Low-flow anaesthesia

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Modern inhalational anaesthetic agents are metabolized to a small extent only and are largely exhaled unchanged. The use of breathing systems fitted with carbon dioxide absorption units and comprehensive gas monitoring permits the exploitation of this to perform economical and safe 'low-flow anaesthesia'.

There is no universally accepted definition of low-flow anaesthesia, though it certainly implies a carrier gas flow less than that attainable with a non-absorber breathing system. Baum's suggestion of 'a rebreathing fraction of greater than 50%' gives too high a figure,[1] since it is at a rebreathing fraction above 75% that the special characteristics of low-flow anaesthesia become apparent. A technique for nitrous oxide–oxygen anaesthesia with a gas flow of 1 litre min^{-1} was described by Foldes in 1952.[2] He sought to define safe nitrous oxide–oxygen mixtures for patients of different weights in the absence of oxygen monitoring. He drew attention to the fact that as the total gas flow was reduced, the gas mixture had to be biased towards oxygen as its uptake would, after the initial few minutes, exceed that of nitrous oxide. This technique and in particular the 1 litre min^{-1} gas flow subsequently became known as low-flow anaesthesia. In 1974, Virtue[3] described a technique using a fresh gas flow of 500 ml min^{-1} which he named 'minimal flow anaesthesia'. He highlighted two important issues: first that the disparity between delivered and inspired oxygen concentration became even more marked and secondly that the significant benefits of economy were by and large already obtained with Foldes' technique.

Modern equipment permits the further reduction of the carrier gas flow to the ultimate degree of providing the patient's requirements and no more. This is 'closed system anaesthesia', where no excess gas is vented. If nitrous oxide is not used, this gas need only comprise oxygen and air in the proportions required to provide an acceptable inspired oxygen concentration. In this article, Foldes' and Virtue's definitions of low-flow and minimal-flow anaesthesia will be used.

Characteristics of low fresh gas flow techniques

A major obstacle to the use of low-flow techniques is the user's fear of the increasing disparity between the gas concentrations set at the anaesthetic machine and those in the breathing system. A gas flow in excess of the minute volume will provide readily predictable inspired gas concentrations, which will be more or less the same for any patient, using any breathing system, at any stage of the anaesthetic and will be unaffected by agent uptake by the patient. However, as the carrier gas flow is reduced and more exhaled gas is retained within the breathing system (increased rebreathing fraction), gas uptake by the patient will increasingly affect the exhaled and hence the inspired gas mixture. Once the flow rate is reduced to near the patient's requirements, the fresh gas mixture will closely reflect the uptake of each of its components by the patient. The increasing deviation of the inspired gas mixture from that set at the rotameters means that these techniques are critically dependent on gas monitoring. This shift towards a quantitative concept of gas delivery is the fundamental defining feature of low-flow techniques.

Requirements for the use of low-flow techniques

These techniques may require significant capital investment in equipment. The key features for gas delivery are flow meters calibrated to flows down to 50 ml min^{-1} and a leak-free circle system. The use of minimal flow anaesthesia is difficult or impossible if the anaesthetic machine has an obligatory oxygen flow of 200 ml min^{-1}, since techniques using near basal oxygen requirement will probably require lesser amounts to be delivered. Thankfully, this 'safety feature' no longer appears on current Datex and Datex Ohmeda models.

The cost of gas monitors alone may prevent the use of low-flow techniques in many parts of the world; however, in the UK, the required standards are already covered by RCoA

Key points

The equipment required to deliver safe anaesthesia with low fresh gas flow rates is already standard in the UK.

Low-flow anaesthesia is characterized by economy in the use of anaesthetic agents and reduced atmospheric pollution.

As the carrier gas flow rate is reduced, an increasing disparity develops between the fresh gas and the inspired gas mixtures. The fresh gas composition increasingly needs to reflect the patient's uptake of its components.

A progressive reduction in a practitioner's gas flow rates permits safe and relaxed self-learning of this technique.

Both compound A and carbon monoxide are produced to a significant extent only in CO_2 absorbents containing potassium hydroxide. No such absorbents remain in commercial production.

