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Review

Low-flow anesthesia: Theory, practice, technical preconditions, advantages, and foreign gas accumulation

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Introduction

In this review article, comprehensive information will be given about the theory and basics of low-flow anesthetic techniques. Mainly, however, practical aspects of low-flow anesthesia are discussed to enable the reader to perform this technique safely in clinical practice. If the equipment meets the specific requirements and careful maintenance of the anesthetic machines is assumed, safe performance of low-flow anesthesia with a fresh gas flow rate of 1.0 l·min^{-1} should be possible without any problems in routine clinical practice.

Short history of the rebreathing technique in anesthesiology

As early as 1850, John Snow recognized that a considerable amount of inhalation anesthetics was exhaled unchanged in the expired air of anesthetized patients. He concluded and could prove that the anesthetic effect could be markedly prolonged by reinhaling these unused vapors [1]. About 75 years later, in 1924, rebreathing systems equipped with carbon dioxide absorbers were introduced into anesthetic practice. Whereas Ralph Waters used a to-and-fro system [2], a German gynecologist, Carl J. Gauss, and a chemist, Hermann D. Wieland, advocated the use of a circle system for application of purified acetylene as an inhalation anesthetic [3]. The introduction of the highly combustible anesthetic gas cyclopropane in 1933 urged anesthetists to use fresh gas flows as low as possible to reduce pollution of the operating room and, thus, to minimize the risk of explosion [4].

In 1954 halothane was introduced, a new volatile anesthetic characterized by high anesthetic potency yet narrow therapeutic width. To ensure patient safety, the use of this anesthetic was dependent on knowledge of the applied vapor concentration. This estimation, however, was simple and easy only if a high flow of fresh gas was used and the proportion of rebreathing was kept rather low. The estimation was more difficult because the vaporizers available at that time did not work sufficiently reliably and precisely in the low-flow range. Thus, although nearly all anesthetic machines were already equipped with sophisticated rebreathing circle systems, paradoxically, it became clinical routine to use fresh gas flows as high as 4 to 6 l·min^{-1}, completely excluding any significant rebreathing [4]. In many countries this is still the routine way to perform inhalational anesthesia [5]. However, due to the development of modern anesthetic apparatus, the availability of comprehensive gas monitoring, increasing environmental awareness, the introduction of new advantageous but expensive inhalational anesthetics, and the worldwide restriction of economic resources in medical care, an increasingly strong tendency towards the use of low-flow techniques has been observed for about 15 years and should be encouraged [6].

Low-flow anesthesia: theory

Rebreathing systems can be used in different ways. If used with a fresh gas flow equal to the minute volume of the patient, the share of rebreathing will be negligible. The expired air will be vented out of the system nearly completely as excess gas via the APL valve. The patient gets nearly pure fresh gas. If a flow of 4.0 l·min^{-1} is used, the share of rebreathing will increase to about 20%. The patient inhales a gas whose composition still resembles that of the fresh gas. The share of rebreathing will reach 50% or more only if the flow is reduced to 2.0 l·min^{-1} or lower. Thus, the share of rebreathing will become significant only when low fresh gas flows are used and

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judicious use is made of the rebreathing technique [7].

According to the literature, two different low-flow techniques can be distinguished. The term "low-flow anesthesia" was introduced by F. Foldes, inaugurating an anesthetic technique performed with a fresh gas flow of 1.0 l·min^{-1} [8]. R. Virtue introduced the term "minimal-flow anesthesia" by recommending the use of an even lower flow of 0.5 l·min^{-1} [9]. As emphasized before, the lower the fresh gas flow, the lower is the amount of gas vented out of the breathing system as waste and the higher is the proportion of rebreathing. The general term low-flow anesthesia should be restricted to an anesthetic technique in which a semiclosed rebreathing system is used, recirculating at least 50% of the exhaled air back to the patient after CO_2 absorption. With modern rebreathing systems, this will be achieved only if the fresh gas flow is reduced to at least 2 l·min^{-1} [10].

However, there is a limit of reduction of the fresh gas flow. To prevent gas volume deficiency, at least the gas volume that is definitely taken up by the patient (Fig. 1) has to be delivered into the breathing system.

