

# Inhalation sedation with the 'Anaesthetic Conserving Device' for patients in intensive care units: A literature review

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## Abstract

**Background.** The Anaesthetic Conserving Device is a modified heat and moisture exchanger that enables the application of inhalation sedation with existing ventilators in intensive care units. The following review describes the advantages of inhalation sedation using the Anaesthetic Conserving Device in comparison to standard intravenous sedation for patients in intensive care units and highlights the technical aspects of its functioning.

**Methods.** The literature search was limited to PubMed, Sage Journals and CINAHL databases, using the terms »anaesthetic conserving device«, »volatile anaesthetic reflection filter«, »AnaConDa« independently and in connection with the terms »sedation« and »intensive care unit«. Included are articles published up until December 2014.

**Results.** Use of inhalation sedation with the Anaesthetic Conserving Device enables faster transition to spontaneous breathing and a shorter awakening time than with intravenous sedation. Even short-term inhalation sedation of patients after open heart procedures has a cardioprotective effect and reduces troponin T values. Despite increased concentrations of inorganic fluoride in serum after sevoflurane exposure, no clinical studies to date have shown its nephrotoxic effect, even after long-term (48 h) sedation. The Anaesthetic Conserving Device is accurate in maintaining target values of volatile anaesthetics. However, increased dead space volume was found in several studies, exceeding the internal volume of the Anaesthetic Conserving Device.

**Conclusion.** Results to date show that inhalation sedation with the Anaesthetic Conserving Device may be an effective and safe alternative to existing protocols of intravenous sedation for patients requiring intensive treatment.

**Key words:** anaesthetic conserving device, inhalational sedation, intravenous sedation, intensive care unit

## **Introduction**

Effective sedation and analgesia are indispensable elements of treating patients in intensive care units (ICU) in order to reduce pain, anxiety, and agitation during mechanical ventilation and when other invasive diagnostic and therapeutic interventions are performed. (1,2) Current guidelines for analgesia and sedation of patients in ICU favour the use of intravenous forms of sedation. (3) Propofol and midazolam are the most often used drugs for sedation of critically ill patients; however, the literature highlights numerous adverse effects of such intravenous anaesthetics. (4,5)

Compared to most intravenous anaesthetics, volatile anaesthetics, such as sevoflurane and isoflurane, offer better control of sedation since they do not accumulate or develop tolerance. Emergence times of patients sedated by inhalation are therefore shorter and more predictable than

after intravenous sedation. (6) The end-tidal tension of a volatile anaesthetic accurately reflects arterial partial pressure, providing a precise indicator of the volatile anaesthetics partial pressure and concentration in the central nervous system. (7) Volatile anaesthetics act primarily on the cerebral cortex, depressing the consciousness and have analgesic properties even at low concentrations, while leaving many autonomic functions such as temperature control, blood pressure regulation or respiration undisturbed. (8) In comparison with intravenous anaesthetics, they are mainly excreted via the respiratory system, so only a minor part is metabolised by the liver or kidney. (6) In humans, the metabolism degrades approximately 0.2 % of isoflurane and 2-5 % of sevoflurane. (9) They have a bronchodilatory effect (10) and protective properties on numerous organs (above all cardioprotective and cerebroprotective). (11,12)

Initial attempts at conserving anaesthetic vapours using an open system involved the development of a reflector that incorporated zeolite crystals. (13) However, because of the possibility of zeolite inhalation causing pulmonary toxicity (14), one proposed solution was to use a charcoal filter instead of a zeolite one. (15) The principle of the charcoal filter was further developed, leading to the creation of a device for inhalation sedation AnaConDa™ (Anaesthetic Conserving Device; Sedana Medical, Uppsala, Sweden), which enables sedation and analgesia of patients in ICU with isoflurane and sevoflurane. (16)

