UniversitätsKlinikum Heidelberg

Interdisciplinary Symposium for physicians, nursing staff and all other interested parties

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The AnaConDaY – Inhalation sedation in the Intensive Care Unit (ICU)

Volatile anaesthetics in the ICU – From the insiders' tip to an established alternative?

About ten years back the first experiences were made with the AnaConDa® to perform inhalation sedation. AnaConDa® is the first and unique system that allows inhalation sedation outside of the operating theatre. The AnaConDa® is easily inserted between the ET-tube and the circuit, and enables delivery of volatile anaesthetics via a syringe pump with a standard ventilator and a gas monitor. The first fields of application were limited to bridging short periods of time between end/termination of surgery and extubation as well as last resort treatment of status asthmaticus. Since then the use of the AnaConDa® for inhalation sedation with Isoflurane and Sevoflurane (still: off-label use in the ICU) has significantly developed further. The dissemination of this technique across areas of medical expertise and borders have been followed by systematical studies regarding safety, recovery and extubation times, relevance of accumulation of metabolites, and long-term sedation over several days. These studies have established a basis for the AnaConDa® as an alternative sedational concept. The AnaConDa® is currently being used in Germany in more than 100 intensive care units with an increasing trend. The implementation of inhalation sedation concept into the S3-guidelines for inhalation sedation in 2010 is trend-setting.

Volatile anaesthetics have not only the obvious advantages in the daily clinical use like providing potent sedation, good controllability, minor accumulation, fast on/off-effect, low consumption, savings on analgesics and uncomplicated patient transport. Exiting is the intensive care and longer term use based on the multitude of experimental and planned clinical studies about organ protection especially regarding lungs, heart and brain.

The latter has brought us to start using inhalation sedation in the ICU in our Neurosurgical Center in Heidelberg. There are some specific considerations beside the common intensive care problems to be made for patients with especially cerebrovascular brain damages like cerebral perfusion pressure and blood flow at impaired autoregulation, increase of the intracranial pressure, epileptic disposition and risk of delirium. The need to mechanically ventilate or analgosedate patients with a severe stroke or cerebral haemorrhage deteriorates considerably the prognosis. To alleviate this it would be highly desirable when administering substances through the ventilator circuit and crossing the blood brain barrier to have neuroprotective properties. However, before using such a substance the following areas should be monitored closely: safety issues, effects on cerebral blood flow, oxygenation and especially the intracranial pressure. The reason behind this is a possible increase of intracranial pressure induced by volatile anaesthetics. At the moment our centre is conducting a surveillance study to monitor effects using multi-modal invasive and non-invasive methods.

Whereas the target organ of analgosedation is the brain it is not just neurologists that have shown interest in this special topic in the past. To point a way to develop this technique further, we felt that we needed to initiate a symposium that brings together users from all areas to collate valuable information around a new and innovative method. We were pleased to see that so many AnaConDa®- experts from different medical areas have accepted our invitation and contributed significantly with their scientific expertise and their long-term experience in using the device to make this symposium a success. Topics such as organprotection, technical aspects, long-term usage and side effects as well as the treatment of special ICU indications were presented in lectures and in practical workshops. This symposium has been a great enrichment for us as organizers hopefully as well for all other participants from the medical and nursing area, we would like to thank all supporters and look forward to be working together with you in the future.

Dr. Julian Bösel
Senior Physician Neurology, Heidelberg

Prof. Dr. Thorsten Steiner
Assistant Medical Director Neurology, Heidelberg

Neurological Intensive Care Unit, University Hospital Heidelberg

Organprotection with the volatile anaesthetics Isoflurane and Sevoflurane

Prof. Dr. Franz Kehl, MD
Medical Center for Anaesthesia and Intensive Care Medicine, Hospital Karlsruhe

Volatile anaesthetics are the centerpiece of anaesthesia. Next to its main effect, sedation, Isoflurane, Sevoflurane and Desflurane have organ-protective side effects: Preconditioning with these substances reduces ischaemic damages of heart, brain, kidneys and lung, stated **Prof. Dr. Franz Kehl, MD, from the Hospital in Karlsruhe.**

A paradoxical intervention, which means preconditioning by one or more ischaemic episodes, increases the resistance towards longer lasting ischaemia occuring in the future. The hypoxic damage is lower than without pre-conditioning. Prof. Kehl's deciding argument to use volatile anaesthetics (VA) in his ICU was that VA without ischaemic induction demonstrate a similar organ-protective effect. Additionally the introduction of the AnaConDa® in 2004 enabled administration of volatile anaesthetics outside of the operational theatre in a safe and simple way.