During the course of anesthesia, oxygen is taken up constantly by the patient in the range of the basal metabolic needs. It can be calculated by applying a simplified version of Brody's formula [11]:

$$\dot{V}_{O_2} = 10 \times \mathrm{BW}\,(\mathrm{kg})^{3/4}. \quad (\mathrm{ml \cdot min^{-1}})$$

BW: body weight of the patient

The uptake of nitrous oxide and the volatile anesthetic, however, follows a power function. The nitrous oxide uptake of an adult patient of normal body weight

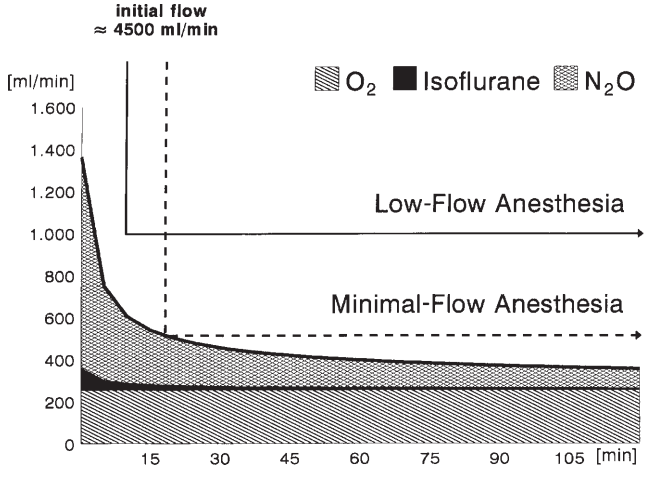

Fig. 1. Common characteristics of anesthetic techniques with low fresh gas flow: following an initial phase using high flow, the fresh gas flow rate is reduced and thus adapted to the total gas uptake, which continuously decreases during the course of anesthesia

can be roughly estimated by applying Severinghaus' formula [12]

$$\dot{V}_{N_2O} = 1000 \times t^{-1/2}. \quad (\mathrm{ml \cdot min^{-1}})$$

t: time, i.e. duration of anesthesia

and the uptake of inhalational anesthetics may be calculated by H. Lowe's formula [13]:

$$\dot{V}_{AN} = f \times \mathrm{MAC} \times \lambda_{B/G} \times \dot{Q} \times t^{-1/2}. \quad (\mathrm{ml \cdot min^{-1}})$$

$f \times$ MAC: desired anesthetic concentration, fraction of MAC
$\dot{Q}$: cardiac output (dl/min)
t: time

Thus, assuming a constant gas composition circulating within the breathing system, the total gas uptake, the sum of oxygen, nitrous oxide, and inhalational anesthetic uptake, follows a power function. Initially it is high and declines sharply during the first 30 min, but it is comparatively low and decreases only slowly during the following course of anesthesia. This exponential character of the gas uptake results from the fact that the partial pressure difference of anesthetic gases between the alveolar space and the blood, which is initially high, decreases continuously with increasing saturation of the blood and tissues. If the anesthesiologist, by frequent alterations of the settings at the gas controls, could succeed in approximating the total gas uptake, anesthesia with a closed rebreathing system would be realized. In clinical practice, however, continuous adaptation of the fresh gas flow according to the continuously changing individual gas uptake will be impossible. However, by applying very simple and safe standardized dosing schemes, low-flow techniques such as minimal-flow and low-flow anesthesia can be performed safely with already available anesthetic equipment in routine clinical work [7,14].

Low-flow anesthesia: practice

Induction

Premedication and induction of low-flow anesthesia are performed according to the usual induction scheme. Preoxygenation by applying pure oxygen via a face mask is followed by intravenous injection of a hypnotic. After neuromuscular relaxation and endotracheal intubation or insertion of a laryngeal mask, the patient is connected to the breathing system. In about 85% of all cases, the gas tightness of the laryngeal mask will allow the fresh gas flow to be reduced to 0.5 l·min^{-1}, even if controlled ventilation is performed [7,15]. There are no procedure-specific requirements for premedication and induction.

