and pain on swallowing after extubation. Furthermore, age, sex, racial origin, type of surgery, ASA Physical Status, active smoking, grade of intubation, length of anesthesia, and angiotensin converting enzyme (ACE) inhibitors prescription were recorded.

Patients underwent standardized general anesthesia with an induction consisting of propofol (0.5–3 $mg \cdot kg^{-1}$), optional midazolam (0.5–2 mg), fentanyl, sufentanil, or remifentanil at the discretion of the attending anesthesiologist, and succinylcholine and/or rocuronium. General anesthesia was maintained using desflurane (end-tidal concentration of 0.8–1.2 minimum alveolar concentration adjusted for age [MAC_{age}]) in a mixture of air and oxygen. Nitrous oxide, lidocaine, dexmedetomidine, ketamine, and nonsteroidal anti-inflammatory drugs were not allowed during the surgery. Tracheal intubation was performed by either direct laryngoscopy or using a videolaryngoscope. The cuff of the endotracheal tube (Shiley^{TM} HiLo Oral/Nasal Tracheal Tube; Covidien LLC, Mansfield, MA, USA) was filled with air and its pressure was adjusted after intubation to be within 20–25 cm H_2O. After intubation, patients were placed on a controlled mode of mechanical ventilation with the objective to maintain an end-tidal CO_2 concentration between 33 and 37 mm Hg. This setting was kept throughout the surgery and for the emergence. Opioids were allowed until ten minutes (remifentanil) or 20 min (fentanyl, sufentanil) before the expected end of the surgery. When the end of surgery was confirmed (after the last surgical stitch), based on the randomized group, either a propofol (0.5 $mg \cdot kg^{-1}$) or a normal saline (NS) (0.05 $mL \cdot kg^{-1}$) bolus was administered to the patient at 1 MAC. Total body weight was used in this study. Thereafter, desflurane was discontinued and fresh oxygen flow was increased to 12 $L \cdot min^{-1}$. A standardized "no touch" emergence technique was used. When a patient reached a MAC of 0.15 of desflurane, every 30 sec a blind assessor asked the patient to open their eyes. The patients were then extubated if they opened their eyes (spontaneously) after verbal request or if they tried to extubate themselves. The blinded assessor noted the incidence and severity of cough during emergence from anesthesia on a four-point (0–3) scale,[11] up until five minutes after extubation. Time to extubation, PONV, and respiratory complications were also recorded. These recovery profiles and hemodynamic parameters were compared between the groups. All patients in the two groups received PONV prophylaxis via administration of *iv* dexamethasone (8-mg bolus after induction) and *iv* ondansetron (4-mg bolus 20 min before the end of the surgery).

Participants were allocated by our pharmacy with the use of a computer-generated list of random blocks of six patients. The syringes containing the randomized bolus dose were prepared based on the allocation group by a pharmacist otherwise not part of the study and were delivered in an opaque container. Another caregiver, also not part of the investigating team and not caring for randomized patients in any other way, was asked at the right moment to hide and administer the randomized syringe and flush the intravenous line with 10 mL of NS. Researchers, caregivers, and patients were blinded to group allocation.

The primary outcome measure was the incidence of cough at emergence from anesthesia evaluated in the period between the discontinuation of desflurane (T0) and reaching a MAC_{age} of 0.15.

Secondary outcomes were the incidence of cough between T0 and T5; severity of the cough between T0 and MAC_{age} of 0.15; cumulative incidence and severity of cough (see Table 2) at emergence at 0.1 and 0.2 MAC_{age} and until five minutes after extubation; the time between desflurane discontinuation and extubation; the level sedation at extubation, at two minutes after extubation, at five minutes after extubation, and every 15 min in the postanesthesia care unit (PACU) according to the Observer's Assessment of Alertness/Sedation Scale;[12] hypoventilation (defined as a respiratory rate $< 8\ min^{-1}$); hypoxemia (defined as a peripheral oxygen saturation $< 90\%$) after extubation; variation ($> 20\%$) in noninvasive blood pressure and heart rate between T0 and T5; agitation during emergence; PONV at PACU admission; and sore throat at PACU admission measured using a visual analog scale (VAS) score of 0 to 10.[12] A summary of the study protocol during and after surgery is presented in Fig. 1.

