

Existence of Reverse Second Gas Effect with Enflurane

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Abstract

Objective: To investigate the existence of 'reverse second gas effect' with enflurane and to find out any influence of the variables; age, gender, body weight and American society of anaesthesiologist (ASA) status of the patient over the existence of reverse second gas effect.

Methods: This double blinded randomized control trial included forty eight adult ASA I and II patients divided in two groups 'A' and 'B'. The existence of reverse second gas effect was investigated in terms of rate of decline of exhaled concentration of enflurane with and without nitrous oxide. Collected data included age, weight, gender, ASA status, rate of decline of exhaled enflurane, heart rate & blood pressure of patients during the research protocol.

Results: Independent 't' test was used to compare the rate of decline and exhaled concentration of enflurane with and without nitrous oxide ($p = 0.22$). 'T' test was also used ($p = 0.45$ & 0.97 respectively) to observe the influence of age and weight. For the influence of ASA status and gender, chi square test was applied ($p = 0.99$ and 0.77 respectively).

Conclusion: From the results of our study, we concluded that reverse second gas effect does not exist with enflurane. Furthermore, no influence of the variables age, gender, ASA status and body weight could be found on the existence of reverse second gas effect (JPMA 56:261;2006).

Introduction

Combinations of anaesthetic gases are often used to speed up the onset of anaesthesia and to diminish the dosage of the individual gas. Nitrous oxide (N_2O), though rarely used as a sole anaesthetic, has been known to facilitate the induction of anaesthesia by accelerating the rate of rise of inspired concentration of adjunct inhalation anaesthetic agent in the pulmonary capillaries. This phenomenon is known as second gas effect.¹⁻³

The uptake of large volumes of N_2O during the induction of anaesthesia accounts for the second gas effect.^{1,2,4} On recovery from anaesthesia, nearly all factors governing the rate of increase in the alveolar anaesthetic concentration during induction are reversed and are equally important in determining the rate of elimination of adjunct inhalational agent and thus recovery.⁵⁻⁷ N_2O has been suggested to increase the induction rate, therefore, its elimination at emergence from anaesthesia should facilitate the

decline of the adjunct inhalation agent.^{5,6}

At emergence when both N_2O and volatile anaesthetic agents are turned off, N_2O diffuses rapidly from the pulmonary capillaries to the alveoli leaving a higher concentration of volatile inhalation agent in the pulmonary capillaries.⁵ This relative increase in the concentration of volatile anaesthetic agent in the pulmonary vasculature should be responsible for its faster elimination, this concept has been named as reverse second gas effect.⁵⁻⁷ This effect, so far, has been studied with two inhalational anaesthetics, halothane and isoflurane.^{5,6} The elimination of N_2O has been found to increase the elimination of halothane⁵, but it has less influence on the elimination of isoflurane.⁶ Studies with other volatile agents in this context have not been done.

A method that allows faster elimination of inhalation agent from alveoli may account for the rapid emergence from general anaesthesia and may be seen as more cost

effective in terms of utilization of operation theatre time and duration of anaesthesia⁶, and this forms the rationale of our study.

The objective of this study was to investigate the existence of 'reverse second gas effect' with enflurane and to see whether the variables like age, gender, body weight and American society of anaesthesiology (ASA) status of the patient has any influence on the existence of the reverse second gas effect with enflurane.

Patients and Methods

This was a double blinded randomized control trial, conducted in the operating rooms of the Aga Khan University hospital, between January and April 2002.