Initial high-flow phase

According to the guidelines given by Foldes or Virtue, during the first initial phase, lasting 10 to 15 min, a high fresh gas flow has to be used. The author [7,16] recommends setting the oxygen flow at 1.4 l·min^{-1} and the nitrous oxide flow at 3.0 l·min^{-1}. In most patients, this fresh gas composition guarantees an inspired oxygen concentration of at least 30%, meeting the recommendations of Barton and Nunn [17,18]. The following settings of the vaporizers are used routinely during the initial phase: enflurane 2.5 vol%, isoflurane 1.5 vol%, sevoflurane 2.5 vol%, and desflurane 4.0%–6.0%. If these settings are used over the first 10 to 15 min, an expired concentration of about 0.7 to 0.8 times the minimum alveolar concentration (MAC) of the respective volatile agent will be gained in adult normal body weight patients. In addition to a nitrous oxide MAC of about 0.6, corresponding to a nitrous oxide concentration of 60%, this will result in a common MAC of 1.3 representing the AD_{95}, the anesthetic gas concentration guaranteeing a sufficient depth of anesthesia for 95% of all patients to tolerate the skin incision without any movement. Furthermore, an initial high fresh gas flow is indispensable for sufficient denitrogenation and washin of the aspired gas composition into the whole gas-containing space. Last but not least, if the flow is reduced too early and too much, inevitably gas volume deficiency will result, compromising adequate ventilation [7,16].

Flow reduction

If low-flow-anesthesia is to be performed, the fresh gas flow can be reduced to 1.0 l·min^{-1} after 10 min. Flow reduction will lead to a significant increase in rebreathing. The inspired gas, thus, contains a markedly increased proportion of the exhaled gas which already has passed through the patient's lungs and contains less oxygen. The resulting decrease of oxygen content in the gas mixture has to be compensated by increasing the fresh gas oxygen content, which must increase with decreased flow. Thus, to maintain a safe inspired oxygen concentration of about 30% in low-flow anesthesia, the fresh gas oxygen concentration has to be increased to 50%, but at least to 40%. With the fresh gas flow reduction, furthermore, the amount of anesthetic vapor delivered into the system is markedly reduced. This has to be compensated by a corresponding significant increase in the concentration of the agent in the fresh gas. Only in this way can the aspired anesthetic concentration with in the breathing system be kept constant. In low-flow anesthesia, the fresh gas concentration of enflurane is increased to 3.0 vol%, of isoflurane to 2.0 vol%, and of sevoflurane to 3.0 vol% [7,16,19]. Because of its specific pharmacokinetic properties, only the fresh gas desflurane concentration can be maintained unchanged [20]. When these standardized schemes are executed, the expired anesthetic concentrations will be maintained in the aspired range of 0.7 to 0.8 times the MAC.

If minimal-flow anesthesia is to be performed, the initial high-flow phase should last about 15 min. A sufficiently long initial high-flow phase will prevent accidental gas volume deficiency, which will always result when the gas loss via individual uptake and leakage is higher than the gas volume delivered into the system. To maintain a safe inspired oxygen concentration of at least 30%, oxygen fresh gas concentration has to be increased to 60%, but at least to 50%, when the flow is reduced to 0.5 l·min^{-1}. Simultaneously the anesthetic concentration of the fresh gas has to be increased to 3.5 vol% when enflurane is used, to 2.5 vol% with isoflurane, and to 3.5 vol% with sevoflurane, and the desflurane concentration is standardly raised by 1 vol%. By applying this dosing scheme again, the concentration of an expired agent will be maintained in the range of 0.7 to 0.8 times the respective MAC [7,16,19,20].

Inspired oxygen and nitrous oxide concentration

After reduction of flow from 4.4 to 0.5 l·min^{-1}, an initial increase in FiO_2 over the next 30 to 45 min can be observed. It will be more pronounced in small or elderly patients with low oxygen uptake than in strong, young, or athletic patients. This initial increase is followed by a slow but continuous decline in the inspired oxygen concentration to lower values, which is more pronounced higher the oxygen uptake of the patient (Fig. 2). Whenever the lower alarm limit of the oxygen monitoring is reached, which must be carefully adjusted to 30%, the oxygen flow has to be increased by 10% of the total

