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Which is most pungent: isoflurane, sevoflurane or desflurane?

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We compared the pungency and tolerability of three inhaled anaesthetics in a randomized, double-blind study. Eighty-one unpremedicated patients (n=27, each group) inhaled 2 MAC of isoflurane (2.3%), desflurane (12%) or sevoflurane (4%) for 60 s from an anaesthetic breathing circuit via a mask. Two blinded observers recorded coughing, complaints of burning and irritation, and how long the inhalation was tolerated. One sevoflurane patient coughed, but completed the study period, whereas 11 isoflurane patients and 20 desflurane patients coughed, objected verbally or removed the mask forcefully. All sevoflurane, 20 isoflurane and seven desflurane patients completed the study period (average 60, 49 and 33 s, respectively, P<0.05). The irritability grading was: desflurane > isoflurane > sevoflurane (P<0.05). Sevoflurane is the least irritating agent for inhalation at 2 MAC concentration.

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Volatile anaesthetics vary in their pungency. This limits their use for induction of anaesthesia. We assessed the acceptability of equally potent (2 MAC) inhaled concentrations of three commonly used volatile anaesthetic vapours.

Materials and methods

Eighty-one male patients, requiring or requesting general anaesthesia for their surgical procedure, were included in this randomized, double-blind investigation, approved by the institutional review board. Patients with signs of active or severe pulmonary disease were excluded. Smoking was not an exclusion criterion, unless patients were coughing frequently or were wheezing. No pre-medication was given. Standard monitoring and an intravenous infusion of a crystalloid solution were started. A table of random numbers was used to assign the anaesthetic vapour. One investigator (M.I.G.) primed the anaesthetic circuit and 3-litre reservoir bag with vapour and oxygen. To confirm the 2 MAC concentration in the circuit, a Datex Capnomac gas-analyser was used in addition to the Ohmeda respiratory gas monitor. Priming was considered to be complete when vapour concentrations were identical in both analysers (4%, 2.3% and 12% for sevoflurane, isoflurane and desflurane, respectively) and remained constant for at least 1 min. Two observers (M.T. and C.H.) were at the patient's side, blinded to treatment, vaporizers and gas-analysers.

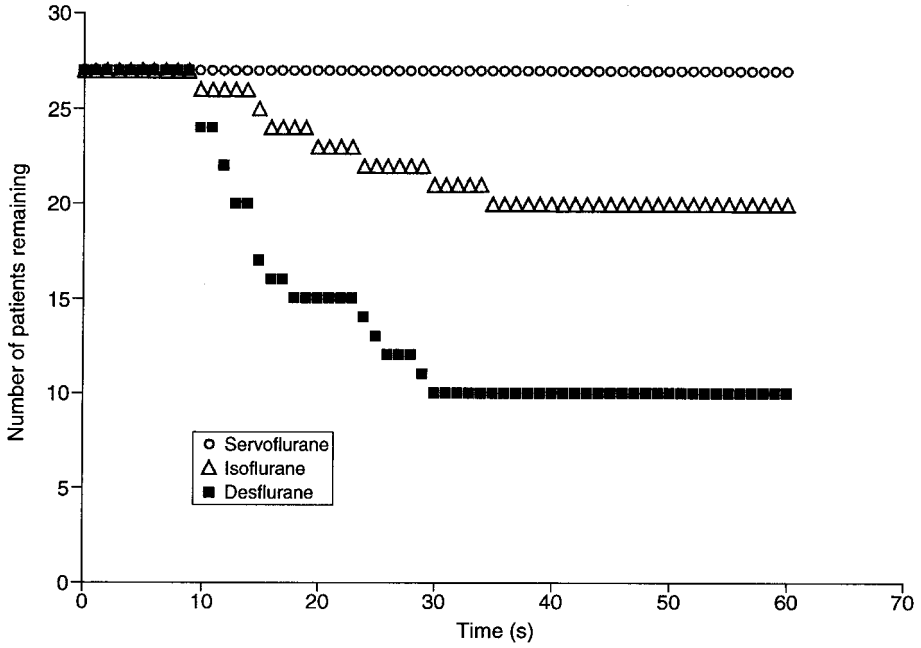

Fig 1 Patients who continue to breathe the anaesthetic versus time from the start of the inhalation.

