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Gas exchange with a reflecting system for inhalational anaesthesia

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Gas exchange with a reflecting system for inhalational anaesthesia

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Louise Walther Sturesson

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Gas exchange with a reflecting system for inhalational anaesthesia

Abstract

In order to reduce comsumption of inhalational anaesthetsics during high flow anaesthesia a system open in regard to oxygen, nitogen and nitrous oxide, but closed to inhalational anaesthetics, was developed. This was achieved by a reflecting filter for inhalational anaesthetics made of active carbon. The principle has been developed into the commersially available Anesthetic Conserving Device (ACD, AnaConDa®).The ACD is a modified heat- and moisture exchanger (HME) containing av bacterial and viral filter as well as a carbon filter. The ACD can be used during surgery for administering the inhalational agents isoflurane and sevoflurane as an alternative to low-flow anaesthesia systems. It can also be used in intensive care units to administer sedation using isoflurane or sevoflurane to critically ill patients. The thesis is based on four papers.

In **paper I** it is shown that that the wash-in kinetics for sevoflurane delivered by the ACD is similar to a vaporiser. With the ACD, end-tidal sevoflurane accurately reflects arterial sevoflurane tension whereas inspired tension may be underesteimated. Despite an increase in tidal volume of patients in a group with an ACD corresponding to the larger internal volume of the device compared to a conventional HME, the $PaCO_2$ was considerably higher in this group.

In **paper II** CO_2 exchange and airway dead space is compared using an HME, ACD without reflecting filter and ACD with reflecting filter in a laboratory set-up. It is shown that the ACD binds CO_2 resulting in a dead space effect 180 ml in excess of its internal volume. This is due to adsorption of CO_2 in the ACD during expiration and return of CO_2 during the following inspiration.

In **paper III** the ACD is used without inhalational anaesthetics in patients as well as in a laboratory set-up with varying temperature and humidity. It is confirmed that an ACD used in humans as well as in a test lung increases the dead space effect and CO_2 rebreathing to a greater extent than can be explained by its internal volume. This is caused by adsorption of CO_2 in the ACD during expiration and release of CO_2 during inspiration. It is also shown that rebreathing of CO_2 is attenuated but not abolished by humidity.

In **paper IV** the ACD is used with sevoflurane in humans and in a laboratory set-up. It is shown that sevoflurane attenuates but does not abolish rebreathing of CO_2, thereby reducing the dead space effect of the ACD.

In conlusion, the ACD causes a dead space effect larger than its internal volume due to CO_2 rebreathing. This may influence the clinical use of the ACD.

Key words
Gas exchange, carbon dioxide, inhalational anaesthesia, anesthestic conserving device

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Gas exchange with a reflecting system for inhalational anaesthesia

LUND UNIVERSITY

Louise Walther Sturesson

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To Anders, Karl and Emma

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List of papers

This thesis is based on the following papers which will be referred to by their Roman numerals:

I. Sturesson LW, Johansson A, Bodelsson M, Malmkvist G.

Wash-in kinetics for sevoflurane using a disposable delivery system (AnaConDa®) in cardiac surgery patients.

British Journal of Anaesthesia 2009; 102: 470-476.

II. Sturesson LW, Malmkvist G, Bodelsson M, Niklason L, Jonson B.

Carbon dioxide rebreathing with the anaesthetic conserving device, AnaConDa®.

British Journal of Anaesthesia 2012; 109: 279-283.

III. Sturesson LW, Bodelsson M, Johansson A, Jonson B, Malmkvist G.

Apparent dead space with the anesthetic conserving device, AnaConDa®. A clinical and laboratory investigation.

Anesthesia and Analgesia. Resubmitted after revision.

IV. Sturesson LW, Bodelsson M, Jonson B, Malmkvist G.

CO_2 rebreathing and dead space effect of the anaesthetic conserving device AnaConDa® when used with sevoflurane.

In manuscript.

Abbreviations

ACD	Anesthetic Conserving Device
AnaConDa®	ACD trade name, Sedana Medical
ARDS	Acute Respiratory Distress Syndrome
CO_2	Carbon dioxide
CO_{2lung}	CO_2 transducer on the patient side of the tested device
CO_{2vent}	CO_2 transducer on the ventilator side of the tested device
E_TCO_2	End-tidal CO_2
HME	Heat- and Moisture Exchanger
kg	Kilogram
LPV	Lung Protective Ventilation
min	Minute
$PaCO_2$	Arterial tension of CO_2
SBT-CO_2	Single Breath Test for CO_2
V_{Daw}	Airway dead space
V_ICO_2%	Re-inspired fraction of expired CO_2 volume
V_T	Tidal volume

Background

Inhalational anaesthetics

Ever since nitrous oxide and ether were demonstrated to possess analgesic and narcotic properties in the middle of the 19th century, inhalational anaesthetics have been used for surgical anaesthesia and analgesia. The first modern halogenated inhalational anaesthetic, halothane, was presented by Charles Suckling in 1954. Halothane was followed by enflurane and isoflurane. Sevoflurane and desflurane are the most recent contributions to the family of halogenated inhalational agents.

Pharmacokinetics

Having reached the alveoli, inhalational anaesthetics rapidly diffuse across the alveolar membrane and are transported by the blood to all perfused organs. The rate at which the alveolar (end-tidal) concentration rises towards the inspired concentration is for all inhalational anaesthetics mainly dependent on the blood-gas partition coefficient i.e. the relative solubility of the anaesthetic. The onset of anaesthetic effect of a poorly soluble inhalational agent with a low blood-gas partition coefficient (e.g. sevoflurane) is faster than that of a more soluble anaesthetic with a higher blood-gas partition coefficient (e.g. halothane). Other factors influencing the rate at which equilibrium is established are ventilation (hyperventilation decreases the time required), cardiac output (high cardiac output increases the time), rate of uptake by different tissues (high uptake rates increases the time to equilibrium between blood and gas) and matching of ventilation and perfusion in the lung (mismatch increases the time to equilibrium).[1] Factors determining the rate of uptake of inhalational anaesthetic to a specific tissue are the tissue-blood solubility coefficient, tissue volume, blood perfusion (proportion of cardiac output) and arterial to tissue partial pressure difference. Concentrations in tissues with high blood flow (e.g. brain, heart and kidney) approach equilibrium with blood concentrations within hours, while tissue with low blood flow (e.g. fat) need several days to reach equilibrium.[1]

Inhalational anaesthetics are mainly eliminated through the lungs. However, all inhalational anaesthetics are metabolised to a varying degree.[2] Thus, about 15-

20% of inhaled halothane is metabolised,[3] while approximately 5% sevoflurane is metabolised[4] and 0.2% isoflurane is metabolised.[5] Metabolism of desflurane is 0.02%.[6] Modern inhalational anaesthetics undergo mainly hepatic metabolism by cytochrome P450 with liberation of several metabolites including inorganic fluoride, which are excreted in urine.[2, 6]

Pharmacodynamics

MAC has since the 1960s been used as a common measure of potency of inhalational anaesthetics.[7] One MAC of an inhalational anaesthetic is defined as the concentration preventing muscular movement in response to surgical stimulation in 50% of subjects. MAC values vary for different agents and are age-dependent. In neonates 1 MAC of sevoflurane is approximately 3.3% and at age 40-50 approximately 2%.[8]

Central Nervous System effects

The mechanisms of action of inhalational anaesthetics are only partially understood.[9, 10] For more than a century, the Meyer-Overton rule implying a correlation between the lipid solubility of inhalational anaesthetics and their anaesthetic potency influenced theories of mechanism of action.[11, 12] The unitary theory of narcosis, implying a common target site of action for all inhalational anaesthetics[13] has been abandoned as knowledge increases on receptor modulation by different inhalational anaesthetics in different parts of the central nervous system.[9]