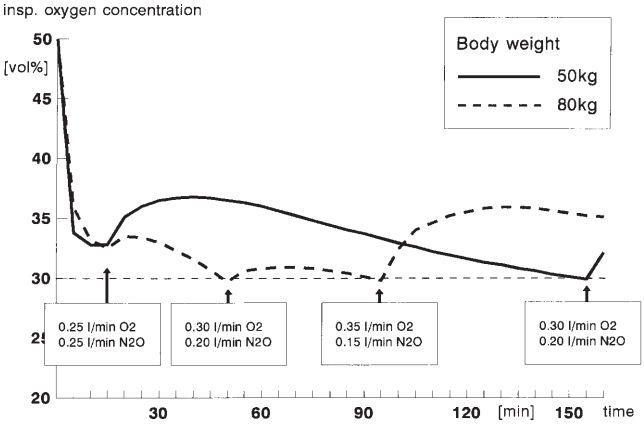

Fig. 2. Inspired oxygen concentration during the course of minimal-flow anesthesia as a function of body weight (correlated with oxygen uptake). At flow reduction, oxygen and nitrous oxide flows are set to 0.25 l·min^{-1} each. Whenever the concentration drops to 30%, oxygen flow is increased by 0.05 l·min^{-1} and nitrous oxide flow is decreased by the same value

fresh gas flow, whereas the nitrous oxide flow must be decreased by the same amount. Thus, in minimal-flow anesthesia, the oxygen flow has to be increased by $50\,ml{\cdot}min^{-1}$ and the nitrous oxide flow reduced by $50\,ml{\cdot}min^{-1}$. After these adjustments, a slow increase in FiO_2 will be followed by a slow but continuous decrease. Whenever the lower alarm threshold is reached again, the oxygen flow has to be increased again by 10% of the total fresh gas flow and the nitrous oxide flow reduced by the same amount. In low- and minimal-flow anesthesia, the oxygen concentration within the breathing system changes slowly but continuously during the course of the anesthetic procedure [7,16].

Concentration of inhalational anesthetics

If the fresh gas concentration of the volatile anesthetic is increased with reduction in flow according to standard schemes, a slight decrease in the inspired and expired anesthetic concentration can be observed. The vaporizers of all modern anesthetic apparatuses are switched into the fresh gas line (VOC). Thus, the reduction in flow results in a corresponding significant decrease in the amount of anesthetic vapor delivered into the system. In all anesthesia machines, likewise, the breathing system, the ventilator, the connecting hoses, and the patient hose assembly contain a gas volume of about 5 to 6l. This, in addition to the gas volume of about 2.5l contained in the lung of an adult patient, is the distribution space for the anesthetic vapor delivered into the system [7]. If a fresh gas flow as low as $500\,ml{\cdot}min^{-1}$ is assumed, a change of the setting of the vaporizer from zero to 5 vol% will raise the amount of vapour from 0 to $25\,ml{\cdot}min^{-1}$, a small volume compared with the distribution space. Thus, in low-flow anesthesia there is a marked difference between the fresh gas concentration of the anesthetic and its concentration within the breathing system, and this difference increases with decreasing fresh gas flow, but decreases with decreasing solubility of the anesthetic agent [19–21] (Fig. 3). If the concentration of the volatile anesthetic is changed, the vaporizer has to be adjusted to a concentration considerably exceeding the aspired nominal value.

Time constant

The time constant is a measure of the time it takes for alterations of the fresh gas composition to lead to corresponding alterations of the gas composition within the breathing system. According to a formula given by Conway [22], the time constant (T) can be calculated by dividing the volume of the system (V_S) by the difference between the amount of anesthetic agent delivered into the system with the fresh gas (V_D) and the individual gas uptake (V_U):

$$T = V_S \big/ \left(\dot{V}_D - \dot{V}_U\right).$$

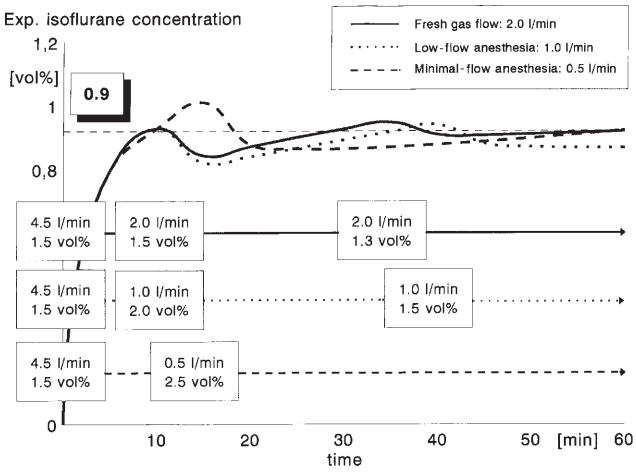

Fig. 3. Expired isoflurane concentration (desired nominal value 0.9% = 0.8 MAC) resulting from different vaporizer settings at different fresh gas flows. Patient's assumed body weight: 75 kg

