Oxygen in air (FiO_2 0.4) improves gas exchange in young healthy patients during general anesthesia

[La présence d'oxygène dans de l'air (FiO_2 de 0,4) améliore les échanges gazeux chez de jeunes patients en bonne santé pendant l'anesthésie générale]

Anil Agarwal MD,* Prabhat K. Singh MD,* Sanjay Dhiraj MD,* Chandra M Pandey PhD,† Uttam Singh PhD†

Purpose: One hundred percent O_2 is used routinely for preoxygenation and induction of anesthesia. The higher the O_2 concentration the faster is the development of atelectasis, an important cause of impaired pulmonary gas exchange during general anesthesia (GA). We evaluated the effect of ventilation with 0.4 FiO_2 in air, 0.4 FiO_2 in N_2O and 100% O_2 following intubation on the development of impaired gas exchange.

Methods: Twenty-seven patients aged 18–40 yr, undergoing elective laparoscopic cholecystectomy were administered 100% O_2 for preoxygenation (three minutes) and ventilation by mask (two minutes). Following intubation these patients were randomly divided into three groups of nine each and ventilated either with 0.4 FiO_2 in air, 0.4 FiO_2 in N_2O or 100% O_2 . Arterial blood gases were obtained before preoxygenation and 30 min following intubation for PaO_2 analysis. Subsequently $\text{PaO}_2/\text{FiO}_2$ ratios were calculated. Results were analyzed with Student's *t* test and one-way ANOVA. *P* value of ≤ 0.05 was considered significant.

Results: Ventilation of the lungs with O_2 in air (FiO_2 0.4) significantly improved the $\text{PaO}_2/\text{FiO}_2$ ratio from baseline, while 0.4 FiO_2 in N_2O or 100% O_2 worsened the ratio (558 ± 47 vs 472 ± 28 , 365 ± 34 vs 472 ± 22 and 351 ± 23 vs 477 ± 28 respectively; $P < 0.05$).

Conclusion: Ventilation of lungs with O_2 in air (FiO_2 0.4) improves gas exchange in young healthy patients during GA.

Objectif : Cent pour cent d' O_2 sont utilisés habituellement pour la préoxygénation et l'induction de l'anesthésie. Plus la concentration d' O_2 est élevée, plus vite peut se développer l'atélectasie, une cause importante d'anomalie des échanges gazeux pulmonaires pendant l'anesthésie générale (AG). Nous avons évalué l'effet de la ventilation avec une FiO_2 de 0,4 dans de l'air, FiO_2 de 0,4 dans du N_2O et 100 % d' O_2 après l'intubation quand apparaissent les anomalies des échanges gazeux.

Méthode : Vingt-sept patients de 18–40 ans, devant subir une cholécystectomie laparoscopique non urgente ont reçu 100 % d' O_2 pour la

préoxygénation, pendant trois minutes, et la ventilation au masque, pendant deux minutes. Après l'intubation, ces patients ont été répartis de façon aléatoire en trois groupes de neuf et ventilés avec 0,4 FiO_2 dans de l'air ou 0,4 FiO_2 dans du N_2O ou 100 % d' O_2 . La gazométrie du sang artériel a été obtenue pendant la préoxygénation et 30 min après l'intubation pour l'analyse de la PaO_2 . Par la suite, les ratios $\text{PaO}_2/\text{FiO}_2$ ont été calculés. Les résultats ont été analysés selon le test *t* de Student et une analyse de variance à une voie. Une valeur de $P \leq 0,05$ a été considérée comme significative.

Résultats : La ventilation pulmonaire avec de l' O_2 dans de l'air (FiO_2 de 0,4) a sensiblement amélioré le ratio $\text{PaO}_2/\text{FiO}_2$, comparativement aux données de base, tandis que 0,4 FiO_2 dans du N_2O ou 100 % d' O_2 l'ont altéré (558 ± 47 vs 472 ± 28 , 365 ± 34 vs 472 ± 22 et 351 ± 23 vs 477 ± 28 respectivement; $P < 0,05$).

Conclusion : La ventilation pulmonaire avec de l' O_2 dans de l'air (FiO_2 0,4) améliore les échanges gazeux chez les jeunes patients pendant l'AG.

GENERAL anesthesia (GA) per-se with or without paralysis causes impairment in gas exchange with decreased blood oxygenation.^{1–3} Atelectasis is an important cause of this impairment in gas exchange during GA. Atelectasis is caused by two mechanisms and both must be present to produce collapse. The two mechanisms are: loss of respiratory muscle tone causing reduction in functional residual capacity (FRC) and resorption of gases. An alveolus or a lung region that is closed off from the ambient air slowly collapses because of absorption of oxygen (O_2) into the blood stream whereas carbon dioxide (CO_2) delivered to the closed unit will dissolve in the surrounding tissue. The

From the Department of Anesthesia,* and Biostatistics,† Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India.