The Anaesthetic Conserving Device (ACD, AnaConDa™) is a modified heat and moisture exchanger, which is inserted between the Y-piece of the breathing circuit and the endotracheal tube (ET-tube) (figure 1) and can be used with any type of ICU ventilator (17,18) without a heated humidifier. The ACD contains active lipophilic carbon fibres, which have the capacity to bind 90% of the expired volatile anaesthetic. These are again released with the following inspiratory cycle. Leakage of the anaesthetic into the environment is thus limited and use of the volatile anaesthetic is also more economical and safer for medical personnel. The lost amount of volatile anaesthetic (10%) is replaced by liquid

anaesthetic, which is uninterruptedly supplied to the equipment by a standard syringe pump and then through a miniature evaporator rod vaporises into the breathing gas with which the patient is ventilated. (8,19) A sampling port located on the patient side of the device allows the expired gas concentration to be continuously displayed on the gas monitor (figure 2). (20) Expired gas should be actively or passively scavenged at the gas outlet of the ventilator. (16) Enlund et al. (17) first described its clinical use for anaesthesia, and Sackey et al. (21) reported its safe use for inhalational sedation in ICU patients.

The following review describes the advantages of inhalation sedation using the ACD in comparison to standard intravenous sedation for patients in ICU and highlights the technical aspects of the functioning of the ACD.

## **Methods**

A literature search was conducted using the electronic databases of PubMed, Sage Journals and the Cumulative Index to Nursing & Allied Health Literature (CINAHL) using the following terms: “anaesthetic conserving device”, “volatile anaesthetic reflection filter”, “AnaConDa”; independently and in connection with terms “sedation” and “intensive care unit”. The extract of hits was limited in the databases by the requirements: scientific journals, peer-reviewed articles and entire text. Works that presented protocols of research, letters to the editor and works that dealt with the use of the ACD in the operating room were not included. Thirty-seven articles were found corresponding to the aforementioned criteria and 29 were retained. We additionally excluded four review papers. Twenty-five articles that met the criteria were included in our review. Articles selected for this review were published in English before December 31, 2014.

## **Results**

Twenty-five articles were included in our review, nine of which are

randomised clinical studies (table 1), twelve are prospective observational studies, two case reports and two studies were performed in a laboratory environment (bench study). Most research into the ACD has been done in Sweden (8), France (6) and Germany (5). The number of patients in clinical studies varied from six to 126 patients.

### **Inhalation sedation with the ACD in ICU – Clinical trials**

The majority of clinical studies evaluated the feasibility of inhalation sedation with the ACD and ascertained its advantages over intravenous forms of sedation. They primarily compared the awakening time of patients after sedation, which was assessed as the time from ending sedation to removal of the ET-tube and the time to an appropriate verbal response of the patient. The quality of sedation and awakening was evaluated by assessment of the depth of sedation, stability of the cardiovascular system of patients, the occurrence of delusions and hallucinations, the occurrence of adverse effects, the length of stay in the ICU and in hospital and an assessment of the costs of sedation and analgesia in the ICU. Table 1 presents the main findings of randomised clinical studies that were included in the literature review. The majority of the studies showed that the awakening time of patients sedated with volatile anaesthetic using the ACD was shorter than with intravenous sedation. (21-25) Patients sedated with volatile anaesthetics needed a shorter period of mechanical ventilation, the ET-tube was removed more quickly and cognitive functions normalised faster, irrespective of the length of sedation.

Sackey et al. (21) analysed the influence of prolonged sedation (>12 hrs) on the awakening time of sedated patients. They compared sedation with isoflurane with sedation with midazolam in a heterogeneous group of patients in ICU. The removal of the ET-tube was faster in patients sedated with volatile anaesthetic (isoflurane:  $10 \pm 5$  min) than in patients on intravenous sedation (midazolam:  $252 \pm 271$  min); patients after isoflurane followed simple verbal instructions faster ( $10 \pm 5$  min) than patients after midazolam ( $110 \pm 132$  min). Sevoflurane, because of its

pharmacokinetic properties, provides faster induction and recovery in comparison with isoflurane. Mesnil et al. (22) analysed patients who required sedation >24 hrs and compared inhalation sedation with sevoflurane ( $n=19$ ) with intravenous sedation with propofol ( $n=14$ ) or midazolam ( $n=14$ ). In addition to faster removal of the ET-tube and a shorter awakening time of patients sedated with volatile anaesthetic (sevoflurane:  $33.6 \pm 13.1$  and  $18.6 \pm 11.8$  min) in comparison with the other two groups on intravenous sedation (propofol:  $326.11 \pm 360.2$  and  $91.3 \pm 35.2$  min; midazolam:  $599.6 \pm 586.6$  and  $260.2 \pm 150.2$  min), the authors also found a better quality of awakening. Patients were less agitated and had fewer hallucinations. Studies that dealt with short-term sedation (<12 hrs) showed similar findings. (23,24)