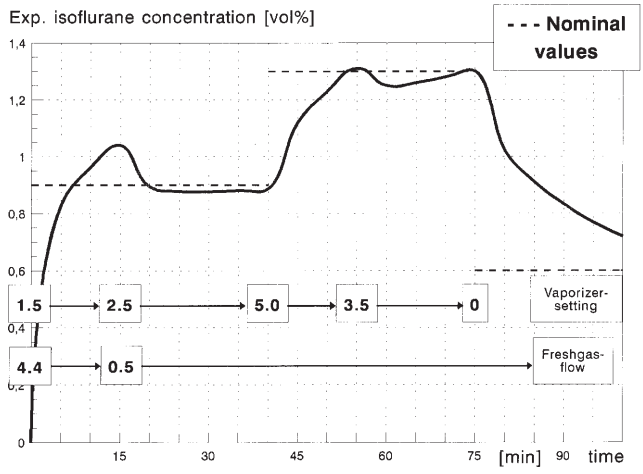

Fig. 4. Minimal-flow anesthesia: alteration of the expired isoflurane concentration to new desired nominal values only by variation of the vaporizer setting. Anesthesia management using the long time constants characterizing low-flow techniques

Assuming a given volume of the system and a given individual gas uptake, the time constant is inversely proportional to the fresh gas flow. The marked increase in the time constant has to be taken into account when switching from high to low fresh gas flows (Fig. 4). Whenever the gas composition within the breathing system needs to be changed rapidly, the fresh gas flow has to be increased to adequately accelerate the washin of the newly aspired gas composition. If low-flow anesthesia is performed with the newer volatiles that are characterized by low anesthetic potency and solubility, such as sevoflurane and desflurane, the time constants will be

significantly shorter, as V_D can be raised considerably and V_U is extremely low [19–21,23].

Recovery phase

According to the long time constant, the vaporizer can be closed about 15 to 20 min before the definite end of the surgical procedure. If the low flow is maintained, the decrease in anesthetic concentration is delayed and slow. During that time, recovery of spontaneous breathing can be induced by using the synchronized intermittend mandatory ventilation mode (SIMV) or by manual assistance of ventilation. About 5 min before extubation, the anesthetic gases are washed out by switching to a high flow of pure oxygen. The recovering patient is cared for in the usual manner [7,16].

Characteristics of low-flow anesthesia

If commercially available anesthetic machines are used, with low- and minimal-flow anesthesia the maximum of flow reduction is reached that can be gained in routine clincal practice. Both techniques are extreme variants of the semiclosed use of rebreathing systems, since a small amount of excess gas is still used. The performance of low- and minimal-flow anesthesia becomes very simple if standardized schemes are used to control the fresh gas flow and its composition. These schemes require only rare adjustments at the gas flow controls and vaporizers. The anesthetist, however, must accept that the gas concentrations within the breathing system will not remain constant at the aspired values but rather will change slowly and continuously during the course of anesthesia.

Last but not least, standardized schemes for the performance of low-flow anesthesia can only be guidelines. The fresh gas flow and its composition always must be adapted to the individual patient's reactions and the current requirements of the surgical procedure.

Technical preconditions for safe performance of low-flow anesthesia

Monitoring and alarm thresholds

Because of its specific characteristics, continuous monitoring is essential for safe performance of low-flow anesthesia [6,7,16]. As the difference between the gas concentrations in the breathing system and the fresh gas increases with the extent of flow reduction, the anesthetic gas composition cannot be reliably assessed from the composition of the fresh gas. Thus, continuous monitoring of the inspired oxygen concentration is absolutely indispensable. The same applies to the concentration of volatile anesthetics, if a fresh gas flow lower than 1 l·min^{-1} is used. The lower threshold for the inspired oxygen concentration should be set to 30%, and the upper alarm limit of inspired anesthetic concentration to 2.0–3.0 vol% for halothane, enflurane, and isoflurane, to 5.0 vol% for sevoflurane, and to 8.0 vol% for desflurane. The fresh gas volume must always be large enough to compensate for the gas loss via individual uptake and leakage. Otherwise, gas volume deficiency will occur, inevitably leading to an alteration of the ventilation. Continuous monitoring of the airway pressure or, alternatively, the minute volume is also therefore indispensable. The disconnect alarm should be set to a value 5 mbar lower than the peak pressure, and the lower alarm limit of the minute volume monitoring to 0.5 l·min^{-1} lower than the desired minute volume. If low-flow techniques are performed consistently, the soda lime consumption will increase fourfold. By continuous monitoring of the inspired carbon dioxide concentration, soda lime exhaustion can be reliably detected. If this monitoring is not available, jumbo or double absorber canisters should be used and the soda lime changed after each day of work [7,24].