Address correspondence to: Dr. Anil Agarwal, Type IV/48, SGPGIMS, Lucknow 226 014, India. Fax: +91 522 668017, 668047, 668078; E-mail: aagarwal@sgpgi.ac.in

Accepted for publication June 4, 2002.

Revision accepted September 6, 2002.

higher the O₂ concentration, the faster is the rate of adsorption and formation of atelectasis.

O₂ 100% is used routinely for preoxygenation and for ventilation during induction of anesthesia. Use of a high fractional inspiratory O₂ concentration (FiO₂) allows more time for endotracheal intubation before life-threatening hypoxemia develops.⁴ This increased safety is obtained at the cost of development of atelectasis. Whether it contributes to postoperative complications has not been analyzed but remains a possibility. Almost 3% of patients undergoing elective abdominal surgery do suffer from postoperative pulmonary complications.⁵ Even a moderate decrease in the complication rate could reduce the numbers substantially. After induction of anesthesia, patients are usually ventilated with different concentration of O₂ in nitrous oxide (N₂O) or air. O₂ 100% and O₂ in N₂O both favour the development of atelectasis, while O₂ in air has been found to retard the development of atelectasis.⁶ We postulated that ventilation with FiO₂ 0.4 in air following preoxygenation (three minutes) and mask ventilation (two minutes) with O₂ 100% would improve pulmonary gas exchange during GA.

Methods

Following approval from the Institutional Research and Ethic's Committees, informed consent from all patients was obtained for this study. Twenty-seven patients of both sexes, aged 18–40 yr, ASA class I and II, under-

going elective laparoscopic cholecystectomy in the supine posture were included in this randomized, prospective study. Smokers and patients with abnormal preoperative pulmonary function tests were excluded from the study. Patients were premedicated with ranitidine 150 mg *po* and lorazepam 2.0 mg on the night prior to and 2.0 hr before surgery. All patients were preoxygenated (three minutes) and ventilated during induction of anesthesia (two minutes) with 100% O₂. Anesthesia was induced with fentanyl (3 µg·kg⁻¹ *iv*) and thiopentone sodium (4–5 mg·kg⁻¹ *iv*). Intubation was facilitated by vecuronium (0.1 mg·kg⁻¹ *iv*). Following intubation patients were randomized into three groups A, B and C of nine with the help of a computer-generated table of random numbers and maintained on gas mixtures as follows along with isoflurane (0.6–1%), A: 0.4 FiO₂ in air; B: 0.4 FiO₂ in N₂O and C: 100% O₂.

Patients were ventilated in volume-controlled mode with a tidal volume of 8 mL·kg⁻¹. Respiratory rate was adjusted so as to keep the end tidal carbon dioxide levels at 35–40 mmHg as measured by Datex Ohmeda 5250 capnograph. Blood gas analysis (ABG) was performed without any temperature correction by i STAT, Abbott, USA, before preoxygenation and 30 min following intubation (end of the study period) for determination of PaO₂. Subsequently, PaO₂/FiO₂ ratios were calculated and analyzed as an indicator of pulmonary gas exchange. Surgical intervention started only after the end of the study period.

TABLE I Patient characteristics

	FiO ₂ (0.4) in air (Group A; n = 9)	FiO ₂ (0.4) in N ₂ O (Group B; n = 9)	100% O ₂ (Group C; n = 9)
Age (yr)	26.2 ± 9.1	27 ± 7.4	29.5 ± 8.2
Sex (M/F)	03/06	04/05	03/06
Weight (kg)	61 ± 12	58 ± 09	56 ± 10
Height (cm)	160 ± 07	158 ± 08	164 ± 06
Baseline PaO ₂ (mmHg)	94.3 ± 5.5	94.4 ± 4.4	95.5 ± 4.9
Baseline PaO ₂ /FiO ₂ ratio	471.4 ± 24.8	472 ± 22	477.5 ± 28.2

**P* ≤ 0.05 compared with Group A. Results mean ± SD.

TABLE II PaO₂ and PaO₂/FiO₂ ratios in the various groups

Group (n = 9)	PaO ₂ (mean ± SD)		PaO ₂ /FiO ₂ ratio (mean ± SD)		Statistical significance control/final
	Baseline	Final	Baseline	Final	
A	94.3 ± 5.5	223.2 ± 18.6	471.6 ± 27.5	558 ± 46.6*	< 0.0001
B	94.4 ± 4.4	146.2 ± 13.5	472.5 ± 22	365.5 ± 33.9	< 0.0001
C	95.5 ± 4.9	351.5 ± 22.9	477.5 ± 28.2	351.5 ± 22.9	< 0.0001
One way ANOVA (<i>P</i>)		0.78	0.00		

PaO₂ values were not compared as these were obtained at different FiO₂. *Newman-Keul (post hoc test) *P* ≤ 0.05.