The cardio-protective effect of preconditioning was first demonstrated with 0.25 – 1.25 MAC Isoflurane in dogs[1]. Already subanaesthetic concentrations (0.25 MAC) were able to reduce the size of the infarct significantly after 60 minutes of coronary occlusion. It was also a dose-effect relationship observed between a collateral coronary blood flow and the amount of volatile anaesthetic administered. The more anaesthetic that was directed to the ischaemic myocard, the better the circulation. Also post-conditioning in the early reperfusion period seems to protect the myocard: Sevoflurane and Desflurane were able to reduce the myocardial reperfusion damage 30 minutes after coronary occlusion in rabbits significantly in comparison to the animal control group.[2]

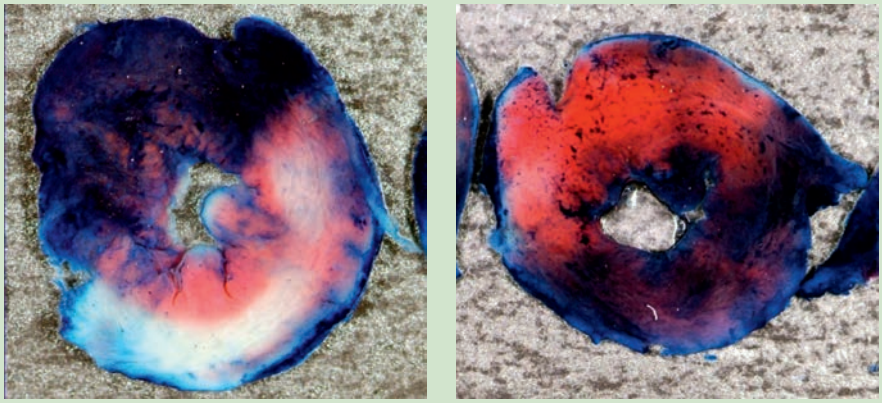

Figure 1. Anaesthetic-induced preconditioning of hearts in mice. The size of the infarct (white areas) is reduced significantly when comparing the untreated control group (left) with the treated group (right).

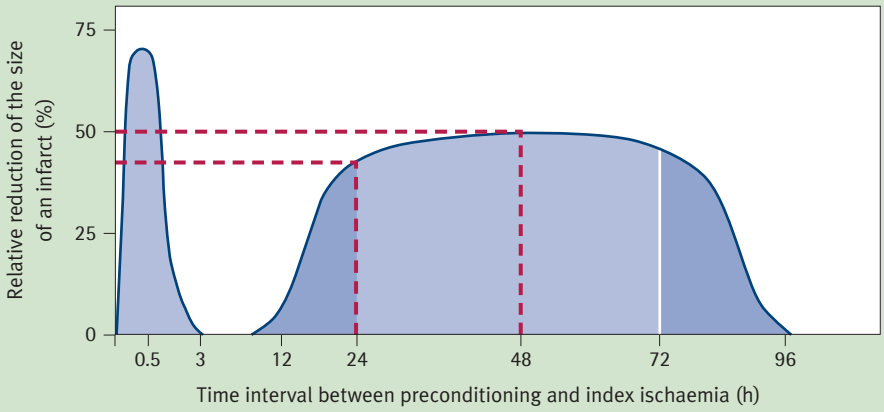

Figure 2. Two-phase cardioprotection: There are two protection phases after preconditioning (immediate and delayed protection) and a gap (no protection) between 3rd hour and 12th hour.

No ischaemic protection between 3rd and 12th Hour

The cardioprotective effect of volatile anaesthetics can be divided into two phases. The myocard is protected directly after the preconditioning for around 3 hours, followed by a gap of around 9 hours and then the second protection phase starts and lasts up to approximately the 96th hour. (fig.2). Volatile anaesthetics are effective if administered before as well as after the ischemic period up to the time of reperfusion (postconditioning). During the ischemic period there is no protective effect. Even with a combination of pre- and post-conditioning the protective effect will not be greater than with using one of them i.e. a complete anaesthesia from the first incision to the closure of the wound will not increase the protective effect.

Inhaled anaesthetics are protective not only through the activation of sarkolemm receptors. As opposite to opioids, which only have a superficial contact to the sarkolemm, the lipophilic volatile anaesthetics pass through the cell membrane and activate intracellular ATP- regulated potassium channels of the mitochondrion. Signals are being transferred from the sarkolemn to the mitochondria through a complex cascade. The opening of the mitochondrial potassium channels prevent the cell death because the cell is able to sustain the APT-level despite ischaemia and reperfusion and therefore no signals inducing apoptosis are being sent.