Anesthetic apparatus

The technical features of the anesthetic apparatus have to comply with the following requirements [7,10]. The flow control system must feature needle valves and flowmeter tubes calibrated and reliably working even in the low-flow range. The vaporizers must be compensated for fresh gas flow. The rebreathing system has to be sufficiently gas-tight: the leakage must not exceed 100 ml·min^{-1} at a pressure of 20 mbar to meet the requirements for minimal flow anesthesia. The performance of low-flow techniques is significantly facilitated by the availability of an anesthetic gas reservoir, by which small accidental gas volume deficiencies can be balanced. Such a gas reservoir can be the end-inspiratory volume contained in the bag of a bag-in-bottle ventilator, the bellows of a ventilator with standing or hanging "floating" bellows, or the manual ventilation bag in machines equipped with a fresh gas decoupling valve. If an anesthetic apparatus is used featuring continuous flow of the fresh gas into the breathing system, it must be considered that each alteration of the fresh gas flow will lead to a corresponding alteration of the tidal volume. The preset tidal volume will be delivered independently of the fresh gas flow range only if an anesthetic ventilator is used featuring fresh gas flow compensation. Fresh gas flow compensation can also be achieved by discontinuous delivery of the fresh gas into the breathing system or by automatic electronic control of the performance of the ventilator corresponding to the fresh gas flow rate. With the use of

modern anesthetic equipment, low-flow techniques are advantageous and can be executed safely, even in pediatric anesthesia [7,25,26].

Advantages of low-flow anesthesia

The advantages of low-flow anesthesia are obvious and indisputable and were already comprehensively listed in Waters's paper [2]: the reduction of anesthetic gas and vapor consumption, the decrease in atmospheric pollution with inhalation anesthetics, the improvement in anesthetic gas climate, and the significant reduction in costs.

In comparison with 2 h of continuous high-flow (4.5 l·min^{-1}) isoflurane anesthesia, the use of minimal-flow (0.5 l·min^{-1}) isoflurane anesthesia reduces the consumption of oxygen by 115 l, the consumption of nitrous oxide by 300 l, and the consumption of isoflurane vapor by 5.6 l [7]. If high-flow techniques, using fresh gas flows of about 4.5 l·min^{-1}, were replaced consistently by low-flow anesthesia in Germany and the UK, the resulting reduction in gas and anesthetic vapor consumption would be about 350 million l of oxygen, 1000 million l of nitrous oxide, 33,500 l of fluid isoflurane, and 46,250 l of fluid enflurane [10]. The conclusion is very simple and obvious: the lower the flow, the less the gas consumption [27,28].

Anesthetists also have to deal with increasingly stringent official regulations on the maximum acceptable workplace concentrations of anesthetic gases [29]. Careful maintenance of the anesthetic apparatus and scrupulous attention to leaks from breathing systems assumed, even the extremely low anesthetic gas concentrations stipulated by the US National Institute of Occupational Safety and Health can be achieved easily only by the use of low-flow techniques [30,31]. Most operating theaters, however, are nowadays equipped with central gas-scavenging systems, and it is possible to stay within the defined limits even if high fresh gas flows are used. Nevertheless, high-flow anesthesia will inevitably result in pollution of the atmosphere beyond the operating theater. Both nitrous oxide and the volatile anesthetics contribute to the destruction of the ozone layer and to the greenhouse effect. The ozone destructive potential of the volatile anesthetics halothane, enflurane, and isoflurane, which are partially halogenated chlorofluorocarbons (CFCs), is assumed to be only 0.1%–1% of that of all fully substituted CFCs. Furthermore, the amount of nitrous oxide emitted from hospitals is only about 1% of the total amount of nitrous oxide polluting the atmosphere. Most is derived from bacterial metabolism in fertilized soil. Nevertheless, even if emitted anesthetic gases are a comparatively small fraction of the total polluting gases, anesthetists are morally obliged to minimize pollution in an age of increasing environmental awareness, and it is their duty to use all technical facilities available to achieve this [32–36]. Desflurane and sevoflurane, which are halogenated only with fluorine, are assumed to have nearly no ozone-depleting potential but may contribute considerably to the greenhouse effect.