FIGURE Mean PaO₂/FiO₂ ratios at baseline and 30 min after ventilation (final) in various groups. *Newman-Keul (post hoc test) $P \leq 0.05$.

Assuming 10% variability in PaO₂ and 99% power, the minimum sample size required in each group was six. Anticipating some dropouts we included nine subjects in each group. Student's *t* test was applied to determine the significance between the control and final PaO₂/FiO₂ ratios of the same group. Means for groups in homogeneous subsets were compared by one-way ANOVA. Post hoc analysis for inter-group difference was carried out using Student-Newman-Keuls test. A P value ≤ 0.05 was considered significant.

Results

Patients of the three groups were comparable with respect to demographic variables (Table I). PaO₂ and PaO₂/FiO₂ ratios of the three groups were also comparable at baseline (Table I). A significant increase in the PaO₂/FiO₂ ratio was observed 30 min after induction of anesthesia in patients maintained with 0.4 FiO₂ in air (Group A) when compared to baseline values. On the contrary, a significant decrease in PaO₂/FiO₂ ratio was observed 30 min after induction of anesthesia in patients maintained with 0.4 FiO₂ in N₂O or 100% O₂ (Groups B and C) when compared to baseline values (Table II; Figure).

One-way ANOVA revealed a similar baseline PaO₂/FiO₂ ratio in all three groups, however a significant difference in the final PaO₂/FiO₂ ratios was observed in the three groups. Post hoc test demonstrated that Groups B and C were similar while Group A was significantly different from the other two groups. A significant increase in final PaO₂/FiO₂ ratio was observed in Group A when compared to final PaO₂/FiO₂ ratios of

Groups B and C. However, no difference was observed in the final PaO₂/FiO₂ ratios of Groups B and C. The best PaO₂/FiO₂ ratios were observed in patients ventilated with FiO₂ of 0.4 in air (Table II).

Discussion

Ventilation of the lungs with 0.4 FiO₂ in air significantly improved the PaO₂/FiO₂ ratio in relation to baseline values, following preoxygenation (three minutes) and mask ventilation (two minutes) with O₂ 100% during induction of anesthesia. On the contrary, ventilation of the lungs with 0.4 FiO₂ in N₂O or 100% O₂ significantly worsened the PaO₂/FiO₂ ratio in relation to baseline values. The best PaO₂/FiO₂ ratio was achieved in the group of patients ventilated with FiO₂ of 0.4 in air during GA. Therefore, our study suggests that the composition of gases used for ventilating the lungs during GA plays an important role on subsequent pulmonary gas exchange.

Computed tomography (CT) of lungs densities developing during GA is the available evidence suggesting the occurrence of atelectasis. These studies also successfully established the relationship between the oxygen concentration used for ventilating the lungs and the extent of atelectasis.

There have also been attempts to prevent and correct atelectasis during GA. Studies have suggested that the use of 100% O₂ during standard anesthesia induction needs to be re-evaluated.⁶ Approaches might include the use of a gas mixture containing air during induction of anesthesia.⁷ Alternatively, re-expansion by hyperinflation should be considered to eliminate atelectasis during GA.^{8,9}

In this study, the PaO₂/FiO₂ ratio was used to estimate the extent of impaired gas exchange during GA,¹⁰ since absolute PaO₂ values obtained at different FiO₂ cannot be compared. Atelectasis results in intrapulmonary shunting and mismatching of ventilation/perfusion (V_A/Q), leading to impaired gas exchange. The PaO₂/FiO₂ ratio reflects the mismatching of V_A/Q and intrapulmonary shunting. However, there are other factors, apart from atelectasis, such as displacement of blood from the thorax to the abdomen, reduction in the thoracic diameter and displacement and dysfunction of the diaphragm, which can also contribute to impairment of oxygenation.¹¹⁻¹³

Rothen *et al.* studied the effect of gas composition on the recurrence of atelectasis after lung re-expansion during GA. They observed that if the lungs are ventilated with 0.4 FiO₂ in air, re-expansion of atelectasis is sustained with respect to atelectasis, shunt, and PaO₂. However, lung collapse reappears within a few minutes if the lungs are ventilated with 100% O₂.¹⁴

The estimated time to collapse of completely closed off lung units from ambient air is six to nine hours if the unit contains air (21% O₂ in N₂), about three hours if it contains 30% O₂ in N₂, and about eight minutes if it contains 100% O₂.^{15,16} Because of the high solubility of N₂O a lung unit will collapse even faster if it contains a mixture of O₂ and N₂O.¹⁵ The composition of inspired gases may also influence the formation of atelectasis in conscious subjects breathing at low lung volumes (i.e., close to residual volumes). For example, despite chest strapping, which reduces FRC by 0.6 L, no atelectasis was found with CT in subjects breathing air.¹⁷ Conscious subjects breathing 100% O₂ at reduced lung volumes, by contrast, showed direct or indirect evidence of atelectasis, although no CT was done.^{18,19}