Statistical analysis

Statistical analyses were processed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Based on a 30% incidence of emergence cough after a desflurane-based anesthesia

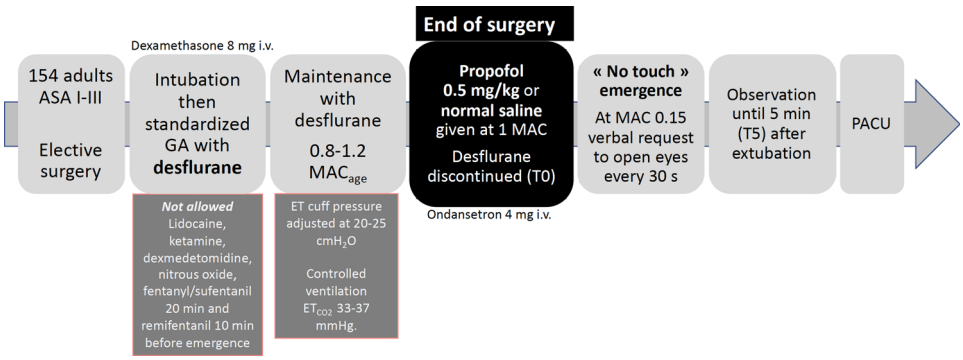

Fig. 1 Summary of study protocol during and after surgery. ET = endotracheal tube; *iv* = intravenous; GA = general anesthesia; PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting

(institutional data from a preliminary unpublished study) and a two-sided alpha of 0.05, a sample size of 70 patients per group was necessary to give us 80% power to detect a clinically significant reduction in cough incidence of 50%. To account for possible loss to follow-up, we recruited a total of 154 patients.

We used Student's *t* test for two samples to compare our groups on continuous variables after confirming the normality of the distribution, and the Chi square test to compare categorical variables. A two-sided *P* value of 0.05 was considered statistically significant. All analyses were carried out using the intention-to-treat principle.

Results

A total of 216 patients were assessed for eligibility, 62 of which did not meet inclusion criteria. One hundred and fifty-four patients were randomized, 77 in each study group. Eleven patients were lost after randomization (three in the propofol group and eight in the placebo group), and two had missing data (one in each group) (Fig. 2). Patients' baseline and perioperative clinical characteristics are shown in Table 1. Five patients in the propofol group and four patients in the NS group were intubated using a videolaryngoscope *vs* a standard laryngoscope.

Regarding our primary outcome measure, the incidence of cough between T0 and a MAC_{age} of 0.15, only 27/68 (40%) in the NS group and 13/73 (18%) in the propofol group regained consciousness before reaching a MAC_{age} of 0.15, hindering our ability to draw inferences. Similarly, 7/68 (10%) patients in the NS group and 11/73 (15%) patients in the propofol group were still under anesthesia at a MAC_{age} of 0.10.

Overall, there was no statistically significant difference between the NS and propofol groups in the coughing incidence during the T0 to T5 interval (84% *vs* 96%; $P = 0.06$) (Table 2). There also was no significant difference in cough intensity between the groups when moderate to severe cough (grade 2–3) was compared with no or mild cough (grade 0–1) (Table 2). Coughing occurred at an average of 0.12 MAC of desflurane in each group. In the propofol group, the mean time to extubation was prolonged by three minutes 27 sec (ten minutes 41 sec *vs* seven minutes 14 sec; 95% confidence interval of the difference, 1 min 7 sec to 4 min 47 sec; $P < 0.001$), there was a need for more vasopressors at emergence ($n = 8/73$ *vs* $n = 1/68$; $P = 0.02$) and the mean (SD) sore throat score was higher (VAS, 1.7 (2,1) *vs* 1.1 (1.8), $P = 0.03$). During recovery, the incidence of respiratory complications, PONV, agitation, and sedation were not different between groups (Table 3).