Neuroprotection: More pyramidal cells survive

Prof. Kehl demonstrated a substantial dosage-related hypoxia protection with Sevoflurane in hippocampal slices of rats[3]. Under controlled conditions 50% of the CA1-pyramidal cells survived a 13 minutes lasting ischaemia, whereby 70% of these cells survived with a preconditioning of 3.0 MAC Sevoflurane. It was also shown in a fluorescence image that Sevoflurane reduces the membrane potential of mitochondria[4]. Furthermore there was a neuroprotective effect in window one and two in rats with cardiac arrest[5]. When controlling a nucleous pycnosis in the CA1 region confirming cell death by histological examination the effects on the brain on the preconditioned animals were comparable to the control group. The cardioprotective effect of Sevoflurane was also demonstrated by the detection of less pronounced increase of troponin. Another finding was that anaesthetized patients with volatile anaesthetics needed less catecholamines than Propofol-patients. A metaanalysis of coronary bypass operations concluded, that volatile anaesthetics were able to increase the cardiac index and to reduce the length of time on mechanical ventilation[7]. ■

Experiences after six years of inhalation sedation

Prof. Dr. Weber, MD
Medical Center for Anaesthesia and Intensive Care Medicine, Ruhr-University, Bochum

In the Hospital of the Ruhr-University in Bochum inhalation sedation with the AnaConDa® has become standard. This technique using especially Isoflurane as the number one gas proved successful against all odds in the beginning. With an early integration of nursing staff in a new weaning-concept, it was possible to break down the barriers, stated the head of the department **Prof. Dr. Weber.**

Isoflurane and Sevoflurane are suitable for inhalation sedation as well as Desflurane with its convincing pharmacological features. However, the low boiling temperature of Desflurane (23.5° C) makes it unsuitable for administration via the AnaConDa®.

Technique: The AnaConDa® saves gas

A syringe pump supplies the mini-vaporizer on the AnaConDa with the volatile anaesthetic. The conserving medium in the AnaConDa® reflects more than 90 % of the exhaled gas which is available at the next inhalation. Only carbon dioxide is passing through the filter. This enables low agent consumption. The actual consumption is dependent on the minute volume where more gas is lost at higher minute volume leading to a lower gas concentration. In extreme situations patients could wake up told Prof. Weber. This design increases safety and could prevent overdosage.

Gaining acceptance through active communication

A key success factor for inhalation sedation is the acceptance of hospital staff. New techniques like inhalation sedation need to be explained properly when being introduced into clinical routine. All objections should be discussed at large, otherwise when people get tired they easily blame the gas.

A closed scavenging system of the waste gas is recommended but if that is not technically feasible then a passive filter system can be used. Volatile anaesthetics have advantages for the personnel: It is more difficult to control the sedation depth when using IV sedation and many patients become tolerant to the drugs.

Prof. Weber has together with his nursing team developed and in routine implemented to 90 % an interdisciplinary anaesthetic gas – weaning concept. The involvement of nurses is important since they have the most frequent contacts with patients and are routinely controlling vital signs parameters.

Weaning philosophy: Switch between Training mode and Recovery mode

The term Anaesthetic gas – weaning concept carries fundamentally different procedures than with Propofol sedation. In Bochum we switch between Training mode based on hard measurable individual parameters and Recovery mode. This proce-

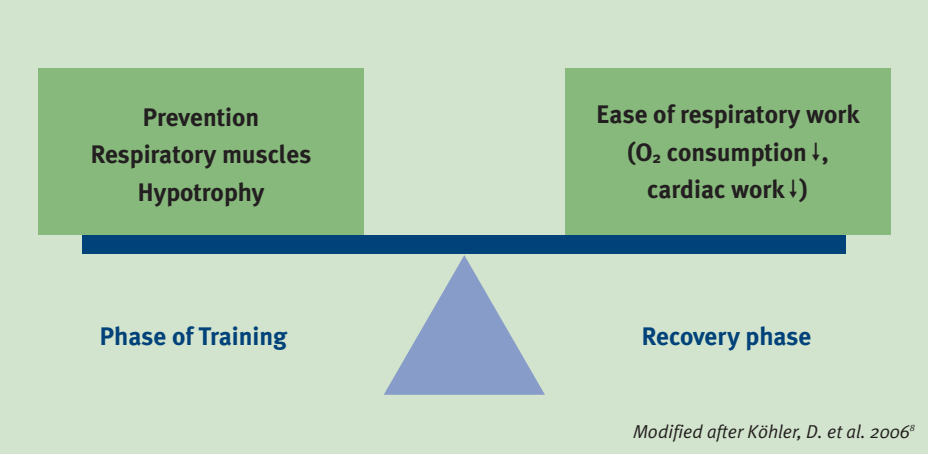

Figure 3: A switch between a phase of training (left) and a recovery phase (right) is the key for a successful ventilation regimen. If possible each patient should be breathing spontaneously for a few hours per day.