Inhalational anaesthetics modify electrical activity of the central nervous system, as measured with EEG. Desflurane and isoflurane do not produce epileptic activity, while enflurane may increase epileptic waves.[14] Data concerning sevoflurane in this respect is controversial. Convulsions in patients with intractable epilepsy may, however, be suppressed by isoflurane and sevoflurane.[15] Inhalational anaesthetics partially uncouple the reactivity of cerebral blood flow to CO_2. In clinical concentrations, desflurane and isoflurane preserve reactivity of cerebral circulation and coupling of changes in CO_2 and metabolism to blood flow in the brain.[16] In the presence of sevoflurane autoregulation of cerebral blood flow is preserved below 1.5 MAC.[17]

Cardiovascular effects

Inhalational anaesthetics reduce mean arterial pressure and cardiac output in a dose-dependent manner. The reduction of mean arterial pressure by isoflurane, desflurane and sevoflurane is primarily determined by a reduction in systemic vascular resistance.[18, 19]

In 1985 Freedman and colleagues[20] reported that enflurane could improve post ischemic myocardial recovery in isolated rat hearts. The following year it was demonstrated that exposure to inhalational agents mimic the cardioprotective effects of repeated ischemia[21], a phenomenon called pharmacological preconditioning. There has been extensive research on the potential benefits of myocardial protection by anaesthetics in both animals and humans. Preconditioning is treatment before and postconditioning is treatment after an ischemic event aiming at myocardial protection by minimizing ischemia-reperfusion injury of the myocardium.

The mechanisms of protection and pre- and postconditioning by inhalational anaesthetics have been extensively studied *in vivo* and *in vitro*. These include:

Opening of mitochondrial K_{ATP} channels[22-24], increase in mitochondrial reactive oxygen species[24, 25] as well as activation or translocation of protein kinase C, tyrosine kinases and p38 mitogen-activated protein kinase.[24] These mechanisms decrease cytosolic and mitochondrial calcium loading.[26]

Two meta-analyses[27, 28] have shown cardioprotective effects of inhalational anaesthetics that result in decreased morbidity and mortality in patients undergoing cardiac surgery. A recent study[29] demonstrated that late pharmacological conditioning with inhalational sevoflurane might mediate cardiac protection, even with a late, brief and low-dose application.

Respiratory effects

Inhalational anaesthetics depress spontaneous breathing by reducing tidal volume.[30] The threshold for activating respiratory centres to CO_2 is raised by inhalational anaesthetics and the decrease in ventilation leads to CO_2 accumulation.[31, 32] Sevoflurane decreases airway resistance.[33] Several case reports have shown successful treatment of status asthmaticus using sevoflurane.[34-36]

Clinical implications of the pharmacodynamic properties of inhaled anaesthetics

It can be concluded that inhalational anaesthetics have beneficial effects for a wide spectrum of patients in anaesthesia and intensive care. These include status epilepticus, exacerbations of obstructive lung disease and ischemic heart disease. The use of inhalational anaesthetics in an intensive care setting is, however, complicated if conventional anaesthetic circuits must be used.

Sevoflurane metabolism and toxicity

Inorganic fluoride

Hepatic metabolism of sevoflurane forms carbon dioxide, inorganic fluoride and hexa-fluoro-isopropanol. Nephrotoxicity of fluoride has been extensively

investigated.[6] After prolonged sevoflurane anaesthesia, there was neither a reduction in renal concentration function[37] nor an effect on renal or hepatic function after long-term (>10 hours) low-flow anaesthesia with sevoflurane.[38] The results from these studies, together with other similar papers and favourable clinical outcome in about 100 million surgical patients, suggest that the elevations of inorganic fluoride concentrations seen during anaesthesia with sevoflurane is not nephrotoxic or otherwise interfering with renal function.[6]

Compound A

The formation and accumulation of fluoromethyl-2,2-difluoro-1-vinyl-ether, usually called compound A, in rebreathing anaesthesia circuits with sevoflurane is especially high with low fresh-gas flows. Histological signs of renal injury from compound A in Wistar rats were observed.[39] There is no evidence that compound A has the potential to produce permanent renal injury in humans.[40] A multicentre study showed no significant differences in routine laboratory renal parameters after low-flow sevoflurane anaesthesia compared with low-flow isoflurane in patients with chronic renal insuffiency.[41] It should be noted that the formation of compound A occurs only in the presence of the alkali components of CO_2 absorbers in a circle system.[6] It is thus not a problem with non-rebreathing circuits for ventilation.

Inhalational anaesthetics and malignant hyperthermia

Malignant hyperthermia is a rare autosomal dominant disorder that results in an extreme form of metabolic crisis. In susceptible patients a crises is triggered by exposure to inhalational anaesthetics, the depolarising neuromuscular blocking agent, succinylcholine, and, in rare cases, stress.[42] The manifestations are primarily due to a gene mutation affecting the ryanodin-1 receptor (RYR-1) receptor, which facilitates calcium release in skeletal muscle.[43] The receptor also binds inhalational anaesthetics, which can start an attack.[42, 44] The pharmacological treatment is dantrolene, which also binds to RYR-1 causing an inhibition of the excitation-contraction coupling and subsequent muscle relaxation.[45] A survey of anaesthesia departments in Denmark found that the overall incidence of fulminant malignant hyperthermia during anaesthetic procedures is low (1/250000 patients) with a mortality rate of 10%. A combination of inhalational anaesthetics and succinylcholine appears to be associated with a higher incidence (1/62000 patients).[46]

The Anesthetic Conserving Device (ACD, AnaConDa®)

In order to reduce consumption of inhalational anaesthetics during high-flow anaesthesia a system open in regard to oxygen, nitrogen and nitrous oxide, but closed to inhalational anaesthetics, was developed. This was achieved by a reflecting filter for inhalational anaesthetics made of zeolite, a porous aluminosilicate material and described by Thomasson and colleagues.[47] Microscopic particles of filter material may reach the lung and some zeolites are hazardous because of their fibrogenic and carcinogenic activity.[48, 49] Instead a carbon filter for reflecting inhalational anaesthetics was evaluated.[50] The principle has been further developed leading to the Anaesthetic Conserving Device (ACD, AnaConDa®), shown in Fig. 1. The ACD is a modified heat-and moisture exchanger (HME) containing a bacterial and viral filter as well as a carbon filter. The ACD is integrated with the respiratory tubing replacing the HME between the Y-piece and the endo-tracheal tube. The internal volume of the ACD is approximately 100 ml.[51] The anaesthetic agent is delivered in liquid form by a standard syringe pump through an infusion line to a porous rod on the patient side of the carbon filter. During inspiration, the fresh gas flow passing the ACD vaporises the anaesthetic agent that has reached the surface of the evaporator rod. Approximately 90% of the anaesthetic agent present in a tidal volume (V_T) of 500 ml will on exhalation be adsorbed to the carbon filter in the ACD.[51] During the following inspiration the adsorbed anaesthetic agent is desorbed and inhaled together with additional agent evaporated on the rod. With the ACD it is possible to administer inhalational anaesthetics with an intensive care ventilator and a non-rebreathing ventilator tubing arrangement. There should be no risk for compound A accumulation with the ACD since no CO_2 absorber is used.

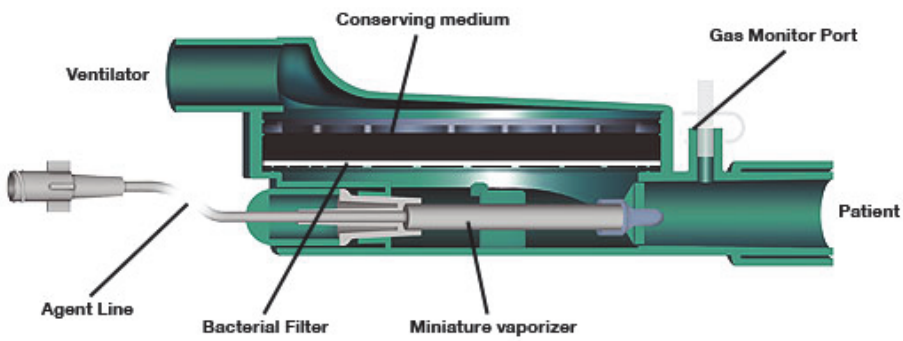

Fig. 1. Cross-sectional view of the ACD. From http://www.sedanamedical.com 26 February 2013.