It is difficult to achieve a suitable depth of sedation with some patients in ICU using standard protocols of intravenous sedation, so higher doses of drugs or their combination are required. This can lead to over-deep sedation of patients and/or haemodynamic instability. L'her et al. (26) found that in the case of patients that needed higher doses of midazolam than the average ( $> 0.05$  mg/kg/h) in the first 24 hrs, an appropriate depth of sedation was achieved faster under inhalational sedation with isoflurane. The same authors also showed a lower use of analgesics (sufentanil) in the case of inhalation sedation. A similar opioid sparing effect of isoflurane was demonstrated in the study by Sackey et al. (21) Mesnil et al. (22) found that the use of opioid analgesics in the period of 24 hrs after removal of the ET-tube was lower in the group of patients on inhalation sedation with sevoflurane than in the group that was on intravenous sedation with propofol or midazolam. Furthermore, the last recorded pain scores were significantly lower in the group on inhalation sedation.

The occurrence of adverse effects, such as arrhythmia, diarrhoea, nausea, vomiting and insufficient respiratory function in patients on inhalation sedation using the ACD has also been investigated and compared with intravenous forms of sedation. (21,22,24) Significant differences in the occurrence of the aforementioned adverse effects between the two forms of sedation were not established. Studies similarly did not demonstrate

statistically significant differences between intravenous and inhalation forms of sedation in the functioning of the circulatory system, liver and kidneys. (23,24,26,27)

Some concerns still remain about the nephrotoxicity of volatile anaesthetics because of the formation of fluoride ions. (21,25) Three studies (22,25,28) ascertained the values of inorganic fluoride in serum with patients sedated with sevoflurane. Despite increased concentrations of inorganic fluoride in serum after sevoflurane exposure, glomerular and tubular renal integrity were preserved in the patients throughout the hospital stay. Furthermore, Perbet et al. (28) demonstrated that following 48 hrs of inhalational sevoflurane sedation using the ACD, washout of sevoflurane was rapid. Marcos-Vidal et al. (29) similarly did not find any differences in creatinine levels in the serum of patients who were sedated after cardiac operations with sevoflurane or propofol. Similar results in relation to the effect of inhalation sedation on renal function have also been shown for isoflurane. (21)

Volatile anaesthetics cause a widening of the brain blood vessels, which in turn increases cerebral blood volume and intracranial pressure (ICP). Bösel et al. (30) analysed the effects of isoflurane on cerebral parameters in neuromonitored ICU stroke patients and showed that it is possible to reach sufficient sedation levels in cerebrovascular ICU patients by applying isoflurane long-term (mean 3.5 days), without a corresponding increase in ICP, if baseline values of ICP are low to moderately elevated. Although ICP values were increased by 2.1 mmHg in the first hour after the transition of patients from an intravenous (with midazolam or propofol) to an inhalation form of sedation, these remained stable during the period of observation. However, after transition to inhalation sedation, a fall in mean arterial pressure and, consequently, cerebral perfusion pressure, was observed in patients, which required the additional use of vasopressors. They therefore propose the mandatory use of extended neuromonitoring of cerebrovascular ICU patients when sedated with volatile anaesthetics. Furthermore, Villa et al. (31) found that isoflurane increases regional cerebral blood flow in comparison to propofol in patients with severe subarachnoid haemorrhage, but the ICP

values did not change significantly between the two forms of sedation. The study only included patients (n=13) with normal (<18 mmHg) and untreated ICP.

Some studies (29,32,33) have assessed whether the administration of volatile anaesthetics during the post-operative period has beneficial effects on markers of myocardial injury. Steurer et al. (32) found significantly lower values of serum troponin T in a group of patients sedated with sevoflurane (2 hrs) than in a propofol group. Studies by Marcos-Vidal et al. (29) and Hellström et al. (33) also confirmed that late postconditioning with sevoflurane might mediate cardiac protection.