dure is mandatory because the diaphragm of ventilated patients becomes hypertrophic after a few days and patients lose the ability to breathe spontaneously. Spontaneous breathing is not always desired. Although the blood flow in the diaphragm is increasing it leads to reduced blood flow in many other organs. If there is no complete Recovery phase without spontaneous breathing in between the increased workload leads to exhaustion of the respiratory system in especially peri-operative patients with trauma, sepsis and patients with reduced lung function (COPD).

Carbon dioxide is the most important marker to assess the function of the respiratory system. Mechanically ventilated critically ill patients that are permanently in a phase of training will not be able to exhale carbon dioxide any more. Recovery phases with a controlled ventilation phase are reducing the risk and lower the carbon dioxide load explained Prof. Weber as the physiological mechanism.

Better outcome with inhalation sedation/ventilation

The outcome of a retrospective analysis conducted in Bochum in 2005 with 61 patients mechanically ventilated for more than 96 hours was clearly in favour of inhalation sedation. Despite the fact that the patients in the inhalational group had a tendency to be sicker than the patients in the iv.-sedation group, the survival rate was significantly higher in the inhalation group with 58% vs. 27% in the iv.-group. ■

Inhalation Sedation – Today's trend, tomorrow's standard

PD Dr. med. Kerstin Röhm
Department of Anaesthesia and Surgical Intensive Care, Klinikum Ludwigshafen

Volatile anaesthetics facilitate superior quality of sedation, realtime monitoring of the depth of sedation, short periods of wakening and extubation, good haemodynamic stability, and a low rate of side effects – that was the bottom line of the presentation made by **PD Dr. Kerstin Röhm from the department of anaesthesia and surgical intensive care at Klinikum Ludwigshafen.** The colleague from Rhineland-Palatinate is convinced that inhalation sedation is not a short term trend but will develop further into a fixed routine.

The first case report on inhalation sedation was about a patient whose epileptic state had been treated by this procedure as a last resort therapy. This was published in 1985[9], and further publications followed. But in view of the lack of suitable equipment at intensive care units, the technique could not be developed until the launch of AnaConDa® reversed the trend. AnaConDa® does not only simplify ventilation, its technique of storing the exhaled gas and reusing it on inspiration also makes it more economic.

Inhalation sedation allows for rapid awakening

In 2004, the first randomised study involving AnaConDa® showed that patients having undergone isoflurane sedation for 12 to 96 hours were able to follow commands substantially sooner than patients sedated with midazolam[10]. Patients were arousable without any problems within 10 to 15 minutes, whereas time to extubation after midazolam sedation was 100 minutes on average. Also after cardiac surgery, sedation with isoflurane permitted earlier extubation, and commands were followed after a shorter period of time, compared to midazolam[11]. Sedation by isoflurane offers a very high quality, its titration is simple, and haemodynamics are stable.

Dr. Röhm presented a study conducted by her own working group to compare sevoflurane (AnaConDa® end-tidal 0.5 – 1 % v/v) versus propofol (2 %, 5 – 7 mL/h, 2 – 4 mg/kg/h) in 70 patients undergoing cardiac surgery. The mean age of the patients was 65 years, and showing appropriate ejection fraction[12]. The AnaConDa® device was inserted between the endotracheal tube and the Y-piece, and the perfusor line flooded with a bolus of 1.2 – 1.5 mL. Since the patients were coming deeply anaesthetized from the anaesthesia department the sedation started on a low perfusion rate of about 2mL/h and an endtidal concentrations of 0,5 % v/v (see figure 4). The necessary dose was ad-