The effective concentration of the inhalational anaesthetic can be monitored also when using an ACD by determining the end-tidal concentration. This may be achieved by sampling on the patient side of the carbon filter, Fig. 1. It was demonstrated that gas monitors may display inspiratory and end-tidal concentrations incorrectly. This was explained by the dead space within the ACD containing CO_2, which will continue to be sampled during the start of inspiration thus offsetting the signal, which indicates start of inspiration. This may cause the monitor to display inspiratory and end-tidal values in lieu with each other.[52]

ACD during surgery

It was in the early 21th century shown that the ACD can be used as an alternative to low-flow systems during major surgery.[53, 54] In a recent comparison with a conventional vaporizer it was shown that the use of an ACD during surgical anaesthesia can reduce sevoflurane consumption when used at concentrations of 1.5-2.0%.[55]

ACD for sedation in intensive care units

Severe disease and invasive procedures, e.g. ventilator treatment, regularly necessitate administration of sedatives and analgesics to critically ill patients.[56] In 1989 isoflurane at subanaesthetic concentrations (0.1-0.6%) was shown to provide satisfactory sedation for a greater proportion of time than midazolam and patients sedated with isoflurane recovered more rapidly from sedation.[57] A comparison between isoflurane and propofol in the early 1990s showed no differences between the two agents concerning sedation and adverse advents in long-term use for at least 48 hours.[58] Administration of inhalational anaesthetics to patients in intensive care units has been simplified considerably by the ACD and provides efficient sedation in such a setting.[59, 60] Despite use for anaesthesia and sedation the wash-in kinetics of inhalational anaesthetics using the ACD was, however, not known when our studies were initiated.

Carbon dioxide (CO_2)

Carbon dioxide (CO_2) is produced by cell metabolism, awake and at rest at a rate of about 3 ml kg^{-1} min^{-1}. CO_2 diffuses from tissue to capillaries and is transported with blood in three different ways to the lungs where it is exhaled. Firstly, CO_2 is dissolved in plasma. Even though it is much more hydrophil than O_2, only about 7% of the CO_2 is transported in this way. Secondly, CO_2 binds to proteins in plasma and blood cells. Twenty-three % of CO_2 is transported this way.

Deoxyhemoglobin has a higher affinity for CO_2 than oxyhemoglobin rendering venous blood a larger capacity to carry CO_2. Thirdly, about 70% of CO_2 in blood is transported in the form of bicarbonate ions (HCO_3^-). In a process catalysed by carbanhydrase in erythrocytes, CO_2 reacts with H_2O to form H_2CO_3, which in turn dissociates to HCO_3^- and H^+.

Hypercapnia

Fresh air is brought into the lungs by cyclic breathing. In an adult a normal tidal breath at rest is approximately 6-8 ml kg bodyweight^{-1} and the respiratory rate is about 16 breaths min^{-1}. Metabolic demand and the efficiency of pulmonary gas exchange will determine the magnitude and rate, provided that the respiratory center in the brain stem is intact and functioning. All gas inspired does not reach the alveoli. Some will stay in the airways and will thus not participate in gas exchange. This gas is about 15% of tidal volume and is called the airway dead space. The remaining part of the inhalational gas reaches the alveoli and respiratory brochioles. Even that partition of tidal volume is not completely used gas exchange because of mismatch between ventilation and perfusion in alveoli causing what is known as alveolar dead space. All subjects, even those with healthy lungs, have some ventilation/perfusion mismatch.[61] Physiological dead space is the sum of airway and alveolar dead space. Physiological dead space is typically 30% of tidal volume in healthy individuals.[62] The part of ventilation which reaches alveoli and respiratory brochioles participating in gas exchange is called alveolar ventilation, which is the tidal volume less the volume of physiological dead space. Effective ventilation is alveolar ventilation, times respiratory rate.

Hypercapnia, i.e. an excessive amount of CO_2 in the blood, may be caused by hypoventilation. Hypoventilation is often defined as ventilation resulting in a $PaCO_2$ above 6 kPa. With this definition, hypoventilation can be present even when minute ventilation is normal if metabolic demand or dead space ventilation is increased.

Hypercapnia during anaesthesia

Malfunctioning anaesthetic circuits including an inappropriately large apparatus dead space, abdominal CO_2 insufflation during laparoscopic surgery or increased metabolic production of CO_2 may all cause accumulation of CO_2 and concomitant acidosis. During anaesthesia with spontaneous breathing inhalational anaesthesia may depress ventilatory responsiveness to CO_2 with the same result. When ventilation is controlled, the anaesthetist needs to control for all the above factors to prevent possible dysfunction in several organ systems, including the heart (e.g.

arrhythmias), lungs (e.g. pulmonary hypertension) and brain (e.g. increased intracranial pressure).[30]

Aims

The initial objective of this dissertation was to determine clinical parameters relevant for guiding sevoflurane anaesthesia to cardiac surgery patients. After analysis of the results from the first paper the focus changed to investigation of dead space effects of the ACD and its causes.

The specific aims of each paper were:

1. To compare a vaporizer and the ACD in a non-rebreathing circuit regarding wash-in kinetics for sevoflurane and to determine if end-tidal values reflect arterial values of sevoflurane in humans.

2. To determine whether CO_2, like inhalational anaesthetics, adsorbs to the ACD during expiration and is desorbed and re-inspired during the following inspiration using a test lung.

3. To determine, in the absence of an inhalational agent, the effect of temperature and moisture on CO_2 rebreathing from an ACD using a test lung and to assess the dead space effect of the ACD in humans.

4. To test the effect of sevoflurane on CO_2 rebreathing from the ACD when used in humans and in a test lung.

Materials

For details on the material used in the present thesis, the reader is referred to the separate papers.

Patients

All patient studies (paper I, III, IV) were approved by the Regional Ethics Committee (Lund, Sweden) in adherence to the standards set in the Helsinki declaration. Paper III and IV were registered at ClinicalTrials.gov before starting recruitment of patients. All patients were adult and written informed consent was obtained from each patient before participation.

Paper I

Sixteen patients presenting for elective cardiac surgery were studied during induction of anaesthesia. All patients had normal echocardiographic left ventricular ejection fraction before surgery. Patients with restrictive lung disease or obstructive disease with more than one inhalational drug were excluded. One additional patient was recruited for detailed measurement of airway gas concentrations during use of ACD.

Paper III

Six patients were studied during routine, intubated sedated postoperative ventilatory support after elective cardiac surgery. The experimental set-up is described in Equipment.

Paper IV

Twelve patients were studied during routine, intubated and sedated postoperative ventilatory support after elective cardiac surgery. The same set-up as in Paper III was used.

Fig. 2. Experimental set-up used in paper II, III and IV. From top to bottom: Computerscreen, ServoVentilator 900C, A/D converter, CO2 analysers and computer.

Test lung

Paper II, III, IV

A test lung in the form of a 20 litre plastic bottle was used. It was connected to the ventilator with a plastic tube penetrating an air tight lid. The test lung was fed with pure CO_2 close to its bottom. Inside gas was mixed with a fan. In studies with humidified gas, moisture was added by wetting cotton towels lining the inner wall of the test lung. Temperature was adjusted with a forced air warming blanket wrapped around the bottle.