Human Subjects protocols were adhered to and informed consent was taken from all patients participating in the study. The study included forty eight adult patients (ASA status I and II of either sex) requiring general anaesthesia with muscle relaxation and endotracheal intubation. Anaesthesia was maintained with enflurane in a mixture of N₂O and oxygen. Subjects with seizure disorder or with evidence of deranged renal function were not considered for study as both conditions are relative contraindications to the use of Enflurane.⁷

Subjects participating in the study were divided into two groups 'A' and 'B' using a sealed envelope method. After induction of anaesthesia with the standard intravenous drugs, anaesthesia was maintained by using 65% N₂O, 35% oxygen and enflurane. All patients received general anaesthesia with "Datex Excel 210 SE anaesthesia workstation with Datex S5 monitor" along with a TEC-5 enflurane vaporizer in a closed circle system. In all patients, we monitored inspired and expired concentration of N₂O, enflurane and end tidal concentration of carbon dioxide with a built-in infrared analyzer. The advantage of using infrared anaesthesia analyzer is rapid and accurate analysis.⁸

Induction, maintenance and emergence from anaesthesia were managed according to the accepted standards of anaesthesia care for the particular surgical procedure and patient's requirements. The researchers were not involved in the planning of the anaesthetic managements of the patients and they were kept blinded to the research technique employed.

Thirty minutes before the end of surgical procedure, based on the anticipated surgical time, research protocol was initiated.

In group A, rate of decline of end tidal concentration of enflurane from a concentration of 0.9% to 0.6% was measured. For this purpose, enflurane vaporizer was turned

off when the infrared anaesthesia analyzer showed a reading of 0.9% end tidal enflurane on the monitor. End tidal concentration of enflurane was allowed to fall until it reached up to 0.6%. Enflurane vaporizer was turned on only when the anaesthesia analyzer showed a reading of 0.6% end tidal enflurane. Time in seconds for the descent of end tidal concentration of enflurane from 0.9% to 0.6% was measured using a stopwatch, which was turned 'on' simultaneously on the turning 'off' of the enflurane vaporizer. Stopwatch was 'stopped' when the end tidal concentration of enflurane on the anaesthesia analyzer reached to 0.6%. This time period measured in seconds was recorded on a specified form.

In group B, rate of decline of end tidal concentration of enflurane from a concentration of 0.9% to 0.6% was measured. For this purpose both the enflurane vaporizer and N₂O flow meter were turned off when the infrared anaesthesia analyzer showed a reading of 0.9% end tidal concentration of enflurane.

The Oxygen flow in litres was increased to compensate for the loss of litres of N₂O. Stopwatch was turned 'on' simultaneously. Time in seconds for a decline of end tidal Enflurane concentration (from 0.9 to 0.6%) as displayed on the monitor was recorded on a specified form. Both the Enflurane vaporizer and N₂O flow meter were turned 'on' when the Enflurane concentration on the monitor reached to 0.6%. To exclude the bias, same infrared anaesthesia analyzer was used for all the patients.

As the elimination of an anaesthetic agent is affected by changing alveolar ventilation⁹, we recorded end tidal CO₂ continuously to ensure constant alveolar ventilation throughout the research protocol. Cardiac output is another variable on to which elimination of anaesthetic agent depends⁹, therefore heart rate and blood pressure (non-invasively) were measured to record any change in the haemodynamic parameters during the research protocol. After recording all the variables including the time in seconds to reach end tidal enflurane from 0.9% to 0.6%, heart rate, blood pressure and end tidal carbon dioxide during that interval, the research protocol was terminated.

Statistical package for social sciences (SPSS 10) was used for data analysis. Independent 't' test was utilized to see the difference between the rate of decline of exhaled concentration of enflurane among the two groups.

Results

The mean duration in group A was 37.4 seconds (SD ± 5.8), whereas in group B, it was 40.7 seconds (SD ± 11.1). Independent 't' test was run for comparison of means. No statistically significant difference was found in both groups (p = 0.22) (Table 1).

Table 1. Duration of decline of exhaled concentration of Enflurane in groups 'A' and 'B'.

	Group 'A' (Mean ± SD)	Group 'B' (Mean ± SD)	P-Value
n	24	24	
Duration (sec)	37.4 ± 5.8	40.7 ± 11.1	0.22

P<0.05=significant

Table 2. Comparison of age and weight in groups 'A' and 'B'.