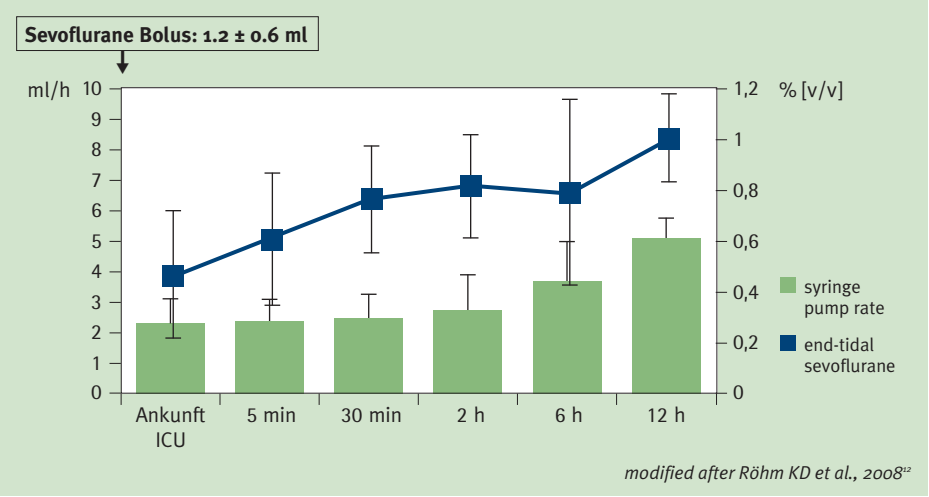

Figure 4: Dosing sevoflurane via AnaConDa® in patients undergoing cardiac surgery in Ludwigshafen

justed over time to the predetermined sedation score (RASS-3) and demanded in the end 4,5 – 5 ml/h leading to an endtidal sevoflurane concentration of 1,0 Vol% (0,5 MAC)

Patients on cardiac surgery benefit from AnaConDa®

Opening eyes, pressing a hand, following commands, and extubation could be performed significantly earlier in the sevoflurane group. Dr. Röhm herself appeared amazed about this remarkable difference, considering propofol to be accepted as agent of first choice for short-term sedation that would allow for rapid weaning also in cardiac surgery patients. Some patients on propofol became apnoic again after extubation and had to be put on the ventilator again. Using sevoflurane reduced the mean time of ventilation by 2.5 hours. There were no differences regarding side effects such as arrhythmias or renal function disorders.

In a further study including 23 critically ill patients having been deeply sedated for up to seven days by sevofluran (6 mL/h, 0.5 – 1.1 % v/v end-tidal), patients were able to press a hand and were easily evaluated neurologically only 15 minutes after switching off the gas[13]. Dr. Röhm stated that titration of sedation depth in long-term patients could be done smoothly, and even in patients suffering ARDS, sevoflurane could be administered easily into the affected lungs. Also patients suffering septicaemia could be extubated within short time after removing the AnaConDa® device.

The most recent German S3 guideline on "analgesia, sedation and management of delirium in intensive care" permits inhalation sedation as an alternative to intravenous sedation, noted Dr. Röhm, despite a restriction by being off-label. There is however sufficient evidence known from literature confirming the safety of isoflurane for long-term sedation (more than seven days).

Occupational exposure

The occupational exposure limit (OEL) for isoflurane is established in Germany to 10 ppm. There are no OEL values determined to date for sevoflurane and desflurane, but a consensus meeting recommended levels of 2 ppm. Dr. Röhm specified the levels detected in her intensive care unit as considerably lower: During sedation of 15 patients for a period of 96 hours with 0.2 – 0.5 % isoflurane, concentrations between 0 and 0.5 ppm were found in the ambient air[14].

Paediatric particulars

AnaConDa® is also suitable for use in paediatric care. Special attention should however be given to the increase of dead space by 100 mL, which may lead to an inadequately high proportion of the dead space in patients whose tidal volume is below 350 ml. Based on her experience, Dr. Röhm advised not to insert the AnaConDa® device between the endotracheal tube and the y-piece, but into the inspirational side piece, and thus to accept the loss of gas via the expirational arm. The escaped gas is then discharged via gas removal systems.

Sevoflurane and kidneys

Though a 7-day sedation using sevoflurane may elevate fluoride levels to 200 µmol/L, Dr. Röhm did never observe renal dysfunctions. She reported fluoride levels with isoflurane never to exceed the threshold of 50 µmol/L, suggesting this agent to be possibly more appropriate for long term sedation. The above mentioned S3 guideline suggests monitoring of fluoride levels when sevoflurane is administered for periods of more than 48 hours, and to switch to isoflurane when levels of 100 µmol/L are exceeded. ■

Inhalation sedation in intensive medical care

Dr. med. Stefan Schmid,
Medical Deparment I, Klinikum St. Marien, Amberg

It is simple and uncomplicated to sedate internal medicine patients with sevoflurane using the AnaConDa®. The haemodynamics remain stable, patients awake soon after switching off the gas, and no relevant side effects have been observed. Volatiles are furthermore highly suitable to treat epileptic state, and after resuscication they may potentiate the cerebroprotective activity of hypothermia. That's how **Dr. Stefan Schmid, consultant at the Medical Department of the Hospital St. Marien in Amberg**, outlines his clinical experience with inhalation sedation.

