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Oral clonidine premedication reduces propofol requirement for laryngeal mask airway insertion

Purpose: To determine the effect of oral clonidine premedication on propofol requirement (ED_{50}) for the insertion of the laryngeal mask airway (LMA) in healthy patients undergoing abdominal hysterectomy.

Methods: After ethics committee approval and informed consent, 41 patients were randomly assigned to receive $5 \mu\text{g}\cdot\text{kg}^{-1}$ clonidine *po* premedication 90 min before entering the operating room ($n = 22$), or no clonidine ($n = 19$). To alleviate pain associated with *iv* propofol, 3 ml lidocaine 2% *iv* were administered. General anesthesia was induced, 30 sec later, with propofol at a rate of $100 \text{ mg}\cdot\text{min}^{-1}$ ($600 \text{ ml}\cdot\text{hr}^{-1}$) *iv*. The dose of propofol at which insertion of the LMA was attempted was predetermined by modification of Dixon's up-and-down method with an initial dose of $2.5 \text{ mg}\cdot\text{kg}^{-1}$ and $0.25 \text{ mg}\cdot\text{kg}^{-1}$ as the step size. An LMA was inserted, without muscle relaxants or other adjuvants 90 sec after completion of the propofol injection, by an anesthesiologist blinded to the treatment of the patient.

Results: The ED_{50} of propofol for LMA insertion in clonidine-treated patients ($2.0 \pm 0.2 \text{ mg}\cdot\text{kg}^{-1}$, 1.8-2.3 $\text{mg}\cdot\text{kg}^{-1}$ [95% confidence interval]), was less than that in patients without clonidine ($2.5 \pm 0.1 \text{ mg}\cdot\text{kg}^{-1}$, 2.4-2.6 $\text{mg}\cdot\text{kg}^{-1}$, $P < 0.01$).

Conclusion: Oral clonidine premedication reduces propofol requirement for LMA insertion.

Objectif: Déterminer l'effet d'une prémédication de clonidine orale sur les besoins en propofol (ED_{50}) lors de l'insertion du masque laryngé (ML) chez des patientes en santé qui subissent une hystérectomie abdominale.

Méthode : Après avoir obtenu l'accord du comité d'éthique et le consentement éclairé des participantes, 41 patientes ont été réparties au hasard et ont reçu une prémédication de $5 \mu\text{g}\cdot\text{kg}^{-1}$ de clonidine *po* ($n = 22$), 90 min avant d'entrer dans la salle d'opération, ou n'ont pas reçu de clonidine ($n = 19$). Pour soulager la douleur associée au propofol *iv*, on a administré 3 ml de lidocaïne *iv* à 2 %. L'anesthésie générale a été induite, 30 s plus tard, avec du propofol à $100 \text{ mg}\cdot\text{min}^{-1}$ ($600 \text{ ml}\cdot\text{h}^{-1}$) *iv*. La dose de propofol à laquelle l'insertion du ML a été tentée était déterminée par une modification de la méthode en dents de scie de Dixon avec une dose initiale de $2,5 \text{ mg}\cdot\text{kg}^{-1}$ et des doses de $0,25 \text{ mg}\cdot\text{kg}^{-1}$ comme palier. Un ML a été inséré, sans myorelaxant ou autre adjuvant, 90 s après l'injection de propofol par un anesthésiologiste impartial.

Résultats: La ED_{50} de propofol pour l'insertion du ML chez les patientes traitées avec la clonidine ($2,0 \pm 0,2 \text{ mg}\cdot\text{kg}^{-1}$; 1,8-2,3 $\text{mg}\cdot\text{kg}^{-1}$ [intervalle de confiance de 95 %]), a été plus faible que chez les patientes sans clonidine ($2,5 \pm 0,1 \text{ mg}\cdot\text{kg}^{-1}$; 2,4-2,6 $\text{mg}\cdot\text{kg}^{-1}$, $P < 0,01$).