Equipment

Paper II, III, IV

The patient or the test lung was ventilated with a Servo Ventilator 900C equipped with two Analyzer 930 (Siemens-Elema AB, Solna, Sweden). One of the CO_2 transducers (CO_{2vent}) was placed between the Y-piece and the device tested. The other CO_2 transducer (CO_{2lung}) was placed between the device tested and the tube connecting to the patient or the test lung, respectively. Signals for airway gas flow from the ventilator and CO_2 signals from both analysers were fed to a personal computer, Fig. 2. Data was collected during measurement sequences comprising 10 consecutive breaths. Data from both transducers were for each breath in the sequence exported to and analysed in an Excel spread sheet.

Methodological considerations

For details on methods used in each paper, the reader is referred to the separate papers.

Measurements

Sevoflurane

End tidal volatile anaesthetic partial pressures can differ widely from those in arterial blood.[63, 64] In order to explore the wash-in kinetics for sevoflurane and to determine if end tidal sevoflurane values from the standard gas monitor reflects arterial sevoflurane levels, the gas chromatography head-space technique described by Smith and colleagues in 1997 was used to measure blood sevoflurane tension.[65] The double head-space analysis employed also allows for a simultaneous calculation of the blood-gas partition coefficient for sevoflurane. Accurate assessment of blood tension of a volatile anaesthetic by chromatographic measurement using the head-space technique is dependent on an accurate value for the blood-gas partition coefficient. The value found in Paper I, 0.76, was higher than reported by Strum and Eger (0.69).[66] Another study by Esper and colleagues in 2007 arrived at the same value (0.76)[67] as in Paper I. The blood-gas partition coefficient only affects the calculation of the absolute value of tension of dissolved sevoflurane. It thus seems reasonable to assume that comparison of relative levels is possible also if the coefficient is slightly offset.

CO_2

CO_2 analyser

Capnometers, capnographs and anaesthetic gas analysers all use the Beer-Lambert law of absorption to quantify the constituents of the respiratory gas stream. The Beer-Lambert law states that if light of known intensity travels a chamber with a known path length, the concentration of a material in the chamber can be determined if the transmitted light intensity is measured. Capnographs and

inhalational anaesthetic gas analysers function by the same principle, but different wave lengths of light are used.

Fowler described in 1949 an infrared analyser for measuring the CO_2 content of gases intended for physiological application.[68] The medical literature was than sparse concerning reports on the use of infrared CO_2 analysers until the 1980s. Since the 1990s it is standard of care to monitor end-tidal CO_2 in patients during anaesthesia[69] and also during intensive care.[70] CO_2 absorbs infrared light with a characteristic peak at a wave-length of 4.3 µm. Several other molecules such as anaesthetic gases, especially nitrous oxide, water vapour and O_2 absorb light in this area of the spectrum interfering with CO_2 measurement.[71] Accurate infrared CO_2 analysis involves a complex continuous data calibration and compensatory procedure to eliminate or at least minimize the effects of overlapping infrared absorption of anaesthetic gases, water vapour, O_2 [72, 73] and those of collisioning broadening of the spectral peaks.[74]

In the CO_2 Analyzer 930 (Siemens-Elema AB, Solna, Sweden), Fig. 3, used in paper II, III and IV such corrections for cross-senitivity are not made.[75] This limitation is due to the fact that no relevant information concerning other gases is available in the apparatus. However, the mentioned problems do not influence the results on which our conclusions are based since they refer to data which are not critically influenced by minor abbreviations in the calibration of CO_2 signals from the analysers. Airway dead space is calculated from the shape of the expiratory limb of the SBT-CO_2 and not from absolute CO_2 values. In the presence of varying water vapour and sevoflurane tensions, volumes of re-inspired CO_2 are expressed in percent of expired volumes of CO_2 from the same breaths and under the same circumstances.

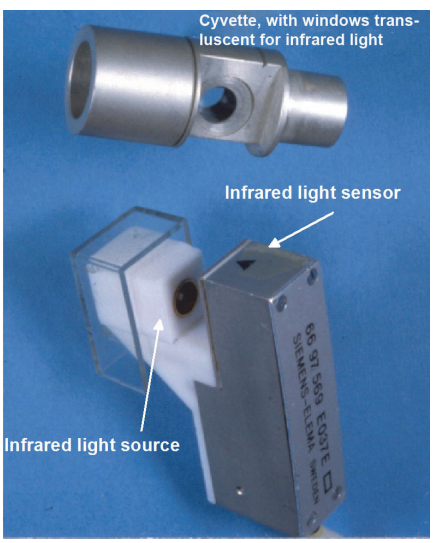

Fig 3. The transducer of the CO_2 Analyzer 930 used in this thesis has two parts. The cyvette connects on the left side to the Y-piece of the ventilator tubing on the right side to the tracheal tube connector. Windows made of saphire glass transluscent for infrared light. The cyvette is placed in the electric transducer so that its infrared light source and sensor are aligned with the windows.

The physical design of capnometers is divided into two categories: mainstream and sidestream. In mainstream capnometers, the light absorption chamber is placed directly in the airway. The light source shines through the chamber with CO_2 being measured during inspiration and expiration directly. The advantage of this technique is a fast response time and the possibility to integrate the CO_2 signal with a simulatnously measured flow for accurate calculation of expired and inspired CO_2-volumes. Disadvantages include a heavy, fragile and expensive infrared measurement device placed directly in the airway at the endo-tracheal tube and that currently availabe systems do not measure inhalational anaesthetic concentrations. The more commonly used side stream capnometers have a sampling line attached to the airway near the endo-tracheal tube and samples are aspirated (200-400 ml min^{-1}) into the measurement chamber located within the monitor itself. The set-up is lightweight and often allows for inhalational anaesthetic as well as CO_2 concentrations to be measured. Disadvantages include delayed response time compared to mainstream capnometers and potential clogging of aspiation tubing.[71]

Blood gas

CO_2 tension in blood is determined by an electrode measuring the change in pH when blood equilibrates with a potassium chloride/sodium bicarbonate solution.[76]

Single Breath Test for CO_2 (SBT-CO_2)

Fraction of CO_2 in expired gas plotted as a function of expiratory flow is useful e.g. for measurement of dead space. This principle has been denoted the single breath test for CO_2 (SBT-CO_2) and developed for use in patients with controlled ventilation by Fletcher, Jonson et al.[77]

The SBT-CO_2 is a recording of fraction of CO_2 in expired air on the Y-axis against expired volume on the X-axis. The first description of SBT-CO_2 in the literature is that of Aitken and Clarke-Kennedy.[78] Using successive samples of expired gas, they were able to deduce the approximate shape of SBT-CO_2. They showed, as did Krogh and Lindhard in 1914,[79] that expired CO_2 increases with increasing expired volume. The single breath tracing can be divided into three phases,[80] as illustrated in Fig.4. Phase I is the CO_2 free phase representing gas from the airways. Phase II is characterised by a rapid S-shaped upswing in the tracing. Phase III represents alveolar gas, and has been called the alveolar plateau, although CO_2 fraction usually rises somewhat also during this phase. The reasons for the gradually rising plateau are believed to be sequential emptying of lung regions with decreasing ventilation/perfusion ratios and continuous release of CO_2 into the alveoli during expiration.[81] Clinical volumetric capnography was first

applied in a study of gas exchange and metabolic rate in infants undergoing cardiac surgery, based on a prototype of CO_2 Analyzer 930.[82]