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guidelines. A near-gas-tight breathing system is needed. These techniques are not applicable to mask anaesthesia, but should be practicable with a well-fitting laryngeal mask.

Advantages of low-flow techniques

The main advantages of low-flow techniques are economy, climatization of the inspired gases, and reduced atmospheric pollution. In addition, the use of these techniques promotes greater understanding of breathing systems and the pharmacokinetics of inhalation anaesthesia.

Economy

The relative cost of volatile agents has declined steadily since the introduction of halothane to the present situation where the price of isoflurane is so low as to be almost negligible. However, the widespread use of desflurane and sevoflurane means that the original goal of improved economy applies just as much today as it did 50 years ago.

Climatization

The advantage of low gas flows in terms of the climatization of the inspired gas is, at least in the UK, no longer generally relevant. The near universal use of patient connection filters means that, due to their heat and moisture exchanger characteristics, the humidity and temperature of the inspired gas is maintained by these devices. In other countries or in paediatric practice, where heat and moisture exchangers may not be in use routinely, the conservation of heat and moisture within the breathing system may still be aided by the use of low fresh gas flows.

Pollution

All gases delivered from anaesthetic machines are ultimately lost to the atmosphere. Halothane, enflurane, and isoflurane contain chlorine and, though not specifically covered by the Montreal Protocol, are believed to have significant ozone depleting potential. The stability of these molecules permits their passage to the stratosphere where increasing UV radiation causes dissociation to liberate free chlorine, which acts as a catalyst in the breakdown of ozone with chlorine monoxide as an intermediate.[4] This reaction is the major cause of the destruction of the ozone layer, especially over the South Pole, which is of considerable ecological significance. Nitrous oxide is also a catalyst in an analogous reaction. While anaesthetists thus have a clear duty to minimize the use, that is to say the release, of these chemicals, it has to be admitted that our practice's contribution to the total global release is small. Desflurane and sevoflurane contain no chlorine and appear to have no greenhouse gas effects.

Disadvantages of low-flow techniques

As stated earlier, the need for capital investment for absorber breathing systems and dependence on gas monitoring may limit the use of low-flow methods in poorer countries. Similarly, the need for and increased consumption of absorbent at low flows may be an issue in some countries. Other disadavantages include the limitations of currently available vaporizers and accumulation of unwanted gases in the breathing system.

Limitations of currently available vaporizers

Modern vaporizers are little different in basic design and function to those of the 1960s. They are designed for use with high fresh gas flows with a consequent requirement for high thermal capacity, temperature compensation, and high accuracy. The use of low carrier gas flows makes these characteristics unnecessary, but it also introduces the problem of delivering an adequate quantity of volatile agent into the breathing system.

Consider a carrier gas flow of 200 ml min^{-1} through a sevoflurane vaporizer. At a setting of 6% a total of 6 g (4 ml of liquid) of sevoflurane will be delivered per hour. (This is a typical adult requirement once equilibrium has been attained). The need to increase the end-tidal sevoflurane, in response, for example, to increased surgical stimulus, poses a problem. The maximum possible delivered concentration of sevoflurane of 8% represents only an extra 2 g (1.3 ml) of sevoflurane per hour. This, delivered into a total gas volume of several litres, will cause only a very slow rise in concentration. This long time constant is a significant practical disadvantage of low-flow techniques using current vaporizers.

The pragmatic solution is to increase the carrier gas flow for a time, which inevitably leads to venting of gas and hence wastage. The use of a vaporizer in the circle (VIC) permits rapid increases, but is impractical for several reasons. There is no currently marketed vaporizer approved for use in circle systems. Some (e.g. Goldman, McKesson, Komesaroff) have delivery characteristics that require very careful handling and the more sophisticated Oxford Minature Vaporizer, though it can be used, carries a warning of failure due to waterlogging of the wicks. In any event, a VIC system cannot comply with current European regulations (EN 740) so it seems unlikely the technique will enjoy a renaissance.