Appropriate humidification and warming of anesthetic gases have a significant impact on the function and integrity of the ciliated epithelium of the respiratory tract. During anesthesia, the absolute humidity of the inspired gas should range between 17 and 30 mgH_2O·l^{-1}, and its temperature between 28° and 32°C. After an initial period of 30–45 min in an actively heated compact breathing system, these values can be achieved only by the use of a low-flow technique [37–41].

Cost savings result directly from the decrease in gas and anesthetic consumption. They are related to the duration of the anesthetic procedure, the price of the anesthetic agent, and the extent of flow reduction [42–44]. If a high-flow (4.5 l·min^{-1}) technique is companed with a minimal-flow (0.5 l·min^{-1}) technique lasting 2 h, assuming the inspired anesthetic concentration at MAC, savings of about US$ 15 can be achieved if enflurane is used, about US$ 21 if isoflurane is used, and about US$ 47 if desflurane is used [16]. By comparison, the additional cost of about US$ 0.60 resulting from increased consumption of soda lime for 2 h is negligible [7]. In relation to the before-mentioned projection, the annual financial savings resulting from reduced gas and anesthetic consumption in Germany and the UK are assumed to total more than US$ 65 360 000 if low-flow anesthetic techniques were performed consistently [10]. It seems to be realistic to assume a cost savings in the range of 50%–75% if low-flow techniques were used consistently in clinical routine practice [7,45,46]. Even the more costly anesthetics such as desflurane could be used without significant increase in costs [47].

Efficiency of inhalation anesthetic techniques

One of the most striking aguments in favour of low-flow anesthesia is the marked increase in efficiency of inhalational anesthesia [48]. The efficiency (Eff) can be calculated by dividing the amount of agent taken up by the patient ($\dot{V}_U$) by the amount of agent delivered into the breathing system ($\dot{V}_D$):

$$Eff = \dot{V}_U / \dot{V}_D .$$

When this algorithm is considered, it becomes obvious that an inhalation anesthetic technique is less efficient the lower the individual uptake and the higher the amount of agent that is delivered into the breathing

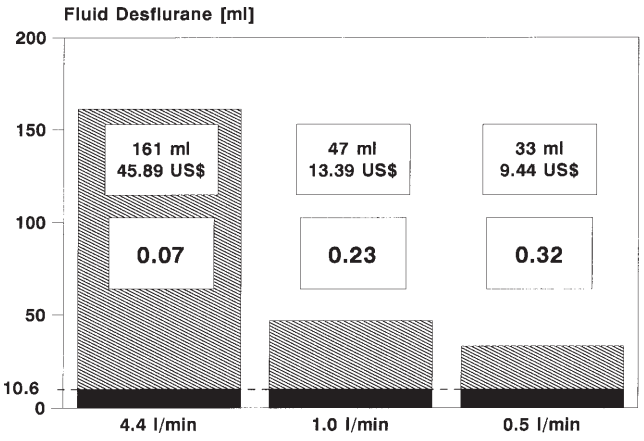

Fig. 5. Comparison of desflurane consumption, costs, and efficiency of application technique resulting from the use of different fresh gas flow rates: high flow, 4.4 l·min^{-1}; low flow, 1.0 l·min^{-1}; minimal flow, 0.5 l·min^{-1}. Basis of calculation: 2 h procedure; inspired desflurane concentration, 6.0%; body weight of patient, 75 kg; cumulative uptake in 2 h, 10.6 ml fluid

system. Since the amount of agent delivered into the system directly is bound to the fresh gas flow, the anesthetic technique will be less efficient the higher the fresh gas flow. This holds especially for anesthetic agents with low solubility and anesthetic potency (Fig. 5). If desflurane, for instance, is used with a flow of 4.5 l·min^{-1} at an inspired concentration of 6.0% over a period of 2 h, the overall efficiency will decline to 0.07. Only 7% of the total amount of agent delivered into the system is really needed and taken up by the patient, whereas 93% is wasted with the excess gas escaping from the breathing system [7]. If this agent is administered at low fresh gas flow rates, the efficiency can be increased to an acceptable range of about 30%. The use of anesthetic agents with low solubility and anesthetic potency, such as sevoflurane and desflurane, for economic and ecologic reasons only can be justified if judicious use is made of rebreathing techniques [47,49,50].