Discussion

In the present trial, we were unable to draw inferences on our primary outcome measure, the incidence of cough between T0 and a MAC_{age} of 0.15, because of an insufficient number of patients who regained consciousness before reaching a MAC_{age} of 0.15. Our principal finding was that a subhypnotic intravenous bolus of propofol administered at emergence from anesthesia did not reduce the incidence of cough during the T0 to T5 interval following a desflurane-based general anesthesia compared with placebo. Furthermore, propofol administration prolonged extubation time by more than three minutes and may be associated with hypotension and sore throat.

The incidence of coughing in both groups may appear high, but it is important to bear in mind that the measurement tool used in this study was very sensitive. As per protocol, a single forceful expiration was attributed a score of 1. Nevertheless, the more clinically significant incidence of moderate to severe coughing (more than two episodes with scores of 2 and 3) was also similar (70% for propofol and 60% for placebo) in both groups. A high incidence of coughing at emergence from anesthesia has also been reported in the literature, ranging from 38% to 96%.[8,13,15–21] One explanation of the results in this study

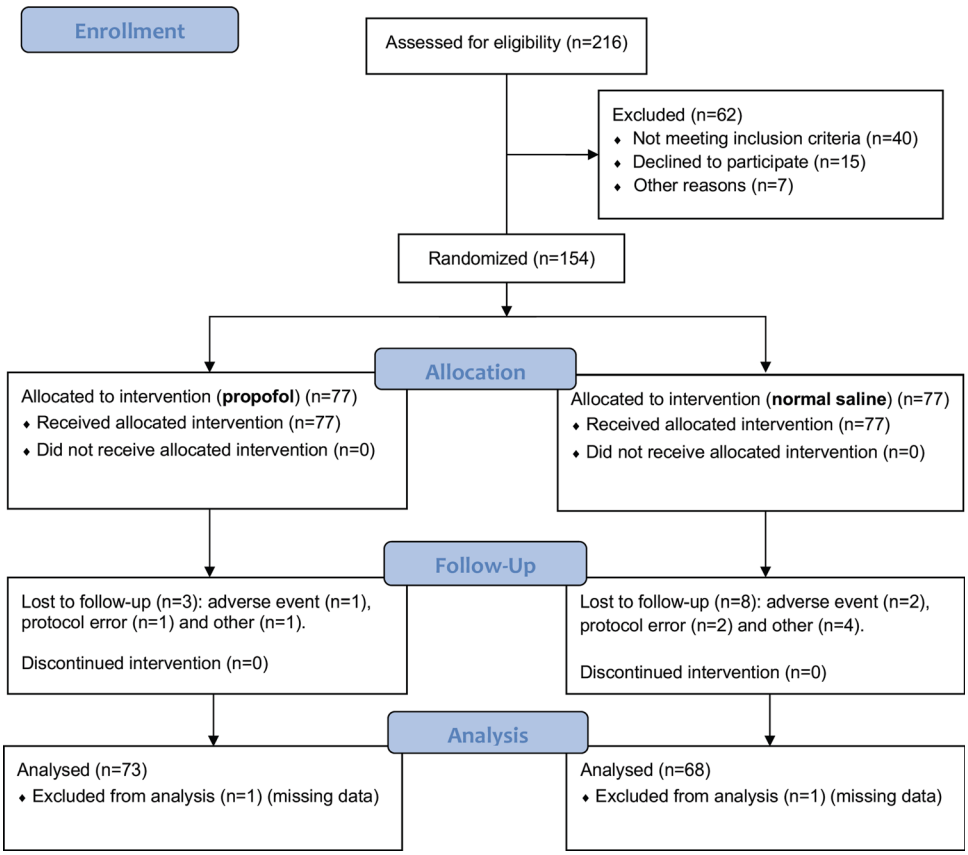

Fig. 2 Study flow diagram

might be that we contraindicated the use of alternative antitussive medication (such as *iv* or intracuff lidocaine) and that we also restricted the use of opioids in the last ten to 20 min before emergence. Another explanation might be that we counted cough for longer than most studies (including our preliminary data), i.e., until five minutes after extubation.