Inhalation sedation was introduced into the clinical practice in the hospital in Amberg for a practical reason: Neurological patients should wake up faster and be assessable to reduce the number of CAT scans needed. Also because of lack of room capacity ventilated patients at Amberg needed to pass through faster. Due to the pleasant smell, lack of irritation of mucous membranes, acting as a bronchodilator, lack of sympathetic stimulation, improved hemodynamic stability, less effect on the vessel wall muscles and more rapid wash-in and wash–out (compared to isoflurane) made them decide using sevoflurane.

A variety of shortcomings with intravenous sedation

In the past, sedation frequently caused problems, and daily arousal, as recommended by the guideline, could hardly be done properly during intravenous sedation. On the other hand, some patients were more awake than intended, and when procedures of care caused undesired reactions, an extra bolus of sedation was required.

During the end of 2006 the AnaConDa® was tested for the first time in Amberg and already in the beginning of 2007 the implementation of the new system started. It involved theoretical and practical training of the personnel to eliminate concerns among nurses and internists. Neither of them knew volatiles from the operating room and had to get used to new values and procedures like MAC, end-tidal concentration and controlling the sedation depth with among other ways also BIS.

Dr Schmidt starts the Sevoflurane sedation with 2 mL/h in a 50 ml syringe pump and is controlling the depth of sedation based on clinical situation, BIS, MAC and end-tidal sevoflurane concentration (aiming for BIS 40-60, 0,2-0,8 MAC). If the level of sedation is insufficient a bolus of 0,1-0,4 mL is given. If tachypnoea or there are signs of pain Dr. Schmidt combines sevoflurane with low dose of remifentanil (5 – 10 mg/24h). High blood pressure, tachycardia or shivering is treated with clonidine (750 µg -3000µg/24 h)

Primary major indication: cerebral bleeding and ischaemia

Initially, sedation by gas was indicated in cerebral bleedings or ischaemia. These patients were seen to awake rapidly, and could undergo neurological evaluation within five minutes after disconnecting the gas supply. Consequently, the number of computer assisted tomograms declined considerably. Anticipated detrimental effects such as increase of intracerebral pressure could not be detected.

Patients requiring deep sedation, as in case of ARDS, are treated in Amberg with a combination of inhalation sedation and low-dose propofol or remifentanil, or sometimes clonidine. In these critically ill patients, the technique of ventilation is alleviated by the concomitant bronchodilatation, improved oxygen supply and circulatory stability due to sevoflurane.

Dr Schmid emphasised that patients suffering exacerbations of COPD or asthma, benefit from a lower rate of bronchospasms, of bronchodilation, reduced hypoxic pulmonary vasoconstriction and preservation of the breathing impulse. Also patients with a history of addiction to alcohol, drug or narcotics can be sedated in an uncomplicated way when the AnaConDa® device is used.

No toxicity through accumulation in septicaemia

In case of septic multi organ failure the toxicity through accumulation associated with intravenous sedatives is avoided by using inhalation sedation. Furthermore, the patients' circulation is more stable, and smaller amounts of catecholamies are required. Hepatic or renal complications of sevoflurane are not to be expected. Though fluoride levels may rise substantially, Dr. Schmid did not detect any impairment of the renal concentration capacity, increase of substances normally excreted by urine beyond those caused by the underlying disease, or symptoms of fluorosis. Increased fluoride levels decline very slowly.

Volatiles have proved to be highly effective in epileptic state refractory to anticonvulsants. Inducing a burst-suppression EEG with about 2 MAC sevoflurane is easier and causes less cardiovascular depression than with barbiturates. BIS evaluation permits bedside monitoring of the treatment success.

Dr. Schmid administers sevoflurane also to wean patients from long term sedation and ventilation, to allow for depletion and elimination of accumulated intravenous hypnotics. When sevoflurane is switched off, patients will awake and can undergo transfer soon. Sevoflurane is also indicated in case of cardiogenic shock requiring ventilation, where it will reduce the need for catecholamine, act cardioprotective and thus improve outcome, and in patients for whom only short-term ventilation is expected, e.g. in hypertensive lung edema, or for protective intubation for endoscopy.