Case reports on the use of the ACD in paediatric ICU are also worth mentioning. Jung et al. (34) reported the use of sevoflurane with the ACD for the sedation of a 30-month old girl with extensive burns. Sackey et al. (35) described long-term sedation with isoflurane with three children in paediatric ICU. In order to minimize the dead space of the ACD (100 mL) and avoid high end-tidal CO<sub>2</sub> concentrations in children (weighing less than 30 kg), they inserted the ACD in the inspiratory limb of the breathing circuit. Recirculation of the anaesthetic gas is deliberately avoided, in a manner requiring a higher infusion rate in order to maintain the desired concentration of anaesthetic vapour.

The economic aspect of the use of inhalation sedation with the ACD is also important. Sackey et al. (36) demonstrated a 75 % lower consumption of volatile anaesthetic with the ACD using high-flow ventilators in comparison with sedation via standard vaporizers. Two studies (24,26) compared the costs of intravenous and inhalation sedation using the ACD. L'her et al. (26) found that inhalation sedation with isoflurane was less expensive (midazolam: 218 ± 111 EUR; isoflurane: 110 ± 19 EUR) than average with patients who needed higher doses of midazolam for achieving a suitable depth of sedation. However, Röhm et al. (24) stated higher daily costs of sedation (including device-related equipment) in the case of inhalation sedation (sevoflurane: 65.49 ± 10.52 EUR; propofol: 13.38 ± 5.91 EUR per patient). However, no study has been based on an exact economic analysis and taken into



account the indirect costs of treatment in ICU, since Röhms et al. (24,25) showed that patients sedated with volatile anaesthetics have a shorter ICU and hospital stay.

### **Technical aspects of inhalation sedation with the ACD**

Some studies have focused on the technical aspects of the ACD, such as the effect of ventilation parameters on ACD performance, the influence of its internal volume (volume of the dead space) on the patient`s mechanical ventilation and the level of ambient pollution with volatile anaesthetics when using the ACD.

Belda et al. (37) demonstrated a high precision of the ACD in maintaining target concentrations of volatile anaesthetic (1.0 vol% and 1.5 vol%) in ICU patients, with the use of a simplified pharmacokinetic model for manually adjusted infusion of liquid sevoflurane. Berton et al. (38) highlighted that ventilation settings (respiratory rate and especially tidal volume) influence the vapour output of the ACD. The expired volatile anaesthetic fraction decreased when the tidal volume increased at a constant infusion flow rate of anaesthetic agent. The influence of respiratory minute volume on the performance of the ACD was also confirmed by Meiser et al. (20) They found that the ACD is accurate in maintaining target values of volatile anaesthetics as long as its reflecting capacity is not exceeded (10 mL of anaesthetic vapour contained in one expired breath; e.g., 1 vol% in 1000 mL or 2 vol% in 500 mL, etc.). An increased minute ventilation therefore necessitates an increased infusion rate in order to keep the desired concentration of volatile anaesthetic in the breathing circuit.

Elevated arterial CO<sub>2</sub> tension (PaCO<sub>2</sub>) has been observed in patients when using the ACD, despite tidal volume compensation. (24,27) The ACD has an internal volume of approximately 100 mL, which additionally increases the anatomical dead space in a ventilated patient. Stureson et al. (39) argue that use of the ACD increases the apparent dead space to a greater extent than can be explained by its internal