Coughing is a common occurrence during emergence from general anesthesia and may result in unwanted sympathetic stimulation, a rise in intracranial pressure, and agitation. Several strategies have been tried to decrease the incidence of coughing. In a recent systematic review and meta-analysis, Tung *et al.*[4] showed that dexmedetomidine, remifentanil, fentanyl, and lidocaine all reduced the incidence of moderate to severe emergence coughing, whereas dexmedetomidine appeared to be the most effective medication for decreasing the frequency of moderate to severe emergence cough. Interestingly, propofol was not evaluated in that study. Propofol is easily available, simple to administer, and is a short-acting hypnotic, with a distribution half-life of two to eight minutes. Infusion of propofol as part of TIVA or target-controlled infusion (TCI) is associated with less coughing at emergence than inhaled anesthetics.[8–10] Nevertheless, there are few data available on the effectiveness of propofol, given as a bolus, to reduce coughing during emergence in intubated adult patients.

The main reasons we decided to use only desflurane in our study were that "green anesthesia" with sevoflurane was not yet widely promoted when we began this study, and that to concentrate on one volatile agent only helped to standardize as much as possible the groups except for the bolus of propofol given at emergence. Furthermore, we had already finished a pilot trial using remifentanil at emergence and it was done using desflurane, so we continued with the same agent. Finally, desflurane is considered the most irritating volatile anesthetic and may increase upper airway reactivity and we wanted to see if propofol administration could be of any help in reducing cough at emergence. Indeed, at 1.0 MAC, sevoflurane is better than desflurane at suppressing cough and is associated with hemodynamic changes caused by deflating/inflating the endotracheal tube cuff.[20] At 2.0 MAC, inhalation of desflurane in unpremedicated patients induced more coughing and complaints of burning and irritation than isoflurane and sevoflurane did.[20] Compared with a perfusion of propofol used as TIVA/TCI, the required half maximal effective concentration (EC_{50}) of plasmatic remifentanil for preventing coughing with desflurane is significantly higher (although not reaching statistical significance *vs* sevoflurane in that

Table 1 Patient characteristics and demographics

	Normal saline *N* = 68	Propofol *N* = 73
Age (yr), mean (SD)	53 (14)	55 (14)
BMI ($kg \cdot m^{-2}$), mean (SD)	29 (7)	27 (5)
Sex, *n*/total *N* (%)		
Male	22/68 (32%)	19/73 (26%)
Female	46/68 (68%)	54/73 (74%)
Ethnicity, *n*/total *N* (%)		
Caucasian	60/68 (88%)	69/73 (95%)
Black	2/68 (3%)	1/73 (1%)
Other	6/68 (9%)	3/73 (4%)
ASA Physical Status, *n*/total *N* (%)		
I	14/68 (21%)	15/73 (21%)
II	40/68 (59%)	47/73 (64%)
III	14/68 (21%)	11/73 (15%)
Alcohol consumption, *n*/total *N* (%)		
None	28/68 (41%)	35/73 (48%)
On occasion	36/68 (53%)	34/73 (47%)
> 10 consumptions/week	4/68 (6%)	4/73 (5%)
Smoker, *n*/total *N* (%)		
Yes	11/68 (16%)	12/73 (16%)
No	57/68 (84%)	61/73 (84%)
On ACE inhibitors, *n*/total *N* (%)		
Yes	7/68 (10%)	7/73 (10%)
No	61/68 (90%)	66/73 (90%)
Type of surgery, *n*/total *N* (%)		
General	31/68 (46%)	34/73 (47%)
Plastic	18/68 (26%)	20/73 (27%)
Orthopedic	6/68 (9%)	6/73 (8%)
Gynecology	9/68 (13%)	5/73 (7%)
Ophthalmology	3/68 (4%)	6/73 (8%)
Vascular	1/68 (1%)	2/73 (3%)
Endotracheal cuff pressure at intubation (cm H_2O), mean (SD)	46 (30)	44 (29)

ACE = angiotensin-converting enzyme; ASA = American Society of Anesthesiologists; BMI = body mass index; SD = standard deviation

study).[20] Selection of a specific inhaled anesthetic could thus theoretically influence the risk of coughing during emergence from general anesthesia.