Conclusion : La prémédication de clonidine orale réduit les besoins en propofol lors de l'insertion du ML.

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Accepted for publication March 10, 2000.

CLONIDINE reduces induction time of sevoflurane,¹ awakening concentrations of sevoflurane and isoflurane,^{1,2} and minimum alveolar concentration (MAC) of sevoflurane required for tracheal intubation.³ These findings suggest that clonidine may also reduce the anesthetic requirement for insertion of a laryngeal mask airway (LMA), which is often accomplished with propofol as the sole agent because of the more profound depression of upper airway reflexes and greater jaw relaxation that it produces in comparison with thiopental.^{4,5} This study was designed to test the hypothesis that oral clonidine reduces the amount of propofol required to insert an LMA in healthy patients.

Method

The protocol was approved by our ethics committee, and informed consent was obtained from each patient. Forty-one patients (25-61 yr), ASA I or II, undergoing total abdominal hysterectomy were studied. Patients were excluded if they were allergic to propofol, or had gastroesophageal, central nervous system, respiratory tract, or psychiatric disorders. They were randomized to clonidine group ($n = 22$) receiving clonidine approximately $5 \mu\text{g}\cdot\text{kg}^{-1}$ plus 20 mg famotidine *po*, or control group ($n = 19$) receiving 20 mg famotidine *po*, 90 min before arrival at the operating room. No other opioids or sedatives were given.

Standard monitoring including electrocardiography, noninvasive blood pressure and pulse oximetry were applied. Oxygen, $6 \text{ l}\cdot\text{min}^{-1}$, was delivered via a face mask for three minutes before general anesthesia induction and was continued until an effective airway was established. To alleviate pain from *iv* propofol, 3 ml lidocaine 2% was first administered. Then, general anesthesia was induced in the supine position 30 sec later with propofol at a rate of $100 \text{ mg}\cdot\text{min}^{-1}$ *iv*. A laryngeal mask airway (size #3) was inserted without other adjuvants 90 sec after completion of the propofol injection. The dose of propofol at which insertion of the LMA was attempted was predetermined by the response of the previous patient, using modification of Dixon's up-and-down method.⁶ The first patient in each group received $2.5 \text{ mg}\cdot\text{kg}^{-1}$,⁴ and the step size was $0.25 \text{ mg}\cdot\text{kg}^{-1}$. All anesthetic management and insertions of the LMA were performed by a single anesthesiologist (TG) blinded to the patients treatment and propofol doses.

Patients response to the insertion of the LMA was described as "no movement" or "movement". "No movement" refers to the absence of bucking or gross purposeful muscular movements until an effective airway was established by confirming the square waveform

TABLE Estimated values of the coefficients of logit $(p/1-p) = B_0 + B_1 X$

	Clonidine group	Control group
Intercept	-13.115	-17.465
Slope	6.680	7.305
Propofol dose	1.963	2.391
<i>P</i>	0.0236	0.0355

Goodness of fit chi-squared clonidine group = 0.9208; control group = 0.7264.

$(P/1-P) = B_0 + B_1 X$, B_0 = intercept, B_1 = slope, $X = \text{ET}_{\text{propofol}}^{-1}$ ($\text{mg}\cdot\text{kg}^{-1}$).

of the capnograph, synchronous thoracoabdominal movement, and the absence of stridor. "Movement" refers to difficult mouth opening, gross purposeful movement, coughing, straining or laryngospasm before or after inflation of the LMA.⁷ If the patient "moved", the maneuver was stopped, and a further attempt was not made until 30 sec after an additional injection of $0.5 \text{ mg}\cdot\text{kg}^{-1}$ propofol. The presence or absence of movement was documented by the anesthesiologist (TG) and the nurse in charge of the case, who also remained blinded to the patients treatment and the propofol dose. When both observers documented any movement, the case was described as "movement". Each patient was tested for a single propofol dose.

