

Title : SUBANESTHETIC CONCENTRATIONS OF HALOTHANE AND ISOFLURANE IN SEVERE CHRONIC ASTHMA

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**INTRODUCTION** : Bronchodilating properties of halogenated anesthetics have been demonstrated in experimental (1) and clinical (2) conditions. Since prolonged hyporesponsiveness of airway smooth muscle after general anesthesia has been recently demonstrated (3), we deemed of interest to investigate if halothane and isoflurane inhalation might have an immediate and prolonged effect on airway constriction in severe asthma.

**METHODS** : Fourteen patients (age = 63.2±10.7 years mean±SD sex ratio 10M/4F) were randomly included in three groups (oxygen n = 4 ; halothane n = 5 ; isoflurane n = 5). The Hospital Ethical Committee approved the protocol and all subjects gave informed consent. All patients suffered from a severe asthma as judged by chronic basal obstruction and few exacerbations and a heavy medical treatment : theophylline, inhaled beta adrenergic agents and steroid therapy given p.o : 5-15 mg prednisolone. The clinical condition of the patients was assessed by 1) number of asthmatic crises 2) peak expiratory flow values measured in triplicate at 8h a.m, 12h, and 8h p.m 3) number of supplemental sympathomimetic inhalations. Steady state in the three weeks preceding the study was a condition of inclusion. After a six hours fast the patients were studied in the operating room in a semi-recumbent position with an intravenous peripheral catheter. Level of consciousness, blood pressure and heart rate were monitored as for routine general anesthesia. The study was conducted in simple blind conditions (anesthetist only aware of the inhaled gas). Administration was performed by a face mask and patients received an inspired concentration of either oxygen (FIO<sub>2</sub> : 1) or halothane (0.5 %) in oxygen or isoflurane (0.8 %) in oxygen during a 15 minutes period through specific precalibrated vaporizers. Respiratory function tests were performed before and 30 minutes and seven days after inhalation of the anesthetic gas. Functional residual capacity (FRC) and respiratory resistance (RAW) were measured by the panting technique in a body plethysmograph (PULMED 3303-IMF, Marseille FRANCE) and specific airway conductance (SGaw) was calculated from conductance (1/RAW) divided the value of FRC. FEV1 was measured on a flow volume curve obtained at the mouth by a pneumotachograph (Lilly - France). Results were computed and stored in a GOUPIL3 microcomputer and were displayed on its screen. The patients were allowed to leave the hospital two hours after inhalation and their clinical condition was assessed

in the three first weeks as previously described (crises and supplemental inhaled drugs, peak flows). Data were expressed as mean±SD and were compared using analysis of variance and Student t test.

**RESULTS** : Patients were comparable in each group as respect to age, medications and initial respiratory functions tests values. During inhalation of anesthetic gases, patients were sleepy but easily arousable with a complete reversibility of effect in the first 15 minutes. Administration of either halothane or isoflurane did not induce any statistically significant change when compared to placebo (Table 1) on the successive tests. No significant difference in their clinical status was observed during the three weeks of follow-up.

**DISCUSSION** : Our data provide evidence that subanesthetic concentrations of inhaled agents do not influence respiratory function in severe chronic asthma. In these patients, the beneficial effect of corticosteroids emphasizes the major role of oedema in bronchial obstruction. A partial reversibility of airway constriction was expected with Halothane or Isoflurane since these agents might either directly relax bronchial smooth muscle or increase beta adrenergic tone (3). The lack of effect reinforces the idea that halogenated anesthetics mainly block airway reflexes after a previous stimulation.

**REFERENCES** :

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**TABLE 1.**  
(mean ± SD)

	ISOFLURANE			HALOTHANE			OXYGEN		
	BEFORE	AFTER	DAY 7	BEFORE	AFTER	DAY 7	BEFORE	AFTER	DAY 7
FRC (liters)	3.66 ±0.30	3.44 ±0.44	3.95 ±0.52	3.4 ±0.71	3.66 ±0.57	3.73 ±0.05	4.43 ±1.43	4.06 ±0.67	4.0 ±0.2
SGaw (Kpa .sec)	0.49 ±0.14	0.47 ±0.20	0.70 ±0.3	0.80 ±0.29	0.66 ±0.25	0.87 ±0.46	0.32 ±0.08	0.23 ±0.05	0.50 ±0.2
FEV1 (liters)	1.6 ±0.35	1.5 ±0.40	1.25 ±0.68	1.74 ±0.30	1.76 ±0.43	1.67 ±0.55	1.04 ±0.39	1.05 ±0.34	1.0 ±0.2