Substantially improved outcome after resuscication

Currently, a recent history of successful resuscication is the most important indication for inhalation sedation. Volatiles are additive to the neuroprotective efficacy of hypothermia without affecting the breathing impulse, and longterm neurological outcome was improved considerably when sedation had been switched to the inhalative administration. Unlike in 2004, when only 35 % of patients could be dismissed from the Amberg hospital in a satisfactory condition, the corresponding percentage rised after introducing hypothermia plus sevoflurane into the treatment schedule to 62 % in 2007, 88 % in 2008 and 86 % in 2009. These patients left the hospital without any neurological deficit, and some of them could even re-enter their occupational life, Dr. Schmid emphasised. Currently, the percentage of patients experiencing a persistent vegetative state fell from 50 % in 2004 to 7 % in 2009. ■

Figure 5: Inhalation sedation with AnaConDa® at the intensive care unit of the Klinikum St. Marien in Amberg (Upper Palatinate)

Inhalation sedation in cardiosurgical intensive care patients

Prof. Dr. med. Beatrice Beck-Schimmer
Institute of Anaesthesiology, University Hospital Zürich

Ischaemic organ damage can be limited by pre- and postconditioning with volatile anaesthetics, said **Professor Beatrice Beck-Schimmer from the Institute of Anaesthesiological at the University Hospital in Zürich.** Its organ protective potential raised the interest for volatile anaesthetics and AnaConDa® among the Zürich anaesthesiologists

To start with, Professor Beck-Schimmer conducted a pilot study to investigate preconditioning with volatile anaesthetics in a study covering 64 patients scheduled for partial liver resection[15]. To limit the intraoperative blood loss, the hepatic blood supply is interrupted during this procedure by a Pringle manoeuvre resulting in hepatic ischaemia. Anaesthesia was performed in all patients with propofol. Prior to ischaemia, the duration of which was 30 minutes or more, 50 % of the patients were preconditioned with sevoflurane, whereas the other 50 % served as control group. The organ protective activity of sevoflurane became detectable by a significantly reduced increase of transaminases (AST and ALT) after surgery. The number of postoperative complications was nine in the sevoflurane group, and 22 in the group without preconditioning, with corresponding rates of severe complications (two versus nine). The number of stays in an intensive care unit could be reduced from nine in the control group to four in the sevoflurane group. The mean duration of stay in the hospital could be reduced by nearly two days, a difference which however did not reach significance.

Postconditioning with volatiles via AnaConDa® has been preliminarily tested in a rat model of endotoxin induced lung damage[16]. Professor Beck-Schimmer presented her considerations that postconditioning would be easier performed directly in the intensive care unit, and thus maybe a smarter technique. After intratracheal administration of endotoxins or sodium chloride the animals received propofol anaesthesia for two hours, followed by continued anaesthesia with either sevoflurane or propofol for four further hours. Bronchoalveolar lavage was performed at the end of the six hours, and lungs were extracted. Oxygenation with sevoflurane was found to be significantly better than with propofol. Postconditioning with sevoflurane had furthermore induced a lower degree of vessel wall permeability, as measured from a significantly lower albumin content in the lavage fluid.

First clinical experience in cardiosurgical intensive care patients

The first use of sevofluran and AnaConDa® took place in the framework of a randomised clinical trial in the cardiosurgical intensive care unit and covered 120 patients having undergone extracorporal circulation. The patients arriving at the intensive care unit had not been extubated in the theatre, and were randomised then to receive continued sedation with sevoflurane via AnaConDa® or with propofol for further four to six hours (late postconditioning with sevoflurane), Cardiac, pulmonal and renal function, incidence of postoperative nausea and vomiting (PONV), and plasma levels of inflammatory mediators were evaluated as endpoints. To be able to perform the study 10 internal trainings for nurses and doctors took place. Also instructions for the use of AnaConDa® were developed.

Overall, 100 patients were analysed, 20 patients had dropped out prematurely. Significantly lower levels of CK-MB and troponin were measured in the first day after surgery in patients on sevoflurane, who also revealed better oxygenation and less pulmonal complications. Renal function and incidence of PONV were comparable. Evaluation of inflammatory mediators is not yet terminated.

Support from specialists in occupational medicine

Because some staff members had raised concern over possible environmental pollution by the volatile anaesthetic, the study was attended by occupational medical investigations. The attending specialists did not only analyse the entire working process diligently, but also implemented essential steps into the working process, such as the safe disposal of the AnaConDa® device (provide with a lid, no handling near the bedside). During the study, the standard operating procedures were adapted accordingly. Measuring was also performed at the bedside. The occupational exposition was determined at three days in five patients who had received sevoflurane for five days and in one non-study patient who had received sevoflurane and isoflurane. The average exposition of the staff members was below 1 ppm. ■

Inhalation sedation in neurological intensive care patients

Dr. med. Julian Bösel, Neurological Department, University of Heidelberg

In the Heidelberg University Hospital, AnaConDa® is used successfully to sedate patients requiring neurological intensive care. Volatile anaesthetics facilitate ventilation, save opioids, and support organ protection. Sedation can be interrupted rapidly to monitor the patient's neurological condition. The additional, anticonvulsive activity is beneficial in patients presenting with epileptic state or severe motion disorders. **Dr. Julian Bösel from the neurological department at the University of Heidelberg** described the procedure of analgosedation with intubation of patients with cerebral lesions, and the adaption of sedation after the first phase of diagnosis and treatment.