Jung *et al*. compared the use of a subhypnotic bolus dose ($0.3\ mg \cdot kg^{-1}$) of propofol to placebo during emergence from a combined sevoflurane and remifentanil ($0.05–0.20\ \mu g \cdot kg \cdot min^{-1}$) anesthesia in 60 patients.[21] The authors reported a significant decrease in the incidence (60% *vs* 87%, $P < 0.05$) and severity (median [interquartile range], 2 [0–2] *vs* $2^{1–3}$; $P < 0.05$) of coughing in the propofol group without delaying wake up or influencing hemodynamics in adults undergoing nasal surgery. A remifentanil infusion was maintained at $0.03\ \mu g \cdot kg \cdot min^{-1}$ and sevoflurane at 1% for the last five minutes before the end of surgery in both groups. Then, sevoflurane and remifentanil were discontinued, fresh gas flow was set at $5\ L \cdot min^{-1}$, and mechanical ventilation was switched to manual ventilation. The randomized medication was administered three minutes after discontinuing sevoflurane and remifentanil. Cough was recorded until five minutes after extubation with the same scale we used in the present study. Time to extubation was approximately 10–11 minutes in both groups, which compares to our time of extubation in the propofol group.[21] Our results cannot readily be compared with those of this study because of important differences in the design. Sevoflurane is not

Table 2 Coughing distribution until five minutes postextubation

	Normal saline $N = 68$	Propofol $N = 73$	P value
Cough occurrence, *n*/total *N* (%)	57/68 (84%)	70/73 (96%)	0.06
Cough grade, *n*/total *N* (%)			
0 (no cough)	11/68 (16%)	3/73 (4%)	
1 (mild, single cough)	16/68 (24%)	19/73 (26%)	
0–1	27/68 (40%)	22/73 (30%)	0.24
2 (moderate, lasting for < 5 s)	18/68 (27%)	29/73 (40%)	
3 (severe, sustained for > 5 s)	23 (34%)	22/73 (30%)	
2–3	41/68 (60%)	51/73 (70%)	0.24
Missing data, *n*	9	4	

Table 3 Recovery profiles in both study groups

	Normal saline $N = 68$	Propofol $N = 73$	P value
Time to extubation, mean (SD)	7 min 14 s (4 min 2 s)	10 min 41 s (3 min 57 s)	< 0.001[a]
MAC_{age} at extubation, mean (SD)	0.14 (0.04)	0.12 (0.04)	0.002
Sedation (OAA/S scale[b]), *n*/total *N* (%)			0.62
At extubation			
4–5	39/68 (57%)	41/73 (56%)	
0–3	29/68 (43%)	32/73 (44%)	
5 min post extubation			0.41
4–5	59/68 (87%)	67/73 (92%)	
0–3	9/68 (13%)	6/73 (8%)	
Respiratory complications, *n*/total *N* (%)	8/68 (12%)	11/73 (15%)	0.56
Hypoventilation, *n*	5	6	
Hypoxemia, *n*	5	6	
Laryngospasm, *n*	1	3	
Agitation, *n*	4	2	
PONV, *n*/total *N* (%)	8/68 (12%)	10/73 (14%)	0.39

[a] Magnitude of difference, mean (95% confidence interval): 3 min 27 sec (1 min 7 sec to 4 min 47 sec)

[b] Range of scale, 5 to 1; a score of 5 corresponds to an alert state and a score of 1 to a deep sleep state

MAC_{age} = Minimum alveolar concentration adjusted for age; OAA/S = Modified Observer's Assessment of Alertness/Sedation Scale; PONV = postoperative nausea and vomiting; SD = standard deviation

associated with the same incidence of airway irritation than desflurane in the literature. In addition, the later timing of their propofol administration, combined with a recently stopped remifentanil infusion and manual instead of mechanical ventilation during extubation precludes direct comparison with our results.