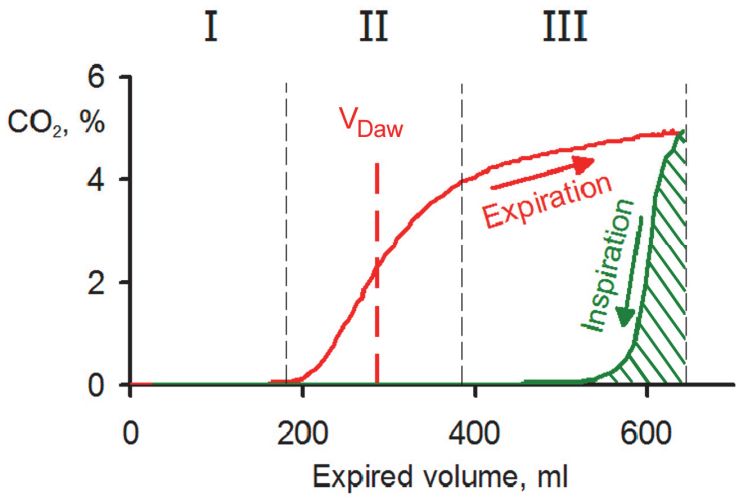

Fig. 4. Expiratory SBT-CO_2 from a patient in paper IV, red curve. During phase I of the expiration, gas free of CO_2 is expired from conducting airways. During phase II airway gas is admixed with increasing amounts of alveolar gas. Approximately at the middle of phase II the volume of conducting airways, the airway dead space (V_{Daw}), is determined, red dashed line. Phase III is considered to represent pure alveolar gas and is denoted the alveolar plateau. It is sloping because of several factors, e.g. continouing delivery of CO_2 to alveoli by venous blood. During ensuing inspiration some CO_2 is re-inspired. During that phase the CO_2 concentration in the cyvette falls, green curve. The volume of CO_2 expired during the breath is presented by the area under the red curve. The volume of CO_2 re-inspired during the breath is represented by the area under the green curve and the volume of CO_2 eliminated by the breath is the difference between these two areas.

A recording of fraction of CO_2 in expired air against expired volume and a simultaneous measurement of arterial CO_2 tension allows determination of physiological dead space and its separation into V_{Daw} and alveolar dead space.[77] Airway dead space can also be calculated by determining the volume expired at the steepest increase in the CO_2 fraction during expiration.[83] This method was chosen in paper II, III and IV for our test lung system as it was stable in its performance and gave reproducible results. In paper III and IV, V_{Daw} in patients were calculated based on the principle suggested by Wolff and Brunner.[84] Their algorithm was modified by Åström et al. to be more robust in the presence of a sloping plateau.[61]

At the end of expiration a certain volume of CO_2 has been expired. At the start of inspiration a part of that volume is re-inspired. The amount of re-inspired CO_2 is in our studies measured with the CO_{2lung} transducer placed between the device tested and the tube to the patient or the test lung in paper II, III and IV. The CO_2 eliminated during a breath is the difference between the total amount of expired CO_2 and the re-inspired CO_2.

Statistics

The presentation of data and the methods for statistical testing of hypotheses used in the four studies were dependent on sample size and whether or not the data was normally distributed (Shapiro-Wilk test).

Paper I

Data were presented as mean (SD). Values expressing changes over time were analysed using two-way repeated measures ANOVA for the two factors time and parameter. The parameters were tension of sevoflurane in arterial blood, inspired gas and end-tidal gas. ANOVA was followed by Holm-Sidak *post hoc* test if ANOVA had indicated statistical significance. Durations were compared using Student's *t*-test. To facilitate comparison of sevoflurane tension between groups, sevoflurane tension for each patient was normalised to the value at the end of the measurement sequence, which can be regarded as close to steady state.

Paper II

Descriptive data

Paper III

Data were presented as median (range). Differences in median values were analysed with Wilcoxon signed rank test. Non-parametric statistics were used due to the small sample size (6 patients).

Paper IV

Data were presented as mean (SD). Differences in mean values between the HME and ACD in the absence of sevoflurane were analysed with the paired Student's *t*-test. Differences in mean values obtained with ACD during zero, 0.4 and 0.8% sevoflurane were analysed with one way repeated measurement ANOVA followed by Holm-Sidak *post hoc* test if ANOVA had indicated statistical significance.

Results and comments

Paper I

Kinetics of arterial sevoflurane tension

In this study we measured 30 min wash-in kinetics of sevoflurane and gas monitor reliability comparing a conventional vaporizer and the ACD. Patients were randomized to receive sevoflurane either by a conventional vaporizer or an ACD. The vaporizer and ACD settings aimed at an end-tidal concentration of 1% in steady state. After detection of sevoflurane by the gas monitor, sevoflurane tension in arterial blood increased steadily and levelled out after 20 and 10 minutes for sevoflurane administered via a vaporizer and ACD, respectively (Fig. 5). The arterial tension in patients receiving sevoflurane via the ACD was lower during the first 5 minutes than for patients receiving sevoflurane via a vaporizer. This relationship was reversed after 10 minutes and from 15 minutes onwards arterial sevoflurane tension was similar in the two groups. Time required to reach 80% of the arterial partial pressure of sevoflurane measured at 30 minutes was similar in the two groups, 8.1 (1.7) and 7.5 (0.34) minutes after detection of sevoflurane by the gas monitor for the vaporizer and ACD groups, respectively, Fig. 5.

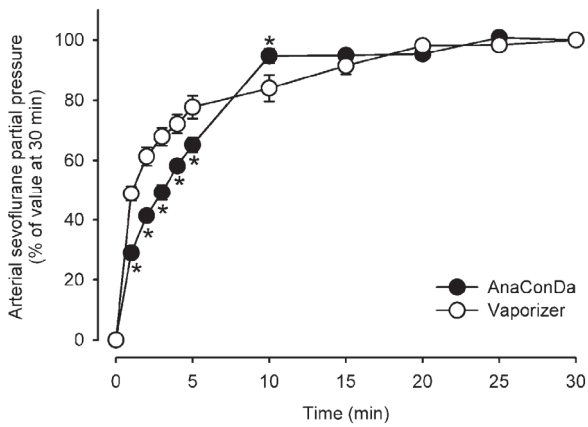

Fig. 5. Wash-in kinetics for sevoflurane using a vaporiser or an ACD. Sevoflurane tensions in arterial blood. Tensions with ACD were lower than with vaporizer during the first 5 min. This relationship was reversed after 10 min and from 15 min on the arterial sevoflurane tension was similar. *Statistically significant difference from value using a vaporizer. Values are mean (SD) were normalised to the value at 30 min (*n*=8 in each group).

Airway sevoflurane

Conventional vaporizer

Mean end-tidal sevoflurane tension at 30 minutes was 0.99 (0.10) kPa. Values for sevoflurane tension in inspired gas given by the gas monitor were significantly higher than the arterial tension at all time points. Values for end-tidal sevoflurane tension given by the gas monitor were slightly, but statistically significantly higher than the arterial partial pressure for the first 10 minutes.

ACD

Mean end-tidal sevoflurane tension at 30 minutes was 1.04 (0.10) kPa. Values for sevoflurane tension in inspired gas given by the gas monitor were significantly lower than the arterial tension at all times. Values for end-tidal sevoflurane tension measured by the gas monitor did not differ significantly from arterial partial pressure.

CO_2 exchange

When the ACD was used, the tidal volume was increased by 50 ml to compensate for the larger internal gas volume of this device compared to the HME used with the vaporizer. Mean $PaCO_2$ was significantly higher at all time points measured in the ACD group compared to the vaporizer group [6.5 (0.7) and 5.4 (0.9) kPa at 30 minutes for the ACD and vaporizer groups, respectively]. Mean $PaCO_2$ values within the groups did not change significantly during the study period.

This study shows that the wash-in kinetics for sevoflurane delivered by the ACD is similar to a vaporizer. End-tidal sevoflurane tension accurately reflects arterial tension whereas inspired tension may be underestimated using an ACD.

