LOW FLOW ANAESTHESIA

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INTRODUCTION:

The technique of reusing the expired gas for alveolar ventilation after absorption of carbon dioxide can be traced to the very beginning of Anaesthesia when Dr. John Snow used caustic potash to absorb CO2 from the expired gas. This concept was considerably simplified by the introduction of “To and Fro” system by Waters and the circle system by Brian Sword, which utilised sodalime for absorption of CO2. It reigned supreme in the early half of this century when expensive and explosive agents like cyclopropane were utilised. The introduction of non-explosive agents like halothane and plenum vaporisers that performed optimally only in the presence of higher flows, resulted low flow anaesthesia becoming less popular. With the added knowledge of the disadvantages of using high percentages of O2 for prolonged periods and the necessity to use a second gas to control the percentage of oxygen, coupled with the complexities involved in the calculation of uptake of anaesthetic agents during the closed circuit anaesthesia, made this technique even less popular. However, the awareness of the dangers of theatre pollution with trace amounts of the anaesthetic agents and the prohibitively high cost of the new inhalational agents, have helped in the rediscovery of low flow anaesthesia.

DEFINITION

Low flow anaesthesia has various definitions. Any technique that utilises a fresh gas flow (FGF) that is less than the alveolar ventilation can be classified as ‘Low flow anaesthesia’. Baum et al. had defined it as a technique wherein at least 50% of the expired gases had been returned to the lungs after carbon dioxide absorption. This would be satisfied when the FGF was less than about two litres per minute.
Baker, in his editorial had classified the FGF used in anaesthetic practice into the following categories:

- **Metabolic flow**: about 250 ml/min
- **Minimal flow**: 250-500 ml/min.
- **Low flow**: 500-1000 ml/min.
- **Medium flow**: 1-2 l/min.

For most practical considerations, utilisation of a fresh gas flow less than 2 litres/min may be considered as low flow anaesthesia.

**The need for low flow anaesthesia.**

Completely closed circuit anaesthesia is based upon the reasoning that anaesthesia can be safely be maintained if the gases which are taken up by the body alone are replaced into the circuit taking care to remove the expired carbon dioxide with sodalime. No gas escapes out of the circuit and would provide for maximal efficiency for the utilisation of the fresh gas flow. The very nature of this system requires that the exact amount of anaesthetic agent taken up by the body be known, since that exact amount has to be added into the circuit. Any error in this could lead to potentially dangerous level of anaesthetic agent be present in the inspired mixture with its attended complications. Hence, there exists a need for a system that provided the advantages of the completely closed circuit and at the same time, reduced the dangers associated with it. Low flow anaesthesia fulfilled these requirements.

Low flow anaesthesia involves utilising a fresh gas flow which is higher than the metabolic flows but which is considerably lesser than the conventional flows. The larger than metabolic flows provides for considerably greater margin of safety and satisfactory maintenance of gas composition in the inspired mixture. Strict compliance to the uptake is not necessary. Hence, the conduct of anaesthesia is greatly simplified and at the same time provides for the economy of the fresh gas flows.
**Equipment**

The minimum requirement for conduct of low flow anaesthesia is effective absorption of CO₂ from the expired gas, so that the CO₂ free gas can be reutilised for alveolar ventilation. Two systems were commonly used in the past, i.e., “To and Fro” system introduced by Waters and the circle system introduced by Brian Sword. The ‘To and Fro’ system because of its bulkiness near the patient and other disadvantages has gone out of vogue. The circle system using large sodalime canisters is in common use. The circle system should have the basic configuration with two unidirectional valves on either side of the sodalime canister, fresh gas entry, reservoir bag, pop off valve, and corrugated tubes and ‘Y’ piece to connect to the patient. The relative position of fresh gas entry, pop off valve, and reservoir bag are immaterial as long as they are positioned between the expiratory and the inspiratory unidirectional valves that functions properly and CO₂ absorption is efficient at all times.

