SEVOFLURANE LOW-FLOW ANAESTHESIA: BEST STRATEGY TO REDUCE COMPOUND A CONCENTRATION

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Sevoflurane low-flow anaesthesia: best strategy to reduce Compound A concentration

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Background: To define the best strategy to reduce Compound A production in Sevoflurane low-flow anaesthesia by experiments *in vitro* and *in vivo* of different absorbers and different anaesthesia machines.
Methods: *In vitro* Compound A has been measured at 45°C *in vitro* following Sevoflurane interactions with potassium hydroxide, sodium hydroxide, soda lime, Dragersorb 800 Plus and Amsorb, a new absorber that does not contain sodium or potassium hydroxide. *In vivo* Compound A concentration in the anaesthesia circuit (inspiratory branch) has been measured using an indirect sampling method through absorber vials (SKC) with active coal granules, during low flows (500 ml / min) general anaesthesia using soda lime, Dragersorb 800 Plus or Amsorb as absorber. Compound A was also measured during low flows (500 ml / min) general anaesthesia using as carbon dioxide absorber soda lime with different anaesthesia machines.
Results: *In vitro* at 45°C Compound A concentration with soda lime and Dragersorb 800 Plus was about 10 times higher than with Amsorb. *In vivo* the Compound A concentrations in the inspiratory branch of the circuit were lower in the group with Amsorb.
Conclusion: The Compound A production is minimal with Amsorb as carbon dioxide absorber.

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Key words: Anesthesia machine; Compound A; low-flow anesthesia; Sevoflurane.

Sevoflurane reacts with carbon dioxide absorbers producing some vinyl compounds, of which the most well known is Compound A (1). Compound A has been demonstrated to be nephrotoxic in rats (2).

Compound A concentration increases with the increase of the temperature of soda lime (3) and therefore in the low-flow anaesthesia due to the higher temperatures of carbon dioxide absorbers. For this reason the 'Food and Drug Administration' advises not to use Sevoflurane with fresh gas flow less than 2 l / min.

Recently, new types of carbon dioxide absorbers to reduce the production of Compound A during the anaesthesia techniques in closed circuit have been introduced (4).

Moreover, some ventilation systems, like Physioflex (Drager) (5–6) have aimed to reduce the Compound A production by maintaining a very high gas circulation inside the circuit, so to maintain the temperature of the carbon dioxide absorber low.

The aim of the study has been to verify if during low-flow anaesthesia (500 ml / min) the production of Compound A is affected by different types of carbon dioxide absorbers and / or by different anaesthesia machines.

Therefore, the reaction '*in vitro*' of various absorbers with Sevoflurane and, *in vivo*, the amount of Compound A production during Sevoflurane low-flow anaesthesia (500 ml / min), with the various absorbers and, with soda lime (ACEF), in different anaesthesia machines has been analysed.

Methods

In vitro

Three carbon dioxide absorbers: soda lime (ACEF), Amsorb (Amstrong) and Draegersorb 800 Plus (Drager) were directly exposed to Sevoflurane at 45°C. (Amsorb contains about 83% of $Ca(OH)_2$, 14.4% of H_2O, $CaSO_4$ and $CaCl_2$; soda lime contains about 80% of $Ca(OH)_2$, 3% of NaOH, 2% of KOH and 15% of H_2O; Draegersorb 800 Plus contains about 82% of $Ca(OH)_2$, 2% of NaOH, 0.003% of KOH and 16% of H_2O). Moreover, Compound A concentration was compared with the ones obtained from Sevoflurane reactions with potassium hydroxide (KOH, Carlo Erba) and sodium

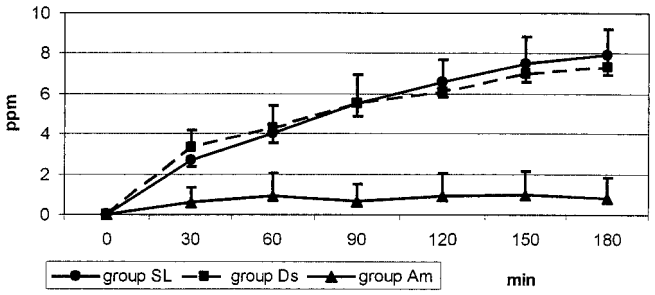

Fig. 1. Inspiratory concentrations of Compound A during low-flow (500 ml/min) anaesthesia in Aestiva 3000. Group SL (n = 5 patients): CO_2 absorber = soda lime; group Ds (n = 5 patients): CO_2 absorber = Dragersorb 800plus (Drager); group Am (n = 5 patients): CO_2 absorber = Amsorb (Armstrong). The difference between group Am and the others is significant at all times.

hydroxide (NaOH, Carlo Erba) under the same conditions.