Furthermore, despite an increase in tidal volume of the patients of the ACD group corresponding to the larger internal volume of the devices, the $PaCO_2$ was considerably higher in this group. We hypothesised that this was caused by adsorption of CO_2 in the ACD during expiration and return of CO_2 during the following inspiration. Since this could be important for safe use of an ACD with patients where the $PaCO_2$ needs to be under tight control, for example, during neurosurgery, this hypothesis was tested in the following study.

Paper II

In this study we compared CO_2 exchange and V_{Daw} with an HME and an ACD with (active) and an ACD without (inactive) reflection filter. A test lung ventilated with dry gas of room temperature was used.

End-tidal CO_2

In the first part of the study, we established a steady state with respect to an end-tidal CO_2 at 5.0 - 5.1 %, while using the HME. When the HME was replaced by the *non-active* ACD and V_T increased by 50 ml as in paper I, end-tidal CO_2 at CO_{2vent} remained stable. When the non-active ACD was replaced by the *active* ACD without any further increase in V_T, end-tidal CO increased gradually indicating accumulation of CO_2 in the test lung. When end-tidal CO approached 10 % V_T was increased stepwise and end-tidal CO_{2vent} decreased. When V_T had been increased by 250 ml compared to baseline V_T with HME, end-tidal CO_2 returned to baseline level as illustrated in Fig. 6.

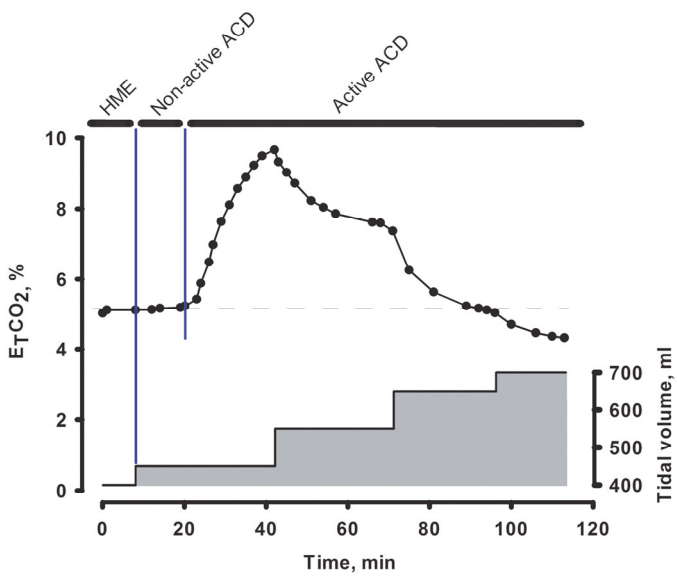

Fig. 6. End-tidal CO_2 measured at the ventilator CO_2 transducer using an HME, inactive ACD or active ACD. Tidal volume is shown in the lower grey part of the graph and was increased by 50 ml corresponding to the difference in the internal volume between the HME and ACD when the inactive ACD was introduced. With the active ACD, when end-tidal CO_2 approached 10%, V_T was increased stepwise in order to restore the original value of end-tidal CO_2.

Dead space effects and CO_2 rebreathing

In a following part of the study, V_T was adjusted to maintain isocapnia and steady state prevailed both when the HME and the active ACD was studied. With the HME, V_{Daw} measured with CO_{2vent}, comprising the volume of the HME and tubing to the test lung was 142 ml and the volume of re-inspired CO_2 (V_ICO_2) from Y-piece and adjacent tubes was 1.6 ml. SBT-CO_2 from CO_{2lung} showed V_{Daw} values representing tubing only (101 ml), while V_ICO_2 included the volume of CO_2 in the HME and accordingly was higher (4.5 ml) than measured with CO_{2vent}. When the ACD was studied with CO_{2vent}, no CO_2 appeared at the transducer until about 200 ml had been expired and V_{Daw} was estimated to 372 ml. V_ICO_2 was similar to breaths with conventional HME. When the ACD was studied with CO_{2lung}, CO_2 arrived rapidly at the CO_{2lung} transducer and V_{Daw} was estimated to 113 ml. During inspiration, the fraction of inspired CO_2 remained high for about 200 ml and then gradually decreased towards zero as CO_2 washout from the ACD progressed. Of the total expired volume of CO_2, more than 50 % was re-inspired. Varying CO_2 flux to the test lung between 85 and 375 ml min^{-1} did not change measured V_{Daw}. Varying respiratory rates between 12 and 24 breaths min^{-1}, with concomitant changes of tidal volume to maintain constant end-tidal CO_2, also did not alter V_{Daw}. Using higher respiratory rate allowed lower tidal volumes to maintain isocapnia.

CO_2 content of the ACD

In order to assess the CO_2 retained in the ACD we used the CO_{2lung} transducer to measure CO_2 volumes washed out from the device during inspiration after disconnecting it from the tubing to the test lung. Steady state end-tidal CO_2 values between 1 and 8 % were achieved by adjusting CO_2-flux to the test lung. During the first breath 95 % of this volume was washed out and after four breaths all detectable CO_2 had been eliminated. A strict proportionally between V_{CO_2ACD} and E_TCO_2 was found: $V_{CO_2ACD} = 3.3 \times E_TCO_2$. Thus, the active ACD contained 3.3 times more CO_2 than the predicted amount present in its 100 ml of gas.

This study indicates that the ACD binds CO_2 resulting in a dead space effect of 180 ml in excess of its internal volume. This is due to adsorption of CO_2 in the ACD during expiration and return of CO_2 during the following inspiration.

Paper III

The experiments in paper II were performed with dry gas at room temperature, which differs from the conditions during clinical use of the ACD. Since the moderate increase in $PaCO_2$ with the ACD found in the patients of paper I contrasted to the massive accumulation of the CO_2 in the test lung of paper II, we hypothesized that temperature and/or humidity reduces the CO_2-binding capacity of the ACD. In this study we tested this hypothesis by measuring CO_2 exchange and V_{Daw} with the ACD in patients and in a test lung at varying temperature and humidity. No inhalational anaesthetics were used in either setting.

Patients

Dead space effects and CO_2 rebreathing were studied with an HME and an ACD.

Dead space effects

CO_{2vent} yielded V_{Daw} values with an HME comprising the volume of the HME and conducting airways of 152 ml (132-183). When the ACD was studied with CO_{2vent}, no CO_2 appeared at the transducer until about 150 ml had been expired and median V_{Daw} was 295 ml (272-314), which was higher compared to the HME ($P = 0.03$). Median difference in V_{Daw} between ACD and HME was 136 ml (120-167). When V_{Daw} values were corrected for the larger internal volume of the ACD compared to the HME by subtracting 50 ml from measured ACD values, the latter was still 86 ml higher (70-117, $P = 0.03$), Fig. 7A. V_{Daw} measured with CO_{2vent} did not differ between an HME and an ACD, Fig. 7B.

CO_2 rebreathing

V_ICO_2 was measured with CO_{2lung} and expressed in percent of the volume of CO_2 expired in the same breaths, V_ICO_2%. Re-inspired CO_2 measured with CO_{2lung} includes CO_2 from the HME or the ACD. With the HME, re-inspired fraction of expired CO_2 was 29% (27-32). Using the ACD, V_ICO_2% was considerably higher (53% (48-58), $P = 0.03$) compared to with the HME, Fig. 7C.