A more elegant approach would be to dissociate the volatile agent delivery from the carrier gas supply by the separate administration of the volatile agent. This may be done by the direct addition of liquid agent which permits rapid increases in concentration with no need to adjust the carrier gas flow. This technique was available commercially in the Physioflex anaesthetic machine (now no longer marketed) and more recently in the Dräger Zeus. It should be noted that, however the volatile agent is introduced, a rapid reduction in the inspired concentration requires an increase in the fresh gas flow. In this case, the wastage incurred is unavoidable. The Physioflex incorporated a charcoal canister to adsorb

volatile agents, but this has not been carried over to the Zeus because of its impracticality with desflurane.

Accumulation of unwanted gases in the breathing system

This is of considerable and abiding interest. It is axiomatic that if you put little gas into the breathing system, then little (or none) will come out. As a result of this failure to flush gases out of the system, any gases introduced which are not taken up by the patient or absorbed chemically will tend to accumulate. Such gases may be exhaled by the patient, be a contaminant of the medical gases, or result from a reaction with the chemical agents used for carbon dioxide absorption.

Substances exhaled by the patient

Substances exhaled by the patient include alcohol, acetone, carbon monoxide, and methane. Therefore, the use of low fresh gas flows is contraindicated in patients who are intoxicated, in uncompensated diabetic states, or who are suffering from carbon monoxide poisoning.

Carbon monoxide is produced as a metabolite of proteins; co-oximetry during a prolonged low-flow anaesthetic will usually show a steady and small rise in COHb. This is unlikely to exceed 3 or 4%, even after several hours. Significant methane is produced by *Methanobacterium ruminatum* in the large bowels of about 30% of the population. It is biologically inert and accumulates to much less than its lower flammability limit. Its relevance is that it absorbs infra-red light at 3.3 μm about 10 times as strongly as does halothane. This wavelength is used by some analysers for halothane recognition and estimation. This can lead to a 'mixed agent' warning which at best will be shown as such (e.g. Datex Ultima) or will cause an undetectable and usually unexpected inaccuracy of the analyser. At worst, during halothane anaesthesia, a falsely high end-tidal concentration will be reported with no other indication of a problem. This has caused problems during anaesthesia for horses.

Contaminants of medical gases

Potential contaminants of medical gas supplies include the lethal gases carbon monoxide and nitric oxide. While the risks of such contamination are vanishingly small, nitric oxide contamination caused a fatality in Bristol in 1965. More benignly, nitrogen and argon may accumulate and cannot be detected by infra-red analysers. Argon is biologically and chemically inert and may be regarded as 'part of the nitrogen'.

Products of reactions with absorbents

It has long been recognized that the chemicals used to absorb carbon dioxide may react with volatile anaesthetic agents. For example, trichloroethylene was known to break down to phosgene (COH_2) which is lethally toxic. It has long been known that halothane reacts with soda lime to produce hydrofluoric acid and bromochlorodifluoroethylene ('BCDFE' $BrClC=CF_2$), although no harm has been attributed to this.

Recent interest in such reactions started in 1994 with reports from the USA of carboxyhaemoglobinaemia in patients anaesthetized at the start of the Monday morning operating session using desflurane with the absorbent Baralyme. This was found to be due to a reaction between desflurane and *dry* Baralyme which produced carbon monoxide, the unused anaesthetic machines having been left switched on over the weekend, thereby allowing drying of the Baralyme by the 'safety' oxygen flow.[5] *In vitro* at 45°C with desflurane, the effluent gas from a Baralyme cannister contained 1.5% carbon monoxide.[6] Enflurane and isoflurane, like desflurane, contain a difluoromethoxy group (F_2HCO-) and will also produce carbon monoxide under such circumstances, but in significantly lower amounts. Baralyme is unique in that it contains 4.7% potassium hydroxide (KOH) as a catalyst. This is around three times as much as used to be found in 'soda lime' in the UK. Eger's group found that with 'soda lime' the amounts of carbon monoxide produced were much lower than with Baralyme and that it had to be dried out to less than 1.5% water (this requires it to be baked in an oven), whereas Baralyme produced significant amounts at 5% water content. Not surprisingly, there have been no cases of carboxyhaemoglobinaemia with desflurane reported in the UK, since Baralyme has never been licensed in this country.