The ED_{50} was estimated from calculating the midpoint dose of all independent pairs of patients involving a cross-over, i.e. "movement" to "no movement". The ED_{50} was defined as the average of the cross-over midpoints in each group. We have studied consecutive patients until six cross-over midpoints were obtained. Statistical analyses were performed using unpaired Student's *t* test, the probit test (SAS proprietary software, Chicago, IL), and a logistic regression test as appropriate. All values are expressed as mean $\pm$ SD, and a *P* value < 0.05 was considered statistically significant.

Results

There were no differences in terms of age (42 ± 7 vs 44 ± 8 yr), weight (53.7 ± 8.6 vs 55.1 ± 9.1 kg), or height (155 ± 6 vs 156 ± 5 cm) between the clonidine and control groups, respectively. The ED_{50} of propofol requirement in the clonidine group ($2.0 \pm 0.2 \text{ mg}\cdot\text{kg}^{-1}$, $1.8\text{--}2.3 \text{ mg}\cdot\text{kg}^{-1}$ [95% CI]) was less than that in the control group ($2.5 \pm 0.1 \text{ mg}\cdot\text{kg}^{-1}$, $2.4\text{--}2.6 \text{ mg}\cdot\text{kg}^{-1}$, (Figure 1) $P = 0.0013$). Logistic regression curves of the probability of no movement upon the LMA insertion in the clonidine and control groups are shown in Figure 2. Maximum likelihood estimators of the logistic regression model parameters and assess-

FIGURE 1 The responses of 22 (clonidine group) and 19 (control group) consecutive patients in whom laryngeal mask airway insertion was attempted, and the propofol dose. Patients are represented by an open circle and a square. Closed circles indicate the midpoint propofol doses of all independent pairs of patients involving a cross-over, *i.e.* "movement" to "no movement". The propofol doses required for smooth insertions of the laryngeal mask airway in the clonidine and control groups were 2.0 ± 0.2 and 2.5 ± 0.1 mg·kg⁻¹, respectively.

ment of goodness of fit are presented in the Table. There were no differences between the observed and the predicted values in both groups. At LMA insertion, no patient developed $\text{SpO}_2 < 97\%$.

Discussion

Our results demonstrated that propofol requirement for the LMA insertion was reduced by oral clonidine premedication. Clonidine reduces the induction dose of propofol in adults,⁸ MAC and induction time of sevoflurane in adults,¹ MAC of sevoflurane required for tracheal intubation in children,³ and awakening concentrations of both sevoflurane and isoflurane in adults.^{1,2} The extent of reduction of these values ranged between 33 and 45 %, ^{2,3,7,8} while in our study propofol requirement was reduced by 20%. These results suggest that clonidine premedication, merely for reducing the propofol requirement, does not seem to be clinically relevant, although clonidine may provide other benefits, such as intraoperative hemodynamic stability, and potentiation of postoperative analgesic regimen.

One may argue that we used lidocaine before propofol injection to reduce pain from *iv* propofol. Lidocaine, 1.5 mg·kg⁻¹, reduces coughing, airway obstruction and incidence of failure in LMA insertion.⁹ Thus, the use of lidocaine before propofol may

FIGURE 2 Dose-response curves for propofol plotted from logit analyses of individual propofol doses and the respective reactions to laryngeal mask airway insertions with or without clonidine pre-medication.

have resulted in underestimation of the ED₅₀ of both groups. Second, although no patient developed hypotension or bradycardia at induction, clonidine alone or in combination with propofol may produce hemodynamic perturbations in the elderly. Finally, there was a wide range in patient age in our study. However, MAC required for LMA insertion in the elderly (65-90 yr) is similar to that of young adults (18-50 yr),¹⁰ suggesting that sensitivity of pharynx to mechanical stimulation may not be age-related.

In conclusion, oral clonidine reduces propofol requirement for smooth insertion of the LMA in healthy surgical patients.

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