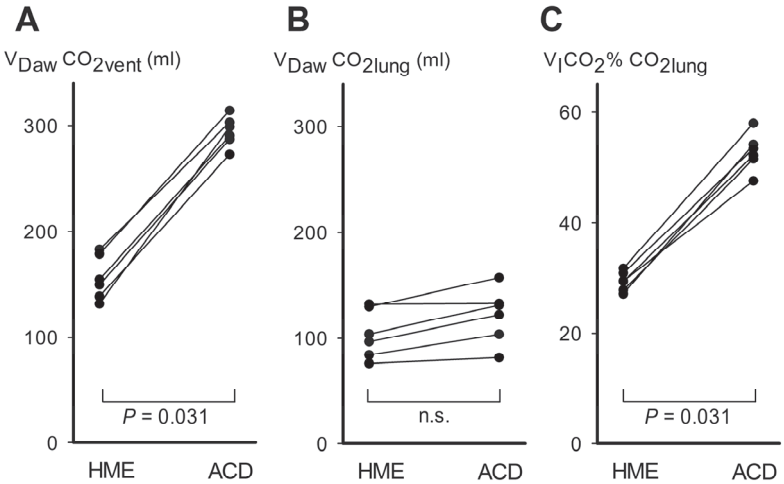

Fig. 7. Airway dead space (V_{Daw}, panels A and B) and fraction CO_2 rebreathing (V_ICO_2%, panel C) in patients using the HME and ACD, measured with CO_{2vent} and CO_{2lung} as shown. V_{Daw} measured with CO_{2vent} and V_ICO_2% were larger with ACD than with HME. Wilcoxon signed rank test. Values from individual patients are shown (*n*=6).

Test lung

The temperature in the test lung was controlled by a forced air warming blanket and the humidity by wetting cotton towels lining its inner wall. At dry conditions, increasing the temperature from room to body like temperature affected V_{Daw} or V_ICO_2% neither at the ventilator nor at the lung side of the ACD. When moist conditions, i.e. relative humidity 85%, were established at 36°C, V_{Daw} measured with CO_{2vent} decreased from 360 ml to 260 ml. After introduction of moisture, V_ICO_2% measured with CO_{2lung} decreased from 62 % to 48%. The values for V_{Daw} and V_ICO_2% after introduction of moisture are within the range observed in patients.

This study shows that an ACD used with patients as well as with a test lung increases apparent dead space and rebreathing of CO_2 to a greater extent than can be explained by its internal volume. This is caused by adsorption of CO_2 in the ACD during expiration and release of CO_2 during inspiration. It was shown that rebreathing of CO_2 is attenuated by humidity.

Paper IV

In paper III we demonstrated that rebreathing of CO_2 from the ACD is attenuated by humidity. We hypothesised that inhalational anaesthetics further reduces rebreathing of CO_2 from the ACD. To test this hypothesis, we measured V_{Daw} and CO_2 exchange in patients and in a test lung with the ACD used with sevoflurane at different concentrations.

Patients

Dead space effects

With the HME V_{Daw} was 180 ml (27). When the ACD was studied without sevoflurane V_{Daw} was 315 ml (30). This was higher compared to the HME ($P < 0.001$). Sevoflurane concentration-dependently reduced V_{Daw} ($P \leq 0.021$). With the ACD and 0.8% sevoflurane, VDaw was 88 ml (6.4) higher than with the HME. Out of this 50 ml is explained by difference in internal volume, while 38 ml (6.4) is caused by CO_2 reflection in the device, Fig 8A.

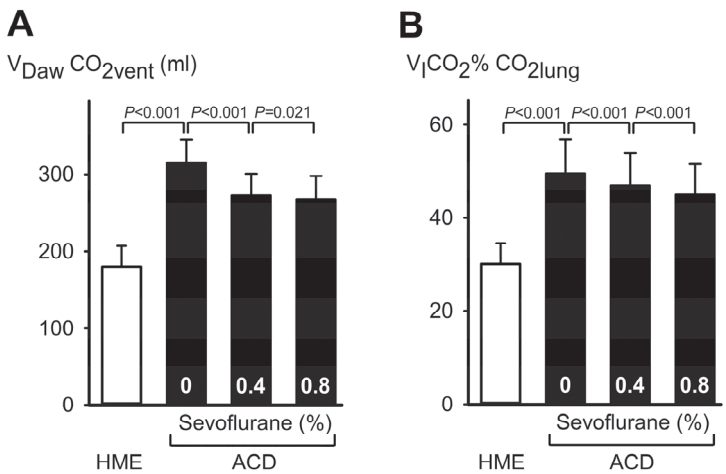

Fig. 8. Airway dead space (V_{Daw}, panel A) and fraction of CO_2 rebreathing (V_ICO_2%, panel B) in patients using the HME and ACD with and without sevoflurane. Values are mean (SD) *P*-values for differences between the means are given. One-way repeated ANOVA followed by the Holm-Sidak *post hoc* test (*n*=12).

CO_2 rebreathing

V_ICO_2 was measured with CO_{2lung} and expressed in percent of the volume of CO_2 expired in the same breaths, V_ICO_2%. Accordingly, V_ICO_2% includes re-inspired CO_2 from the HME or the ACD. With the HME mean V_ICO_2% was 30% (4), Fig. 8B. With the ACD, mean V_ICO_2% was significantly higher (50% (7), $P < 0.001$). Sevoflurane concentration-dependently reduced V_ICO_2% and was 45% at 0.8% sevoflurane ($P < 0.001$), Fig 8B.

Test lung

At humid conditions and body-like temperature V_{Daw} measured with CO_{2vent} was with the ACD 259 ml. At an end-tidal sevoflurane concentration of 0.6%, V_{Daw} decreased to 219 ml. Further increase of sevoflurane to 1%, 2% and 3% reduced V_{Daw} only marginally. V_ICO_2% measured with CO_{2lung} was without sevoflurane 48%. With 0.6% sevoflurane, V_ICO_2% decreased to 44%. Increasing sevoflurane concentration to 1%, 2% and 3% did not noticeably change V_ICO_2% further.

This study confirms that an ACD causes a dead space effect by re-inhalation of CO_2, larger than can be explained by its internal volume. Sevoflurane attenuates but does not abolish rebreathing of CO_2, thereby reducing the dead space effect of the ACD. The CO_2-reflecting properties of the ACD have implications with respect to its use at low tidal volumes and lung protective ventilation.

General discussion

ACD and CO_2 rebreathing

The results from this PhD project imply that the ACD reflects not only inhalational anaesthetics but also CO_2. This causes a dead space effect with the ACD larger than its internal volume. Humidity and sevoflurane attenuates this dead space effect by decreasing CO_2 rebreathing, but a significant effect remains. In patients, the dead space effect was 135 ml higher for the ACD used without sevoflurane compared to the HME, of which 85 ml reflects the CO_2 exchanging capacity of the ACD and 50 ml is due to its larger internal volume. With 0.8% sevoflurane, the dead space effect of the ACD was 88 ml higher than with the HME, of which 38 ml was due to CO_2 exchanging capacity of the ACD. Our test lung results imply that no further reduction of the dead space effect of the ACD should be expected at sevoflurane concentrations providing surgical depth of anaesthesia. These results suggest that when ventilating a patient with a respiratory rate of 16 min^{-1} in order to maintain isocapnia, when switching from an HME to an ACD, tidal volume should be increased by around 140 ml before inhalational anaesthetics are delivered. When sevoflurane is administered with the ACD, a tidal volume increase of 90 ml would be sufficient. In paper I mean difference between $PaCO_2$ values in patients using an HME and ACD was 1.4 kPa at the start of measurements. After 30 minutes of sevoflurane administration with the ACD the difference decreased to 1.1 kPa. This supports our conclusion that sevoflurane reduces the dead space effect of the ACD. The manufacturer's recommended minumum tidal volume of 350 ml may be an underestimation. For detailed recommendations on minimum tidal volume to be used with the ACD further studies seem warrented. The impact of the dead space effect of the ACD using other respiratory rates than 16 min^{-1} in patients was not determined in the present studies. However, data recorded in paper IV makes it possible to calculate the combinations of V_T and respiratory rates which are compatible with maintained CO_2 exchange with the use of an HME, an ACD with and without sevoflurane.