volume. In fact, they demonstrated that the ACD adsorbs exhaled CO<sub>2</sub>, which is returned during the next inhalation cycle, creating an additional apparent dead space. In further studies, the same authors found that the humidity of the gas exhaled by the patient (40) and the presence of volatile anaesthetic in the breathing circuit (41) reduce the rebreathing of CO<sub>2</sub>, although it is still present. A study on patients sedated with sevoflurane using the ACD showed an 88 mL larger apparent dead space than with a conventional heat and moisture exchanger (50 mL due to the larger internal volume of the ACD and 38 mL due to the rebreathing of CO<sub>2</sub>). (41) A larger apparent dead space could be significant in patients with pathological states connected with inefficient oxygen and CO<sub>2</sub> exchange, such as patients with acute respiratory distress syndrome (ARDS), since lung protective ventilation with low tidal volumes is recommended for them. (27,40) Calculations by Sturesson et al. (41) showed that with use of the ACD, it may be difficult to maintain normocapnia in patients with tidal volume <6 mL/kg, even when the respiratory rate is increased. A recent study by Chabanne et al. (42) showed that use of the ACD in ICU patients worsens ventilatory parameters, with significant increases in the work of breathing, minute ventilation, intrinsic positive end-expiratory pressure and inspiratory pressure swings. Sevoflurane use via the ACD (for a light-sedation target) normalizes respiratory parameters, so it might be an alternative method for sedation in ICU patients, at least during the weaning process with pressure-support ventilation.

Various studies have ascertained environmental pollution with volatile anaesthetics using the ACD, since central gas scavenging systems are rare in ICU. (18) In the European Union, the upper exposure limit for isoflurane in the workplace is 50 ppm per hour. (43) Studies in ICU have shown that, with the use of scavenging systems (either active or passive), values of volatile anaesthetics remain below the aforementioned permitted limit when they are administered with the ACD. (18,26,36) Some studies (36,44) have also shown that adequate room air exchanges per hour without using any form of gas scavenging maintains

environmental pollution within permitted limits. Djafari Marbini et al. (44) measured the ambient levels of isoflurane <2 ppm in the vicinity of a patient's head and the predicted nursing area with ten room air exchanges per hour. Stackey et al. (36) looked at ambient isoflurane pollution utilizing active scavenging and four room air exchanges per hour, in 15 patients during ICU sedation for 12 – 96 hrs. Five patients in this study had no active scavenging and relied on room air exchanges alone. The mean levels of isoflurane pollution were <0.5 ppm in all patients. Despite the fact that studies show low environmental pollution with volatile anaesthetics using the ACD, these are based on small samples and a low number of measurements. Similarly, the conditions under which pollution with gas anaesthetics was measured were various. This aspect of the use of the ACD must therefore be additionally studied.

## Discussion

The clinical use of inhalation sedation in ICU was described in the late 1980s for patients with bronchial asthma and patients with drug abuse or addiction syndromes, since in such cases a combination of a variety of hypnotics and analgesics are required for adequate analgosedation. (19) With the arrival of the ACD on the market, inhalation sedation in ICU has been increasingly established in various countries of the European Union and Canada. (18,20,22,23) Research to date has shown that the use of inhalation sedation with the ACD in ICU is simple and safe for both patients and staff. (26,27,37)

The literature included in the review shows that use of inhalation sedation enables faster transition to spontaneous breathing and removal of the ET-tube and a shorter awakening time of patients than with intravenous sedation. (21-23) In addition, patients sedated with volatile anaesthetics need less analgesics (22,26) and the hospital stay is shorter. (24,25) Even short-term inhalation sedation of patients after cardiac operations has a cardioprotective effect and reduces values of troponin T. (29,32) Similarly, inhalation sedation using the ACD enables direct control of the concentration of volatile anaesthetic in the breathing

circuit, so the depth of sedation of a patient can be easily monitored and titrated. (21,33)

Jackson et al. (45) reported that 33 % to 57 % of patients in ICU do not receive appropriate drugs and doses that enable suitable analgesia and depth of sedation. Too-deep sedation and analgesia prolongs the need for mechanical ventilation and increases the risk of occurrence of pneumonia and sepsis, (46) increases the risk of haemodynamic instability, which can prolong the ICU stay and increase the mortality of patients. (1) Too-shallow sedation and analgesia can cause fear, pain, stress and anxiety, which increase the level of endogenous catecholamines, increase the metabolism and use of oxygen, arterial pressure and incidence of tachyarrhythmia, which can cause additional complications in the treatment of a critically ill patient. (47)

