Interactions of inhalational anesthetics and carbon dioxide absorbents

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Summary

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Anesthesia is essential to facilitate most of the surgical procedures performed in hospitals. To make economical use of medical gases like oxygen and inhalational anesthetics, the anesthesiologist uses an anesthesia machine, that contains a circle ventilating circuit that allows rebreathing of expired gases from the patient. To facilitate this rebreathing of medical gases and volatile anesthetics, it is essential that exhaled carbon dioxide does not return to the patient. This is accomplished by using a carbon dioxide absorbent inside the circle ventilating circuit. There are several carbon dioxide absorbents, and they contain calcium hydroxide that binds carbon dioxide, and other chemicals that facilitate the binding of carbon dioxide to calcium hydroxide. Classic absorbents contain strong bases like potassium hydroxide (KOH) and sodium hydroxide (NaOH) as facilitating binding agents. These strong bases, however, are highly reactive and are to a large extent responsible for carbon monoxide (CO) production from inhalational anesthetics and carbon dioxide absorbents that have become desiccated. CO is a toxic gas, mostly produced as a result of incomplete combustion of organic materials. The average CO concentration in the atmosphere is 0.1 ppm (parts per million), but in cities with much traffic it can reach up to 115 ppm. Hemoglobin's affinity for carbon monoxide is 220 times that of oxygen, which can lead to hypoxia if CO concentrations are sufficiently high. A one hour exposure of 1500 ppm of CO is lethal for humans.

With the introduction of sevoflurane, it was soon demonstrated that from the interaction with carbon dioxide absorbents, a nephrotoxic degradation product was formed, named compound A (CA). CA is nephrotoxic in rats after a 3-hour exposure of 50 ppm, as established histologically. In humans however this concentrations does not generate any renal injury, and higher concentrations up to 240 ppm only demonstrates some transient nephrotoxicity in a few studies. CA is produced as a result of degradation of sevoflurane in desiccated as well as hydrated carbon dioxide absorbents. Absorbents without strong bases like KOH and NaOH, produce the lowest concentrations of CA.

In this thesis we investigated the CO production from all modern inhalational anesthetics and CA production from sevoflurane in combination with seven different types of carbon dioxide absorbents containing different concentrations of strong bases. The absorbents were tested in hydrated and completely desiccated condition. For the laboratory studies described in **chapters 2-5** we developed a patient model in which a standard anesthesia circle machine was connected to an artificial lung with a study protocol where volatile anesthetics and fresh gas flow were introduced in accordance with clinical practice. For accurate measurements of CO and CA a portable gas chromatograph was used.

In **chapter 1** we described the history of inhalational anesthetics and carbon dioxide absorption. Also, an overview of recent findings of the interactions between volatile anesthetics and carbon dioxide absorbents is presented. We measured the maximum concentrations of CO produced as a result of interaction between the five modern inhalational anesthetics (halothane, enflurane, isoflurane, sevoflurane and desflurane) and sodalime (i.e. Drägersorb 800 plus®) in hydrated and completely desiccated condition in **chapter 2**. Temperature was measured inside the absorbent, to investigate a possible relationship between temperature of the absorbent and carbon monoxide production. Very high concentrations of CO were measured with desflurane and enflurane, up to 14262 and 10654 parts per million (ppm) respectively. Lower but still toxic concentrations were found using isoflurane (2512 ppm), whereas non-lethal concentrations of CO were measured for sevoflurane (121 ppm) and halothane (210 ppm).

No CO was found with normally hydrated sodalime and no relationship could be established between temperature of the absorbent and the amount of CO production.

In **chapter 3** we investigated the amounts of CO produced as a result of interaction between desflurane and six different types of absorbent containing different concentrations of strong bases. This to establish the relationship between the strong base content of the absorbent and carbon monoxide production. Here we demonstrated that the desiccated absorbents with a relatively large

concentration of NaOH, namely Medisorb® and Spherasorb® produced high concentrations of CO. The absorbents free of strong bases produced small amounts of CO (Loflosorb® and Superia®) or no CO at all (Amsorb® and lithium hydroxide). None of the tested absorbents produced any CO when normally hydrated. Lithium hydroxide, however, is not yet available for medical use in anesthesia machines, because of it's highly corrosive effect. **Chapter 4** focuses on the interactions of sevoflurane and the seven different types of carbon dioxide absorbent described in **chapters 2 and 3**. We tested these absorbents in normally hydrated and desiccated condition and measured the temperature inside the absorbent, to investigate a possible relationship between CA and CO production and temperature inside the absorbent. We demonstrated that absorbents free of strong bases, Loflosorb®, Superia®, Amsorb® and lithium hydroxide do not produce any CA when normally hydrated, in contrast with absorbents containing strong bases. However, the absorbents Amsorb® and lithium hydroxide do produce small amounts of CA when desiccated. Small amounts of CO were produced by the desiccated strong base containing absorbents Drägersorb 800 plus®, Medisorb® and Spherasorb®, accompanied by sevoflurane degradation at the start of these experiments. No CO was produced with any of the absorbents in normally hydrated condition. No relationship between temperature and CA or CO production could be established. All measured concentrations of CA and CO do not appear to be clinically relevant.

Detection methods for the production of carbon monoxide inside an anesthetic ventilating circuit are not built in anaesthetic systems as a standard. We therefore investigated the reliability of an electrochemical CO sensor compared to the gold standard i.e. gas chromatography in **chapter 5**. In this study we found that the electrochemical sensor accurately detected carbon monoxide within the specified range of 0 – 200 ppm. Above this specified range this sensor underestimates the actual amounts of CO produced as measured by a gas chromatograph. However, this underestimated result still provides a warning signal of carbon monoxide production that requires immediate change of the carbon dioxide absorbent. When this sensor is exposed to sevoflurane in combination

with desiccated sodalime, it is not capable of normal operation and will display high and incorrect concentrations of CO within half an hour of operation.

In **chapter 6** we provide indications that carbon monoxide production in anesthetic practice is probably limited. In 40 patients receiving desflurane or sevoflurane anesthesia no CO production was found. This may be due to the effect of a safety protocol that was implemented in the VU University Medical Center with the introduction of desflurane. The purpose of this safety protocol is to prevent carbon dioxide absorbent desiccation. In all 20 sevoflurane anesthesia's, small concentrations of compound A were measured that where clinically insignificant.

In **chapter 7** the main conclusions and a general discussion of this thesis are presented.