The traditionally employed analgosedation, though of major importance, is associated with problems such as hypotension, gastrointestinal motility disorders, drug accumulation, tolerance, withdrawal symptoms, prolongation of coma, delirium, and, finally, longer stay at the intensive care unit.

Specifics of cerebral lesions

In patients with cerebral lesions, consecutive decline of perfusion pressure due to hypotension, and the bleeding risk due to hypertensive episodes associated with insufficient sedation have to be considered. Adequate analgosedation is also crucial to regulate and restrict the intracranial pressure. Furthermore, neurological examination and evaluation should be possible only short time after terminating the sedation.

To make themselves familiar with volatile sedation, the colleagues in Heidelberg modified their sedation schedule about one year ago (figure 6). Sedation is induced with propofol plus remifentanil as before, but after the first diagnostic and therapeutic procedures the patients are allocated according to the expected duration of sedation. When the clinical assessment suggests sedation for more than five days, midazolam plus sufentanil are administered. For expected shorter periods of sedation, isoflurane or sevoflurane, each plus sufentanil or remifentanil, is the combination of first choice. There is however no doubt that individual patients may require deviations from this schedule.

Many advantages with volatiles

Rapid induction and discontinuation of volatile sedation facilitates the neurologic evaluation. Also improved ventilation due to bronchodilative effects, saving of opioids, anticonvulsive effects and, possibly, neuroprotective effects in patients suffering stroke or subarachnoidal bleeding play a role. Patients with neurological disorders requiring ventilation usually are critically ill and their prognosis is poor. This makes a possible reversal from a disadvantageous ventilation into the advantage of potential neuroprotection highly interesting. One should consider risks, such as hypotension and subsequently reduced cerebral perfusion pressure, cerebral vasodilation associated with a risk of increased intracranial pressure. Local effects such as disturbed pupil motility without increased intracranial pressure might furthermore interfere with the neurological evaluation.

To keep records of the inhalation sedation, the colleagues in Heidelberg designed an observational study implementing multimodal monitoring in cerebrovascular intensive care patients undergoing inhalative sedation (Volatile Anesthetics in Neurocritical Ischaemic Stroke and Hemorrhage, VANISH). Patients are monitored during the switch from propofol to isoflurane: intracranial pressure is measured invasively, perfusion by transcranial ultrasound, and cerebral oxygenation (covering venous oxygen saturation plus cerebral oxygen extraction) by near infrared spectroscopy.

No critical increase of intracranial pressure with isoflurane till today

Evaluation of the first 20 patients revealed stable inracranial pressure after the switch to isoflurane. In no patient the threshold of 20 mmHg has been exceeded. In some cases, a decline of cerebral perfusion pressure required antagonisation with catecholamines. No serious problems were observed. There was a tendency of flow increase in the medial cerebral artery which was not significant. Cerebral oxygen extraction remained comparable. ■

Analgosedation – Protocol at the neurological ICU in Heidelberg

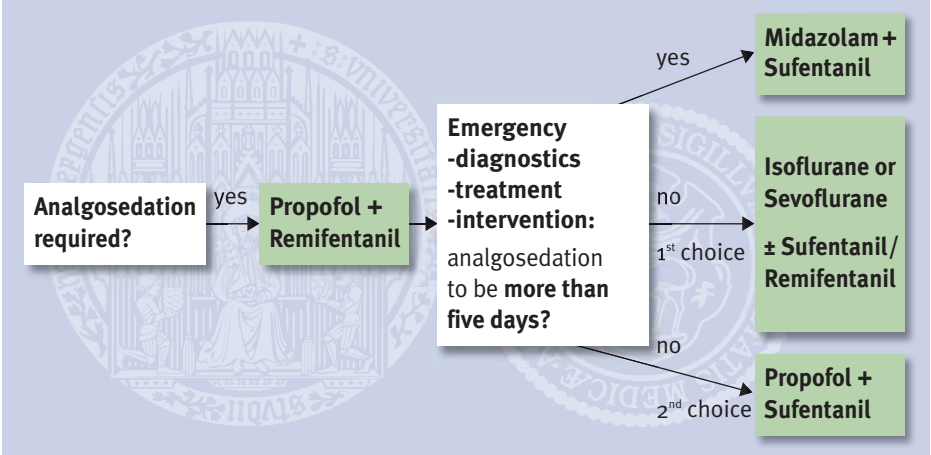

Figure 6: Present sedation model of the neurology department Heidelberg

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