The worldwide introduction of sevoflurane during 1995 and 1996 contributed to the concerns over production of toxic gases. In a reaction identical to that occurring with halothane, an olefin is produced. This product known as 'compound A' was considered by some to pose a risk of renal toxicity. This debate raged for some years with contrary evidence and strongly conflicting views coming from different workers, mainly in the USA. It is accepted that prolonged sevoflurane anaesthesia with low fresh gas flows results in proteinuria, glycosuria, and enzymuria. However, this is not, and has not been shown to be, associated with any clinical manifestations, even when such a technique is applied to patients with pre-existing biochemical renal abnormalities. Furthermore, it occurs if isoflurane is used in place of sevoflurane and seems also to be independent of carrier gas flow rate.[7,8]

Much of the laboratory work on renal toxicity was undertaken on rats, where compound A causes acute tubular necrosis at concentrations in excess of 250 ppm. It is now clear that these studies were invalid due to the marked differences between human and rat renal biochemistry. The generally held view (and that of the author) is that compound A has a considerable margin of safety in humans at the concentrations typically found during low-flow sevoflurane anaesthesia (around 15 ppm).

This specific concern about sevoflurane lead the Food and Drugs Administration (regulatory body for the USA) to set a 2 litre min^{-1} lower limit for carrier gas flow during sevoflurane anaesthesia. In December 1997, this was revised to 1 litre min^{-1} with a 2 MAC hour exposure limit for fresh gas flows between 1 and 2 litre min^{-1}. Canada and Australia still have a 2 litre min^{-1} limit

while Switzerland and Israel have adopted the revised Food and Drugs Administration guideline. Greece, Norway, and New Zealand have abandoned their flow rate restrictions; no restriction was ever imposed in the UK.

It seems that the issues of carbon monoxide and compound A production would have been of little more than academic relevance in the UK had they not led to marked changes in the formulation of absorbents in recent years. For many years 'soda lime' comprised calcium hydroxide with sodium hydroxide (typically around 2–3%) and KOH (typically around 1–2%). It was always taught that the strong alkalis were necessary to catalyse the reaction between calcium hydroxide and the carbonic acid formed by carbon dioxide and water. With the discovery that these strong alkalis were implicated in the production of both carbon monoxide and compound A, manufacturers took a variety of measures. Removal of all KOH was widely adopted and NaOH levels were reduced. Other approaches included the addition of a zeolite (Spherasorb, Intersurgical).

In 1999, a novel absorbent was introduced (Amsorb, Armstrong Medical) which contains no strong alkali.[9] Amsorb utilizes hygroscopic agents to ensure that the calcium hydroxide does not become dry. The main claimed benefits of Amsorb (now marketed as 'Amsorb Plus') are that it produces no carbon monoxide or compound A. All absorbents incorporate a chemical (acidity sensitive) to indicate exhaustion of the product. A trap for the unwary is that the colour change of exhausted absorbent will tend to revert if it is left to rest. Thus, apparently good absorbent in a machine that has not been used for some time may fail with remarkable rapidity. The immunity of Amsorb to this false indication is a definite advantage. Against this must be set its higher cost, somewhat reduced efficiency and the aforementioned doubts about the 'threat', now that KOH-containing absorbents are no longer marketed.

In November 2003, the Food and Drugs Administration issued a 'Dear Health Professional' warning.[10] This related to what now appears to be a total of 16 cases of overheating in breathing systems when sevoflurane was being used. Five of these cases occurred in Germany prior to 1999. The remainder were in the USA and involved the use of Baralyme. It appears that, yet again, the cause was a reaction between the volatile agent and dry, potassium-containing absorbent (Dräger reformulated their absorbents in1999, removing the KOH). The cases reported from the USA included melting of absorber canisters, smoke, and two explosions. No such incidents have ever been reported in the UK and none in Europe since 1999.[11–15]

Future developments

The development of more appropriate volatile agent dosing systems, in particular liquid injection, would greatly improve the ease of use of low carrier gas flows in clinical practice. Non-chemical systems for carbon dioxide removal are currently being developed and evaluated. Such systems should remove any lingering concerns about the generation of unwanted gases in the breathing system.

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Please see multiple choice questions 1–4