Clinical implications

In brief, the larger dead space effect with an ACD compared to its internal volume increases the tidal volume needed to maintain isocapnia. Lung protective ventilation (LPV) is an issue with particular importance in ARDS. The best documented feature of LPV is the use of low tidal volume ventilation.[85-87] Treatment protocols using low tidal volume ventilation should include increased respiratory rates in order to maintain CO_2 exchange, since so called permissive hypercapnia seems to be associated with significant risk of lung injury.[88] Data for two patients in paper IV of very different build show that with the HME used in this study tidal volumes recommended for LPV would be possible at respiratory rates of about 25 min^{-1}. With an ACD at various sevoflurane concentrations, such tidal volumes cannot be achieved even at a respiratory rate of 40 min^{-1}.

Future perspective

Experience has shown that administration of inhalational anaesthetics to patients in intensive care units has been considerably simplified by the ACD.[59] Available methods for residual gas scavenging appear to be efficient.[89] It is thus possible to use the ACD in an enviromentally acceptable way. This could open up the hitherto specialized area of administration of inhalational anaesthestics to non-anaesthetists. With reference to earlier discussions on administration of anaesthesia (e.g. propfol) and analgesia by non-anaesthetists, one should be concerned regarding minimum qualifications needed for safe use of inhalational anaesthetics in intensive care units. Further research on inhalational sedation in intensive care units is important for this reason too since knowledge of today is based on a modest amount of study data.

Sevoflurane and isoflurane have pre- and postconditioning effects. Sevoflurane may suppress intractable epilepsy and successfully treat status astmaticus. The metabolism and toxicity of sevoflurane and isoflurane are considerably less and the elimination is independent of liver and kidney function compared to commonly used intravenous sedating agents. With the exception of malignant hyperthermia, sevoflurane and isoflurane have no known serious side effects in sedating concentrations. Will inhalational sedation contribute to a better outcome for the severely ill intensive care unit patients? Will the ACD make traditional anaesthesia machines redundant?

Conclusions

1. Wash-in kinetics for sevoflurane delivered by the ACD is similar to a vaporizer. End-tidal sevoflurane tension accurately reflects arterial tension whereas inspired tension may be underestimated using the ACD in humans.

2. At dry conditions at room temperature the ACD contributes with an apparent dead space of 180 ml in excess of its internal volume. This is due to adsorption of CO_2 in the ACD during expiration and return of CO_2 during the following inspiration.

3. In humans, the use of an ACD increases rebreathing of CO_2 and the dead space effect to a greater extent than can be explained by its internal volumes. This is caused by adsorption of CO_2 in the ACD during expiration and release of CO_2 during inspiration. Rebreathing of CO_2 is attenuated by humidity.

4. In humans and in a test lung, CO_2 rebreathing and dead space effect with an ACD are attenuated but not abolished by sevoflurane. The use of an ACD may be impossible if lung protective ventilation is indicated.

Populärvetenskaplig sammanfattning

Anesthetic Conserving Device (AnaConDa®) är ett nytt, kommersiellt tillgängligt, hjälpmedel för att ge narkosgaser. AnaConDa® är en förgasare och återandningsfilter, vilken ansluts till patientens andningstub under operation eller intensivvård. Filtret fungerar med hjälp av kolpartiklar som binder utandade narkosgasmolekyler till sig vilka återandas vid nästa inandning. Vid vanlig narkosgasdosering återanvänds mer än 90% av utandad narkosgas vid nästa inandning. AnaConDa® fungerar dessutom som fuktvärmeväxlare vilka alltid används vid ventilatorbehandling för att minska kroppsvätskeförluster via andningsvägarna. AnaConDa® kan användas med narkosgaserna isofluran och sevofluran. Till skillnad från intravenösa narkosmedel verkar narkosgaserna isofluran och sevofluran minska skadan på hjärtmuskeln i samband med syrebrist (s.k. farmakologisk konditionering). Detta har lett till ökad användning av narkosgaser i samband med hjärtkirurgi före, under och efter ingreppet. En förutsättning för att ge narkosgas har hittills varit tillgång till narkosapparat med förgasare vilka i regel bara finns på operationsavdelningar. AnaConDa®:n har löst de tekniska/praktiska och miljömässiga problemen för att kunna ge narkosgas utanför dessa, såsom inom intensivvård där ventilatorvårdade patienter behöver rogivande läkemedel.

Vi har undersökt hur narkosgas tas upp i blodet hos patienter som ska genomgå en hjärtoperation vid tillförsel via en AnaConDa® jämfört med via en vanlig narkosapparat med förgasare (studie I). Likvärdiga koncentrationer av narkosgasen sevofluran uppmättes i blodet oavsett om gasen tillfördes via förgasare eller AnaConDa®. Det finns mätbara skillnader i volym hos en vanlig fuktvärmeväxlare och den större AnaConDa®. Volymen av det inre av anordningen utgör s.k. skadligt rum varmed avses att gasutbyte med blodet inte sker i denna del av andningssystemet. Det större skadliga rummet hos AnaConDa kompenserades med motsvarande ökning av andetagsvolymen hos de patienter som fick narkosgas via AnaConDa®. Trots kompensation för volymsskillnaden mellan fuktvärmeväxlare och AnaConDa® så fann vi att koldioxidhalten i blodet hos patienter där AnaConDa® använts var högre än förväntat. Hög koldioxidhalt i blodet kan leda till oregelbunden hjärtrytm, förhöjt tryck i skallen och i blodkretsloppet genom lungorna.

AnaConDa®:ns eftertraktade egenskap är återandning och –utnyttjande av narkosgas. I studie II undersökte vi om filtret ger återandning av koldioxid i laboratorieförsök med en 20 liters plastflaska som lungmodell. Under dessa förhållanden gav AnaConDa® filtret en betydande återandning av koldioxid. Varje andetag behövde ökas med ca 180 ml (normalt andetag hos vuxen människa cirka 500 ml) för att bibehålla ursprunglig koldioxidnivå i andningsluften när AnaConDa®:n användes istället för en vanlig fuktvärmeväxlare.

I studie III undersöktes om fukt och värme påverkar AnaConDa®-filtrets återandning av koldioxid. Hos patienter efter hjärtoperation kopplades AnaConDa® in istället för en vanlig fuktvärmeväxlare och storleken på det skadliga rummet och koldioxidåterandningen mättes. När AnaConDa® användes hos patienter uppmättes det skadliga rummet betydligt större än skillnaden i intern volym med en fuktvärmeväxlare. Koldioxid återandades betydligt mer vid AnaConDa- användning (53%) jämfört med vid fuktvärmeväxlare (29%). I laboratorieförsök visades att fukt minskade koldioxidåterandning och storleken på det skadliga rummet. Värmehöjning från rumstemperatur till kroppstemperatur påverkade däremot inte koldioxidåterandning och storleken av det skadliga rummet.

När narkosgasen sevofluran användes i AnaConDa®:n i studie IV minskade såväl återandningen av koldioxid hos hjärtopererade patienter som det skadliga rummet. Den återandade halten koldioxid sjönk ju högre koncentration av sevofluran som användes. Det skadliga rummet uppmättes till 40 ml större än AnaConDa®:s fysiska interna volym vid den högsta använda sevoflurankoncentrationen. I laboratorieförsök visades att koldioxidåterandningen avtog i närvaro av sevofluran och storleken på skadligt rum minskade. Sevofluran minskade således, men tog inte helt bort, koldioxidåterandningen och storleken på skadligt rum vid AnaConDa® användning.

AnaConDa® är ett nytt hjälpmedel för tillförsel av narkosgaserna isofluran och sevofluran till patienter i behov av sedering/sövning både på operation och inom intensivvård. Denna avhandling visar emellertid att inte bara narkosgas reflekteras i AnaConDa®:s filter utan också koldioxid. Detta bör beaktas vid användning av AnaConDa®.

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