	Group 'A' (Mean ± SD)	Group 'B' (Mean ± SD)	P-Value
n	24	24	
Age (years)	39.4 ± 17.4	35.7 ± 16.4	0.45
Weight (kg)	64.7 ± 17.3	64.5 ± 16.3	0.97

The age, weight, ASA status and duration of decline of enflurane were compared for each technique group. Both groups were homogenous in terms of age, weight, ASA status and gender.

The effect of age of the patients on the rate of decline of exhaled concentration of enflurane in both the study groups was analyzed with independent 't' test that showed no statistically significant difference (p =0.45) (Table 2).

To analyze the effect of body weight on the rate of elimination of enflurane in both the groups, independent 't' test was utilized. No statistically significant influence of weight of the patients over the rate of decline of exhaled concentration of enflurane in both the research techniques employed was observed (p=0.97) (Table 2).

To see the influence of gender and ASA status on the existence of reverse second gas effect, pearson chi square test was used. The possible effect of gender on the duration of decline of exhaled concentration of enflurane was analyzed in both the studied groups, which showed no statistically significant difference. (p = 0.77).

Similarly, no significant influence of ASA status could be found over the rate of decline of exhaled concentration of enflurane in both the groups (p = 0.99).

Discussion

Masuda first presented the concept of reverse second gas effect in 1984, when she found that the rate of elimination of halothane increases with the simultaneous elimination of nitrous oxide.⁵ After that, Burford et al⁶ studied the presence of reverse second gas effect with isoflurane. They failed to see any significant difference in the rate of elimination of isoflurane with or without nitrous oxide.

We studied the existence of reverse second gas effect with enflurane but the results were inconclusive. Our failure to appreciate the existence of reverse second gas effect with

enflurane can be discussed in terms of solubility and duration of anaesthetic.

Solubility of the anaesthetic agent is one of the most important factors in determining the rate of induction and recovery of volatile anaesthetic.^{9,10}

The lesser the solubility, the lesser is the time required for induction and elimination of the volatile inhalational anaesthetics.^{9,10} It can be seen from two experiments conducted to see the existence of reverse second gas effect that with the lesser soluble drugs, (isoflurane; blood gas solubility 1.6, enflurane; blood gas solubility 1.9) the reverse second gas effect could not be demonstrated. Elimination of nitrous oxide from the alveoli may be one of the factors that determines the rate of decline of alveolar concentration of volatile anaesthetics. It may contribute to the rate of elimination of the alveolar anaesthetic⁵ but it is not the only factor responsible for the rate of decline of anaesthetic agent.^{9,10} Hence, it can be interpreted that, with the soluble inhalational agent like halothane the reverse second gas effect was appreciated⁵ but no such phenomenon was found with the lesser soluble drugs like isoflurane⁶ and enflurane (in our study).

The duration of inhalational anaesthetic administration is one of the determinants of the elimination of alveolar anaesthetic.¹⁰ A longer duration of moderately soluble drug like enflurane puts more anaesthetic into the slowly filled compartments of fat and muscles. Obviously these reservoirs can supply more anaesthetic returning to the alveoli when they are filled than when they are empty and hence can prolong the elimination of the anaesthetic agents.¹⁰ In our study groups, duration of anaesthetic administration was not a constant factor. Therefore, the impact of duration of anaesthesia on the rate of elimination of enflurane with and without nitrous oxide in our patients could not be determined. Based on our study, we cannot support the hypothesis that elimination of nitrous oxide increases the rate of decline of end tidal concentration of enflurane regardless of age, weight, sex or ASA status of the patient.

In this study, we failed to appreciate the existence of reverse second gas effect with enflurane and found that variables like age, gender, body weight and ASA status of the patient do not have any influence on the existence of reverse second gas effect with enflurane. We suggest that anaesthesia providers should not anticipate elimination of nitrous oxide to speed up the descent of enflurane and hasten recovery from general anaesthesia.

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