Although only a minor percentage of isoflurane and sevoflurane is metabolised by the kidneys because of the formation of fluoride ions, concerns about their nephrotoxicity are still present. Plasma fluoride concentrations exceeding 50  $\mu\text{mol/L}$  and the risk of kidney injury have been described with methoxyflurane. (48) Several studies have found elevated values of inorganic fluoride more than 50 or 100  $\mu\text{mol/L}$ . (22,25,28) However, despite increased concentrations of inorganic fluoride in serum after sevoflurane exposure, glomerular and tubular renal integrity were preserved in patients (22,25) even after long-term sedation with sevoflurane. (28) Two factors may explain these differences between methoxyflurane and sevoflurane: a) it is not the peak serum fluoride concentration but the duration of the systemic fluoride that is important. Sevoflurane is less soluble than methoxyflurane in blood and tissues; sevoflurane thus exits the body much more rapidly; and b) the liver is the primary organ of metabolism of sevoflurane, whereas both the liver and kidney metabolize methoxyflurane. (49) The high local (intrarenal) production of fluoride ions from methoxyflurane probably explains the greater capacity of that anaesthetic to produce renal injury from fluoride production. This is in agreement with several studies in which no differences in creatinine levels in the serum of patients who were sedated with sevoflurane, propofol or isoflurane were

reported. (21,29)

Despite the large number of studies investigating the use of inhalation sedation with the ACD in adult patients, almost no research has been carried out on the use of inhalation sedation in critically ill children. It is well known that optimal sedation in critically ill children is often difficult to achieve due to the altered pharmacokinetics and dynamics in children. Tolerance and withdrawal after long-term benzodiazepine use in paediatric ICU has been described. (50) Furthermore, some studies have shown the clinical usefulness of volatile anaesthetics for sedation in children. (51,52) To date, only a few case reports have described inhalation sedation with ACD in paediatric ICU with encouraging results (34,35), and further evaluation of the usefulness of this method of sedation for paediatric patients is still needed.

In adult patients without pulmonary pathology, the additional dead space of the ACD can be considered clinically unimportant, although some studies have identified increased values of PaCO<sub>2</sub> in patients. (24,27) Values of PaCO<sub>2</sub> were therefore balanced with higher tidal volumes and/or respiratory rates. Stureson et al. (41) demonstrated that, with the use of the ACD, normocapnia may be difficult to maintain when using a low tidal volume, even when the respiratory rate is increased. This might limit the usefulness of ACD in clinical settings. In fact, lung protective ventilation (mechanical ventilation with low respiratory volumes, ≤ 6 mL/kg), is of key importance and an integral part of treatment of patients with ARDS. (53) However, hypercapnia is a central component of current protective ventilatory strategies. Increasing clinical evidence supports the use of permissive hypercapnia, particularly in acute lung injury/ARDS, status asthmaticus, chronic obstructive pulmonary disease and neonatal respiratory failure, in order to avoid the deleterious effects of high lung stretch. (54) Additionally, with inhalational sedation, spontaneous breathing can be maintained and, if necessary, may be augmented by various ventilator modes. (8,42) Although some authors (27,41) argue that the use of the ACD might not be appropriate for patients with respiratory diseases with increased

physiological dead space and/or ventilation difficulties, there are still no clear guidelines or research in this field. According to the manufacturer's instructions, the use of the ACD is advised only in patients with a tidal volume >350 mL. (8)

## Conclusion

Because of their pharmacokinetic properties, use of volatile anaesthetics with ICU patients is becoming increasingly interesting, especially for some groups of critically ill patients. With the arrival of the ACD, their use in ICU has finally become available. However, the number of prospective randomised clinical studies investigating the effectiveness and safety of inhalation sedation of ICU patients using the ACD is relatively small. We also highlighted some issues that are still unclear (the influence of the ACD dead space on patient ventilation, gas scavenging, the cost of inhalation sedation with ACD etc.) and need to be additionally explored. Otherwise, the results to date show that inhalation sedation with the ACD can be a useful alternative to existing protocols of intravenous sedation of patients requiring intensive treatment.