To conclude, ventilation of the lungs with 0.4 FiO₂ in air significantly improved PaO₂/FiO₂ ratio during anesthesia. Keeping the patient's safety in mind, we suggest that the practice of using 100% O₂ during pre-oxygenation and induction of anesthesia should be continued. However, the deleterious effect of such a practice on gas exchange can be countered effectively thereafter by ventilating the lungs with an FiO₂ 0.4 in air. Further studies to determine the optimal FiO₂ in air for ventilation during GA are recommended.

References

- 1 Strandberg A, Tokics L, Brismar B, Lundquist H, Hedenstierna G. Atelectasis during anaesthesia and in the postoperative period. *Acta Anaesthesiol Scand* 1986; 30: 154–8.
- 2 Cote CJ, Goldstein EA, Cote MA, Hoaglin DC, Ryan JF. A single-blind study of pulse oximetry in children. *Anesthesiology* 1988; 68: 184–8.
- 3 Moller JT, Johannessen NW, Berg H, Espersen K, Larsen LE. Hypoxaemia during anaesthesia—an observer study. *Br J Anaesth* 1991; 66: 437–44.
- 4 Videira RL, Neto PP, do Amaral RV, Freeman JA. Preoxygenation in children: for how long? *Acta Anaesthesiol Scand* 1992; 36: 109–11.
- 5 Pedersen T, Viby-Mogensen J, Ringsted C. Anaesthetic practice and postoperative pulmonary complications. *Acta Anaesthesiol Scand* 1992; 36: 812–8.
- 6 Hedenstierna G, Edmark L, Ahrendt KK. Time to reconsider the pre-oxygenation during induction of anaesthesia. *Minerva Anestesiol* 2000; 66: 293–6.
- 7 Rothen HU, Sporre B, Engberg G, Wegenius G, Reber A, Hedenstierna G. Prevention of atelectasis during general anaesthesia. *Lancet* 1995; 345: 1387–91.
- 8 Rothen HU, Sporre B, Engberg G, Wegenius G, Hedenstierna G. Re-expansion of atelectasis during general anaesthesia: a computed tomography study. *Br J Anaesth* 1993; 71: 788–95.
- 9 Shambaugh GE, Harrison WG, Farrell JI. Treatment of respiratory paralysis of poliomyelitis in respiratory chamber. *JAMA* 1930; 94: 1371–3.
- 10 Marino PL. Hypoxia and hypercarbia. In: Zinner SR (Ed.). *The ICU Book*, 2nd ed. Baltimore: Williams & Wilkins, 1998: 339–54.
- 11 Hedenstierna G, Strandberg A, Brismar B, Lundquist H, Svensson L, Tokics L. Functional residual capacity, thoracoabdominal dimensions, and central blood volume during general anesthesia with muscle paralysis and mechanical ventilation. *Anesthesiology* 1985; 62: 247–54.
- 12 Kraye S, Rehder K, Vettermann J, Didier EP, Ritman EL. Position and motion of the human diaphragm during anesthesia–paralysis. *Anesthesiology* 1989; 70: 891–8.
- 13 Klineberg PL, Rehder K, Hyatt RE. Pulmonary mechanics and gas exchange in seated normal men with chest restriction. *J Appl Physiol* 1981; 51: 26–32.
- 14 Rothen HU, Sporre B, Engberg G, Wegenius G, Hogman M, Hedenstierna G. Influence of gas composition on recurrence of atelectasis after a reexpansion maneuver during general anesthesia. *Anesthesiology* 1995; 82: 832–42.
- 15 Joyce CJ, Baker AB, Kennedy RR. Gas uptake from an unventilated area of lung: computer model of absorption atelectasis. *J Appl Physiol* 1993; 74: 1107–16.
- 16 Webb SJ, Nunn JF. A comparison between the effect of nitrous oxide and nitrogen on arterial PO₂. *Anaesthesia* 1967; 22: 69–81.
- 17 Tokics L, Hedenstierna G, Brismar B, Strandberg A, Lundquist H. Thoracoabdominal restriction in supine men: CT and lung function measurements. *J Appl Physiol* 1988; 64: 599–604.
- 18 Nunn JF, Williams IP, Jones JG, Hewlett AM, Hulands GH, Minty BD. Detection and reversal of pulmonary absorption collapse. *Br J Anaesth* 1978; 50: 91–100.
- 19 Baker AB, McGinn A, Joyce C. Effect on lung volumes of oxygen concentration when breathing is restricted. *Br J Anaesth* 1993; 70: 259–66.