Trace gas accumulation

A matter of concern remains the accumulation of trace gases resulting from the diminution of the washout of foreign gases, which is less the lower the fresh gas flow. Foreign gases may decrease the concentration of nitrous oxide and oxygen. That may, for instance, be the case if nitrogen accumulates due to insufficient denitrogenation, or the argon concentration may rise due to the use of an oxygen concentrator [51,52]. Methane, physiologically exhaled by the patient, in high concentrations may compromise the measurement and monitoring of halothane concentration [53]. Accumulation of acetone may prolong the emergence from anesthesia and provoke nausea or vomiting. However, this may become clinically relevant only in the very rare cases of severely ketoacidotic patients [54]. Accumulation of these trace gases, even in prolonged low-flow anesthesia, has not been shown to be of clinical importance [55].

All inhalational anesthetics react with carbon dioxide absorbents by absorption and degradation, most avidly if the absorbent is desiccated [56]. The new volatiles desflurane and sevoflurane are more liable to react with the alkaline absorbents than the older anesthetics halothane, enflurane, and isoflurane. Desflurane reacts more than enflurane or isoflurane with absolutely dry carbon dioxide absorbents, generating carbon monoxide. Only partial wetting markedly reduces this chemical reaction, and if soda lime contains only 4.8% and Baralyme only 9.5% water, carbon monoxide generation is suppressed completely [57]. It has been concluded that fresh gas flows lower than 5 l·min^{-1} should not be used in order to avoid accidental carbon monoxide intoxication resulting from trace gas accumulation [58]. This conclusion, however, must be strongly rejected, since only high fresh gas flows are liable to dry out the absorbents. On the contrary, low-flow anesthesia, preserving the moisture content of the absorbents, can prevent carbon monoxide generation [59]. Sevoflurane reacts with dry absorbents more avidly than halothane [60,61]. Both agents, however, also react with normally wet carbon dioxide absorbents, generating haloalkenes: halothane by forming BCDFE (1,bromo-1,chloro-2,2,difluoro-ethylene [62]) and sevoflurane by forming compound A (fluoromethyl-2,2,difluoro-1,trifluoromethyl-vinylether). The concentration of compound A was found to increase with the extent of flow reduction, with the temperature of the absorbent, and the concentration of the agent [63,64]. Some authors regard a load of compound A of 150 to 240 ppmh already as potentially nephrotoxic in humans [65–67] and emphasize that this anesthetic should not be used with flows lower than 2.0 l·min^{-1}. On the contrary, some authors consider low-flow anesthesia with sevoflurane to be safe, arguing that the mean peak concentrations in different studies did not exceed 25 ppm and no signs of renal impairment were observed in any patient [49,68,69]. Mazze recently published the results of an investigation on the nephrotoxicity of compound A in primates, demonstrating that nephrotoxic effects occured only at a load of at least 800 ppmh [70]. If this threshold for nephrotoxic load with compound A was accepted, absolutely no flow restriction would be justified. Even long-lasting minimal-flow anesthesia with sevoflurane could be performed safely, although compound A peak concentrations were found to reach 50 to 60 ppm with this technique [71]. Unlike the case in the United States, sevoflurane has been approved for clini-

cal use without any fresh gas flow restriction in all countries of the European Common Market. Nevertheless, whenever there is a possibility of the accumulation of potentially harmful trace gases, for safety reasons a low-flow technique using a flow of at least 1 l·min^{-1} should be performed, guaranteeing a sufficient continuous washout effect [7].

Summary

Rebreathing systems can be used judiciously only by reducing the fresh gas flow rate considerably. The anesthesiologist, however, must have a clear understanding of how to cope with the specific characteristics of this anesthetic technique and how to overcome its shortcomings and possible disadvantages. Following the given guidelines and standardized schemes will enable the anesthesiologist to perform low-flow anesthesia safely in clinical practice.

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