**Monitoring**

Inspired O₂ concentration should be monitored at all times if N₂O is used in more than 65% concentration, as one of the adjuvant gas. EtCO₂ monitoring seems to be necessary to ensure proper functioning of the absorber. If monitoring of end tidal anaesthetic concentration is available, the administration of low flow anaesthesia becomes very easy. In the absence of that a
few calculations have to be carried out for deciding on the amount of anaesthetic agent to be added to the system.

THE PRACTICE OF LOW FLOW ANAESTHESIA:

The practice of low flow anaesthesia can be dealt with under the following three categories:

1. Initiation of Low flow anaesthesia
2. Maintenance of Low flow anaesthesia
3. Termination of Low flow anaesthesia.

INITIATION OF LOW FLOW ANAESTHESIA.

Primary aim at the start of low flow anaesthesia is to achieve an alveolar concentration of the anaesthetic agent that is adequate for producing surgical anaesthesia (approximately 1.3 MAC). The factors that can influence the build up of alveolar concentration should all be considered while trying to reach the desired alveolar concentration. These factors can broadly be classified into three groups (fig. 1); 1) Factors governing the inhaled tension of the anaesthetic, 2) Factors responsible for rise in alveolar tension, 3) Factors responsible for uptake from the lungs thus reducing the alveolar tension.

Fig 1. Factors affecting the build up of alveolar tension
Factors governing the inhaled tension of the anaesthetic:

1. The circle system is often bulky and has a volume roughly equal to 6-7 litres. Besides this, the FRC of the patient, which is roughly 3 litres, together constitutes a reserve volume of 10 litres to which the anaesthetic gases and vapours have to be added. With the addition of FGF, the rate of change of composition of the reserve volume is exponential. The time required for the changes to occur is governed by the time constant, which is equal to this reserve volume divided by the fresh gas flow. This represents the time required for 67% change to occur in the gas concentration. Three time constants are needed for a 95% change in the gas concentration to occur. Hence, if a FGF of 1L/min is used, then 30 minutes will be required for the circuit concentration to reflect the gas concentration of the FGF. If the FGF is still lower, then correspondingly longer time will be required.

2. The functional residual capacity of the lung and the body as a whole contain nitrogen which will try to equilibrate with the circuit volume and alter the gas concentration if satisfactory denitrogenation is not achieved at the start of anaesthesia. Hence, as a prelude to the initiation of closed or low flow anaesthesia, thorough denitrogenation must be achieved with either a non-rebreathing circuit or the closed circuit with a large flow of oxygen and a tight fitting facemask.

3. The anaesthetic agent could be lost from the breathing system due to solubility of the agent in rubber, and permeability through the corrugated tubes. Though the amount of loss will be minimal, it should be considered at the start if the aimed anaesthetic concentration is low.

Factors responsible for rise in alveolar tension of the anaesthetic agent:

1. Concentration effect: The concentration effect helps in raising the alveolar tension towards the inspired tension, but hinders with it if an insoluble gas is present in the mixture. The rate of rise of alveolar partial pressure of the anaesthetic agent must bear a direct relationship to the inspired concentration. Higher the inspired concentration, the more rapid is the rise in alveolar concentration. At low inspired concentration, the alveolar concentration results from a balance between the ventilatory input and circulatory uptake. If the later removes half the anaesthetic
introduced by ventilation, then the alveolar concentration is half that inspired. The concentration effect modifies this influence of uptake. When appreciable volumes are taken up rapidly, the lungs do not collapse; instead the subatmospheric pressure created in the lung by the anaesthetic uptake causes passive inspiration of an additional volume of gas to replace that lost by uptake, thus increasing the alveolar concentration and offsetting the mathematical calculations. Similarly, if an insoluble gas (e.g., nitrogen) is present in the inspired mixture, as the blood takes up the anaesthetic gas, the concentration of the insoluble gas will go up in the alveoli, reducing the concentration of the anaesthetic agent.