A recent study showed that an intravenous combination of propofol (0.25 $mg{\cdot}kg^{-1}$) and low-dose ketamine (0.15 $mg{\cdot}kg^{-1}$) significantly reduced the incidence and severity among patients awakening from general anesthesia using sevoflurane compared with propofol alone or NS.[22] The design was completely different from ours (drugs administered one minute prior to extubation, intravenous lidocaine allowed, etc.) but also shows that propofol used as an intravenous bolus alone was not different than NS at reducing the incidence and severity of cough. Another study showed that, at the end of general anesthesia with isoflurane in children undergoing tonsillectomy, 0.5 $mg{\cdot}kg^{-1}$ propofol is more effective than 0.5 $mg{\cdot}kg^{-1}$ ketamine in reducing cough response upon emergence from anesthesia, with a lower incidence of nausea and vomiting, as well as lower sedation.[23] In that study, no

control group was used, the population and inhalational agent were different from those in our study, and the study drugs were administered two minutes prior to extubation.

Of note, the absolute incidence of cough at emergence (T0–T5) in our study was numerically (but not statistically) higher in the propofol group, almost reaching predefined statistical significance. While this could be a random effect, the prolonged extubation time associated with propofol may have given more time for patients to cough. This might also explain the increased incidence of sore throat in the propofol group.

It is not clear why the use of a propofol bolus could not mimic the effect of a propofol infusion on the incidence of cough. Given the short distribution half-life of propofol, its antitussive effect may not cover the whole emergence when administered as a bolus. The pharmacokinetics of propofol are variable and we may have obtained another result with a different timing of administration, or with a different dose.

Strengths and limitations

The choice of MAC_{age} of 0.15 was arbitrary and based on the findings of our preliminary study. To recruit similar patients and to standardize the study, we excluded a good number of patients with a higher risk of coughing and adverse effects. Therefore, the results of the present study may not reflect the "real life" situation in the operating room at emergence from anesthesia. The effect of an *iv* bolus of propofol in these populations may need to be evaluated. The nonuse of opioids in the last 10–20 minutes prior to extubation was necessary to evaluate the sole effect of propofol administration on the incidence of coughing at emergence from anesthesia but does not reflect day-to-day practice. Furthermore, the incidence and severity of cough (evaluated using a 4-point scale) may have been too sensitive to appropriately measure our primary outcome in real-life situations. Nevertheless, we recruited a large number of patients using a strict protocol and a multitude of different clinical variables. We obtained interesting data concerning coughing dynamic at emergence.

In conclusion, a 0.5 $mg{\cdot}kg^{-1}$ *iv* propofol bolus administered at emergence did not reduce the incidence of cough occurring between T0 and T5 following a desflurane-based general anesthesia compared with placebo. Furthermore, it prolonged extubation time by 3.4 minutes on average. Finally, during recovery, the incidence of respiratory complications, PONV, agitation, and sedation were not different between groups.

Author contributions *Marie-Félix Ouellet* and *Pierre Beaulieu* contributed to all aspects of this manuscript, including study conception and design; acquisition, analysis, and interpretation of data; and drafting the article. *Alex Moore* contributed to the conception and design of the study, analysis, and interpretation of data; and drafting the article. *Stephan Williams* contributed to the conception and design of the study, data analysis, and drafting the article. *François Girard* contributed to the conception and design of the study. *Julie Desroches* contributed to the acquisition, analysis, and interpretation of data and drafting the article. *Monique Ruel* contributed to the acquisition of data.

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