To ensure a leak-proof fit during the study and prevent potential entrainment of room air during the study period, a facemask was firmly applied to the patient's face. The patient was then instructed to exhale forcefully while the chimney-piece on the mask was occluded. If an air-leak existed around the mask, it was adjusted until no leak could be detected and held in place throughout the 60-s inhalation.

A Fink non-rebreathing valve[1] was used in this study to ensure a constant inspired concentration throughout the study period. It was attached in series to a three-directional valve leading to either room air or to the primed breathing circuit. At the start of the 60-s study period, the three-way valve was turned and the patient was instructed to take a single deep breath followed by normal breathing. The observers looked for signs of irritation, such as coughing, head movement or forceful removal of the mask by the patient. During the study period, the patient was asked whether he could continue or wanted the mask removed. The duration of time the inhalation was tolerated was measured by a stopwatch (C.H.). The study period ended when the patient expressed unbearable irritation, removed the mask, or after 60 s.

Statistical analysis

The chi-squared test was used to compare the responses to the three vapours. Analysis of variance was used to compare the time-of-tolerance. When the *F*-test of the analysis of variance was statistically significant, Bonferroni multiple comparison procedure was performed. A *P*-value less than 0.05 was considered statistically significant.

Results

There were no obvious systematic differences between the patients in the groups. Because this study was performed at a Veterans Affairs Hospital, all patients were male. The number of smokers in each group was similar (13 in the desflurane group, 14 in the isoflurane group and 14 in the sevoflurane group). No patient had a history of symptoms of COPD, asthma or other pulmonary disease.

One sevoflurane patient, 11 isoflurane patients and 20 desflurane patients coughed or objected overtly to inhaling the gas mixture ($P<0.05$). When questioned about burning, irritation or other discomfort, none of the sevoflurane patients complained, while 12 isoflurane and 21 desflurane patients did ($P<0.05$).

With time (seconds) as a variable, the means in all groups were also significantly different when compared with each other ($P<0.05$). Figure 1 shows how long patients tolerated the inhalation and how many completed the 60-s study period.

No correlation could be found between smoking history and reaction to the inhalation.

Discussion

A novel approach to rapid induction by mask is the inhalation of a single deep breath of high concentration of potent vapour. This 'vital capacity breath technique' has been investigated comparing sevoflurane and isoflurane,[2 3] as well as with sevoflurane and halothane[4] in adults. Sevoflurane not only acted more rapidly, but also produced an induction with a lower incidence of coughing and 'better

patient acceptance'.[2 3 5] A different study compared the irritative qualities of four vapours at 1 and 2 MAC in volunteers.[6] Pungency was graded as isoflurane > enflurane > halothane > sevoflurane. Unfortunately, desflurane was not included in this comparison. It has the lowest blood–gas partition coefficient, but is associated with a high incidence of coughing and irritation.[7 8]

Our results show that during a 60-s inhalation of a 2 MAC concentration, sevoflurane is the least irritating anaesthetic agent. Isoflurane is more irritating than sevoflurane, but less so than desflurane, which seems to be unacceptably pungent. Most patients (20 out of 27) objected strongly to the inhalation.

A positive smoking history had no significant effect on the incidence of patient complaints. This may have been due to patient selection, as patients with respiratory symptoms were excluded from this study.

There are some limitations to our study. A 60-s time period was arbitrarily chosen, because we only sought to compare the initial irritability of the vapours. We think it is significant that some patients (seven receiving isoflurane, 20 receiving desflurane, respectively) did not tolerate even 60 s of exposure. We observed that very few patients lost consciousness after a single breath or within the 60-s time period. This needs further evaluation.

Second, the MAC concentration (and its multiple) represents equipotency based upon the response to a standardized surgical incision. It may not represent equipotency for airway irritability. Two MAC of desflurane should perhaps be compared with a higher concentration of isoflurane and sevoflurane. Equipotency in pungency remains conjectural.

Third, modern anaesthesia delivery systems use semi-closed circle systems, which may not be simulated exactly by a non-rebreathing valve. However, this valve allows delivery of only the anaesthetic mixture, the composition of which can be maintained precisely.[9 10] The purpose of its use was merely to deliver a constant anaesthetic concentration.

We conclude that, at the 2 MAC concentration, sevoflurane is significantly less irritating to the airways than isoflurane, and both are significantly less irritating than desflurane. Sevoflurane seems to be the best agent for rapid induction of general anaesthesia by mask.

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