2. Alveolar ventilation: The second factor governing the delivery of anaesthetic agent to the lung is the level of alveolar ventilation. The greater the alveolar ventilation, the more rapid is the rise of alveolar concentration towards the inspired concentration. This effect is limited only by the lung volume, the larger the functional residual capacity, the slower the wash in of the new anaesthetic gas.

Factors responsible for uptake from the lungs thus reducing the alveolar tension:

Uptake from the lung is the product of three factors: solubility of the agent in the blood, the cardiac output and the alveolar to venous partial pressure gradient.

1. Blood gas solubility: “Solubility” is the term used to describe how a gas or vapour is distributed between two media. At equilibrium, that is when the partial pressure of the anaesthetic in the two phases is equal, the concentration of the anaesthetic in the two phases might differ. This is calculated as a coefficient. When it is between blood and gas it is called blood gas solubility coefficient. If other things are equal, the greater the blood/ gas solubility coefficient, the greater the uptake of anaesthetic, and slower the rate of rise of alveolar concentration.

2. Cardiac output: Because blood carries anaesthetic away from the lungs, the greater the cardiac output, the greater the uptake, and consequently the slower the rate of rise of alveolar tension. The magnitude of this effect is related to the solubility: the most soluble agents are affected more than the least soluble agents.
3. Alveolar to venous partial pressure gradient: During induction the tissues remove all the anaesthetic brought to them by the blood. This lowers the venous anaesthetic partial pressure far below that of the arterial blood. The result is a large alveolar to venous anaesthetic partial pressure difference, which causes maximum anaesthetic uptake and hence lowers the alveolar partial pressure.

Considering the above mentioned factors at the start of anaesthesia, two facts become apparent:

1. Induction if performed using low flows would take an unacceptably long time.

2. If induction is done with an intravenous agent, unless special precautions are taken, it may take very long time to achieve the desired alveolar concentrations. Once the desired concentration is achieved, it will be difficult to change it. Hence, termination of action would take a long time after the discontinuation of the agents.

**Methods to achieve desired gas and agent concentration**

**Use of high flows for a short time:**

This is by and far the commonest and the most effective technique of initiating closed circuit. By using high flows for a short time, the time constant is reduced thereby bringing the circuit concentration to the desired concentration rapidly. Often, a fresh gas flow of 10L of the desired gas concentration and 2 MAC agent concentration is used so that by the end of three minutes (three time constants) the circuit would be brought to the desired concentration. The large flows and high agent concentration also compensate for the large uptake seen at the start of the anaesthesia. Mapleson\(^3\) using a spreadsheet model of a circle breathing system has calculated that, by using a FGF equal to minute ventilation and setting the anaesthetic agent partial pressure to 3 MAC, the end expired partial pressure of halothane will reach 1 MAC in 4 minutes and that of isoflurane in 1.5 minutes. The major advantages of this method are the rapidity with which the desired concentration is achieved, the ability to prevent unexpected raise in the agent concentration and the ability to use the commonly available plenum vaporisers to achieve the desired concentration. This also has the added advantage of achieving better denitrogenation, so
vital to the conduct of the low flow anaesthesia. The chief disadvantage would be the high flows required which would compromise on the economy of the gas utilisation and the need for scavenging systems to prevent theatre pollution. This period of using high flows for a short period at initiation goes by the name of "loading".

Prefilled circuit.

The second method is utilising a different circuit like Magills for preoxygenation. Simultaneously, the circle is fitted with a test lung and the entire circuit is filled with the gas mixture of the desired concentration. Following intubation, the patient is connected to the circuit thereby ensuring rapid achievement of the desired concentration in the circuit. But all the factors discussed above will be effective in preventing fast build up of the alveolar concentration to attain surgical anaesthesia.

Use of large doses of anaesthetic agents.