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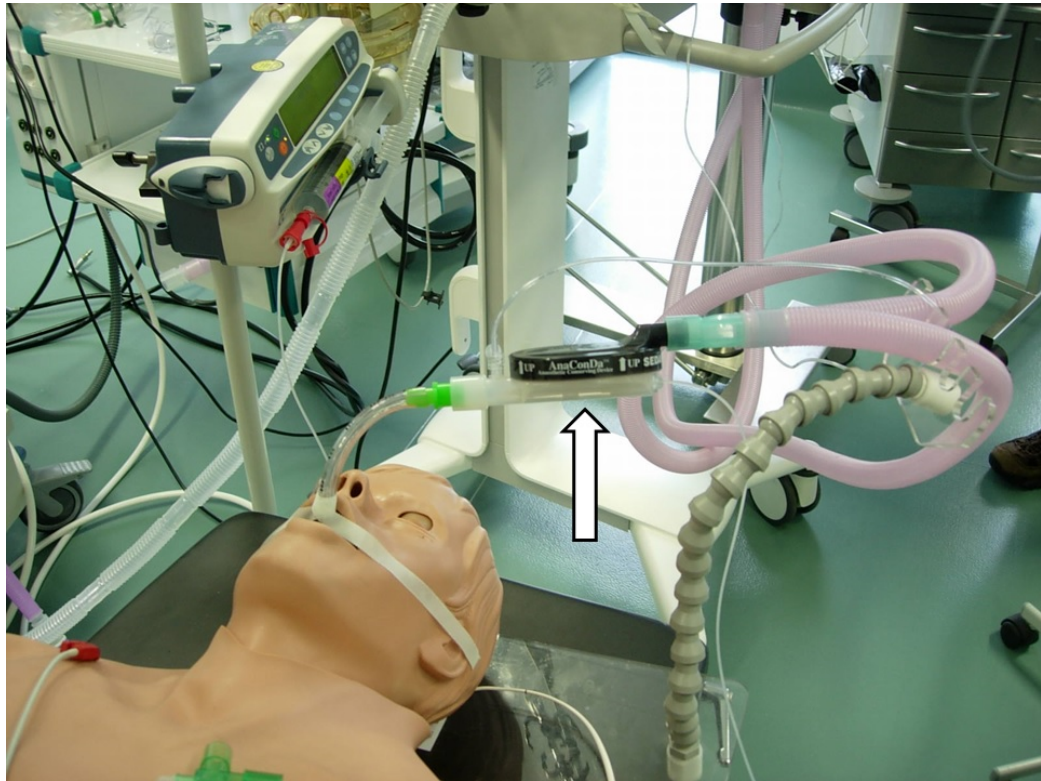
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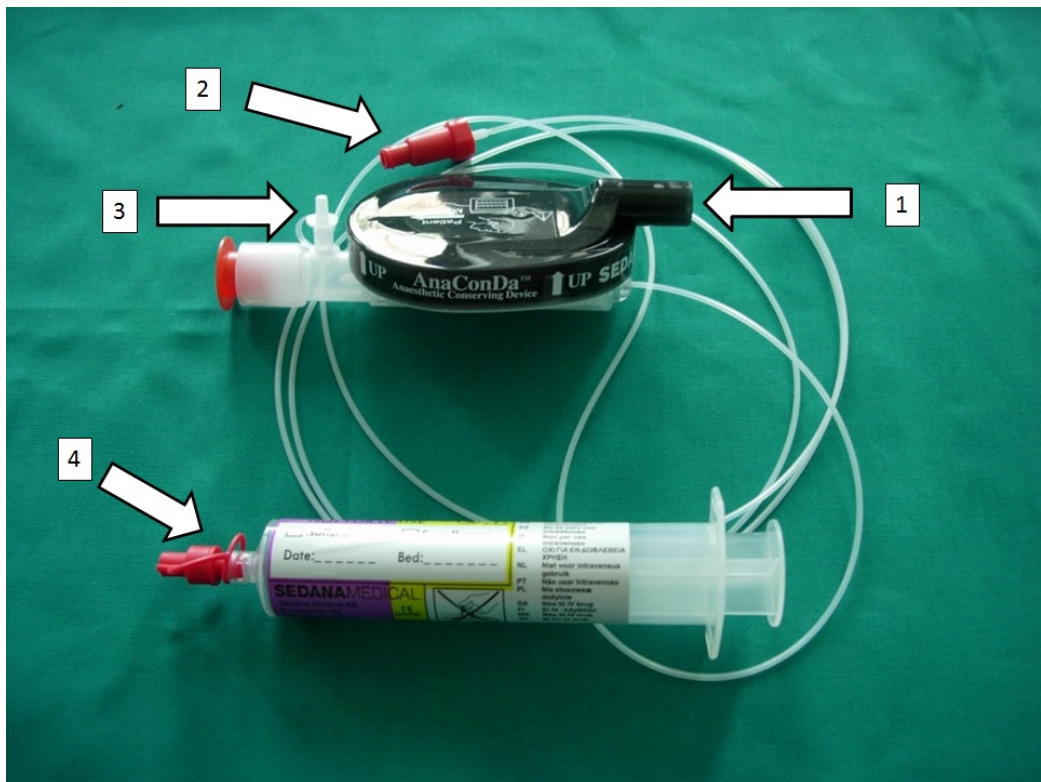
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**Figure 1.** Connection of the AnaConDa (arrow) to the ventilator circuit on high-fidelity simulator.