Compound A concentration was determined analytically by a Varian gaschromatograph CP-3800 model provided with a flame ionization detector (FID); Compound A retention time is 115 s, while Sevoflurane retention time is 180 s.

In vivo

Compound A concentration during Sevoflurane low-flow anaesthesia was assessed first using different absorbers in one machine (Aestiva 3000, Datex-Ohmeda) and second using one absorber (soda lime, ACEF) in two different anaesthesia systems.

Three homogeneous groups of patients scheduled for major general surgery taking longer than 3 h, using an Aestiva 3000 machine, were exposed to general low-flow (500 ml / min) anaesthesia with Sevoflurane: in five patients (group SL) soda lime (ACEF) was used; while in another five patients (group Am) Amsorb was used, and in the other five (group Ds) Dragersorb 800 Plus was used. The anaesthesia was maintained with Sevoflurane (1,5 MAC) with air 70% in oxygen. Compound A concentration was measured in the inspiratory branch of the circuit by an indirect sampling through absorber vials (SKC) with active coal granules. Each vial was connected on one side to the circuit and on the other to a suction pump exactly regulated to a 100-ml / min volumetric flow. Each sampling lasted 30 min and analysis was performed immediately; the samples were analysed with the Varian gas chromatograph (CP-3800) obtaining the gas chromatograph separation of Sevoflurane from its degradation compounds.

In the second clinical test Compound A production *in vivo* in low-flow circuit with two different anaesthesia systems and with soda lime as absorber was evaluated. Ten patients were submitted to low-flow (500 ml / min) anaesthesia for general surgery taking longer than 3 h. In five patients (group S710) Siemens 710 was used; in another five (group A3000) Aestiva 3000 (Datex-Ohmeda) was used. Sampling and measurements of Compound A was performed as before; the temperature observed on the surface of soda lime inside the canister was registered.

The data are reported as mean ± standard deviation. Comparisons between the different groups were done with Student's *t*-test A *P*-value lower than 0.05 was regarded as statistically significant.

Results

In vitro test

Compound A concentrations with soda lime and Dragersorb 800 Plus are about 10 times (at 3 h) higher than with the Amsorb.

In vivo tests

The three groups of patients were homogeneous regarding body surface (group SL: $1.8 \pm 0.1\,m^2$; group Am: $1.7 \pm 0.3\,m^2$; group DS: $1.8 \pm 0.2\,m^2$). In group SL and Ds there was a Compound A concentration after 3 h of anaesthesia of 7.9 and 7 p.p.m., respectively, in the inspiratory branch (Fig. 1). Using Amsorb as a carbon dioxide absorber the concentration of Compound A was less than 1 (p.p.m) (Fig. 1).

The body surfaces of the two groups of patients of the second clinical test were not different (Group S710; $1.68 \pm 0.18\,m^2$, Group A3000; $1.66 \pm 0.216\,m^2$). The results are shown in Fig. 2: Siemens 710 produces the highest level of Compound A and the temperature ob-

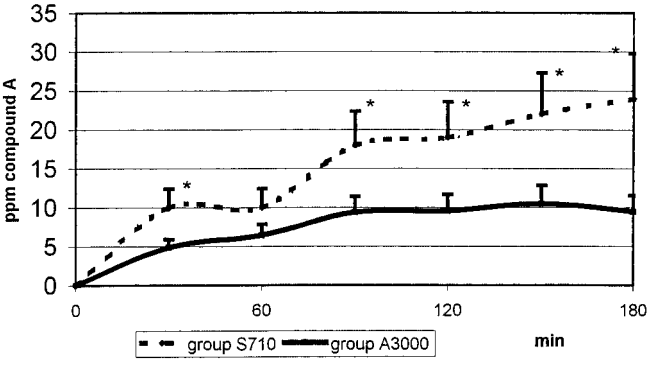

*Fig. 2. Compound A production (p.p.m) during low-flow anaesthesia (500 ml/min) with three different anaesthesia systems. Group S710 = Siemens 710; group A3000 = Aestiva 3000; * = P < 0.01 (Student's t-test), comparison between group S710 and Aestiva 3000 at each time.*

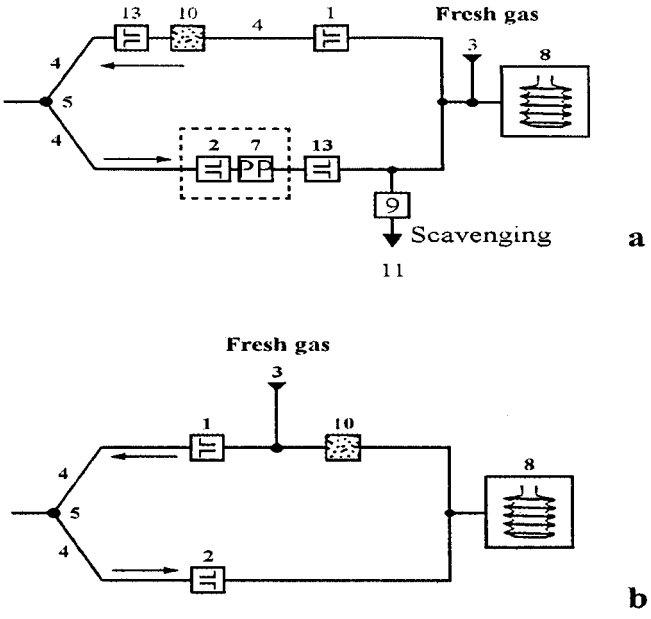

Fig. 3. (a) Siemens 710; (b) simplified scheme of Aestiva (Datex-Ohmeda). 1 = Inspiratory valve; 2 = expiratory valve; 3 = fresh gas inlet port; 4 = breathing tube; 5 = Y- piece; 6 = reservoir bag; 7 = PEEP valve; 8 = ventilator; 9 = overflow valve; 10 = CO_2 absorber; 11 = scavenging port; 12 = valve; 13 = unidirectional valve. Explications in the text. (modified from Zbinden et al. (16).

served in the canister was 31.9 ± 1.1°C and with Aestiva 3000, 28.8 ± 1.5 C ($P = 0.007$, Student's *t*-test).

Discussion

Compound A is a potentially nephrotoxic product (7–10).

The aim of the study was to define the best strategy to minimize Compound A production.

Recently new carbon dioxide absorbers were produced and they appear to be able to reduce the production of Compound A during low-flow general anaesthesia (4, 11).

The elimination of the bases sodium hydroxide and potassium hydroxide from the usual carbon dioxide absorbers decreases production of Compound A, without materially decreasing the capacity of the remaining base, calcium hydroxide, to absorb carbon dioxide (12, 13).

Our results confirm that Amsorb, *in vitro* test at high temperature but also in the clinical one, obtains good results to reduce the production of Compound A because of the absence of strong bases in its formulation. This is confirmed by the literature about the new products that have been put on the market in the recent past (4, 14, 15).

Other clinical observations have shown that some ventilator systems like Physioflex (Drager) (5, 6) also using closed circuit, produce a low concentration of Compound A because, maintaining the circulation of gases inside of the circuit at a high level, they contribute to maintain the temperature of the used carbon dioxide absorber low.

The different position of the canister of carbon dioxide absorbers relative to the fresh gas inflow in the circuit can modify the temperature of soda lime because the fresh gases are cold and dry. The ventilators' circuits that are used in our experiment are schematized in Fig. 3 (modified from Zbinden et al.) (16): in the anaesthesia system Siemens 710 the position of the canister of soda lime is far from the source of fresh gases. This type of composition allows the temperature of the canister to reach the maximum levels in relation to the carbon dioxide produced by the patient.

In the Aestiva anaesthesia systems, where (simplified in Fig. 3b), the source of fresh gases is placed near the CO_2 absorber and the low temperature fresh gases from the central gas system contribute to cool the content of the canister and to limit the production of Compound A.

Conclusion

The production of Compound A is minimal if the composition of soda lime does not provide strong bases and is lower if the fresh gas enters the breathing circuit closely upstream the absorber canister, which cools the absorber mass more effectively than down stream fresh gas delivery.

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