**Figure 2.** AnaConDa system components: 1 AnaConDa device, 2 Agent

supply line with valve and screw cap, 3 Gas measurement port, 4 AnaConDa syringe with screw coupling and screw cap.

**Table 1.** Randomised clinical studies of inhalation sedation using the ACD in ICU patients.

<b>Authors/year</b>	<b>Number of patients (n) and cause of sedation in ICU</b>	<b>Comparable anaesthetics</b>	<b>Duration of sedation</b>	<b>Established advantages of inhalation sedation with ACD</b>
Sackey et al., 2004 (21)	n=40; heterogeneous pathology (respiratory failure, respiratory obstruction, sepsis, trauma etc.)	I/M	Sedation >12 hrs	– time of awakening significantly shorter (faster removal of ET-tube, faster capacity to follow verbal instructions)
Belda et al., 2008 (37)	n=50; patients after major surgical operations	S target conc. 1.0 vol% and 1.5 vol%	6 hrs after operation	– excellent precision of ACD in delivering volatile anaesthetic within 6 hours
Röhm et al., 2008 (24)	n=70; patients after cardiothoracic operations (coronary artery	S/P	Short-term sedation (<12 hrs)	– shorter recovery after sedation (faster removal of ET-tube, faster capacity to follow verbal instructions)

	bypass)			– shorter ICU and hospital stay
				– shorter mechanical ventilation of patients
				– shorter time of hospital stay
Röhm et al., 2009 (25)	n=125; patients after major abdominal, vascular and thoracic operations	S/P	Sedation up to 24 hrs	– despite increased values of inorganic fluorides, renal function was preserved during the time of treatment
				– shorter time of wakening and faster removal of the ET-tube
Mesnil et al., 2011 (22)	n=60; heterogeneous pathology (trauma, pneumonia, sepsis, acute respiratory failure etc.)	S/P and M	Sedation >24 hrs (or < 96 hrs)	– lower use of analgesics (in 24 hrs after extubation)
				– fewer post-sedation hallucinatio

				n episodes
Hellström et al., 2011 (33)	n=100; patients after coronary artery bypass graft surgery	S/P	Min 2 hours	– <i>post hoc</i> analysis showed significantly lower values of cTnT for the period of 12 hours after the operation
Hellström et al., 2012 (23)	n=100; patients after coronary artery bypass graft surgery	S/P	Min 2 hours	– faster removal of ET-tube – faster verbal response of patient
Steurer et al., 2012 (32)	n=117; patients after heart surgery	S/P	Sedation $\geq$ 4 hours	– troponin T values significantly lower on the first day after operation
Marcos-Vidal et al., 2014 (29)	n=126; patients after heart surgery	S/P	Min 3 hours	– troponin T values significantly lower 12 and 48 hours after surgery – no differences between groups in creatinine levels before

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ACD, AnaConDa; ET-tube, endotracheal tube; I, isoflurane; ICU, intensive care unit; M, midazolam; min, minimum; P, propofol; S, sevoflurane.

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