The third method consists of adding large amounts of anaesthetic agent into the circuit so that the circuit volume + FRC rapidly achieves the desired concentration as well as compensates for the initial large anaesthetic gas uptake. To execute this, the patient is connected to the circuit, which is filled with oxygen (used for preoxygenation), after intubation. Fresh gas flow is started with metabolic flows of oxygen and a large amount of nitrous oxide often in the range of 3-5 litres per minute. Oxygen concentration in the circuit, which gradually falls, is continuously monitored and the nitrous oxide flow is reduced once the desired oxygen concentration is achieved (33 - 40%). The obvious disadvantage of this method is the potential for errors and hypoxia if the oxygen monitor were to malfunction. Hence this method is seldom used for N2O. In the contemporary anaesthesia machines it is not possible to administer lesser than 25% of oxygen and the described technique cannot be executed.

The method discussed above is often used to build up the agent concentration in the circuit. The commonly used agents are halothane and isoflurane. This involves setting the VOC to deliver a large amount of the agent while using low to moderate flows so that the required amount
of vapour is added into the circuit. The usual requirement of anaesthetic agent is approximately 400 - 500 ml of vapour in the first 10 minutes which implies an average need of 40 - 50 ml of vapour per minute during the first 10 minutes. Most of the vaporisers allow a maximal concentration of 5% to be delivered. At a setting 5% in the vaporiser, with a FGF of one litre/minute, the required mass of 500 ml of vapour could be added to the circuit so that the alveolar concentration could be built up. The setting in the vaporiser can be brought down to 0.5 – 0.8 % after 10 minutes and titrated according to the surgical needs.

**Injection techniques.**

An alternative method for administering the large amounts of the agents is by directly injecting the agent into the circuit, a form of VIC^4,5,6,7,8. This is an old, time-tested method and is extremely reliable. Each ml of the liquid halothane, on vaporisation yields 226 ml of vapour and each ml of liquid isoflurane yields 196 ml of vapour at 20°C. Hence, the requirement of about 2ml of the agent is injected in small increments into the circuit. The high volatility coupled with the high temperature in the circle results in instantaneous vaporisation of the agent. The injection is made through a self sealing rubber diaphragm covering one limb of a metal t piece or a sampling port, inserted into either the inspiratory or the expiratory limb (fig. 2).

Fig 2. Closed circuit configuration for injection technique
The injection is made using a small bore needle and a glass syringe. Placing a gauze piece or a wire mesh inside the T piece often helps in the vaporisation of the liquid. The intermittent injections are often made in 0.2-0.5 ml aliquots manually. Doses should never exceed 1ml at a time. Doses exceeding 2 ml bolus invite disaster. Intermittent injections can often be easily substituted with a continuous infusion with the added advantage of doing away with the peaks and troughs associated with intermittent injections.

The exact dose to be used is calculated thus:

$$\text{Priming dose (ml vapour)} = \text{Desired concentration} \times \{(\text{FRC} + \text{Circuit volume}) + (\text{Cardiac output} \times \text{BG Coeff.})\}$$

The Cardiac output and the FRC can be estimated for the patient based on standard nomograms. This priming dose is the dose required to bring the circuit volume + FRC to the desired concentration and is injected over the first few minutes of the closed circuit anaesthesia. Besides this, an amount of agent necessary to compensate for the uptake of the body must also be added and this is calculated depending on the uptake model being used (vide infra).

**THE MAINTENANCE OF LOW FLOW ANAESTHESIA.**

This is the most important phase as this is stretched over a period of time and financial savings result directly from this. This phase is characterised by

1. Need for a steady state anaesthesia often meaning a steady alveolar concentration of respiratory gases.
2. Minimal uptake of the anaesthetic agents by the body.
3. Need to prevent hypoxic gas mixtures.

Since the uptake of the anaesthetic agent is small in this phase, the low flow anaesthesia is eminently practical. Adding small amounts of the anaesthetic gases to match the uptake and providing oxygen for the basal metabolism should suffice. If CCA is used, this would be directly equal to the uptake and hence provides for the monitoring of the oxygen consumption and the
agent uptake. If low flow anaesthesia is used, then besides the uptake, the amount of gas, which is vented, is also added to the circuit to maintain steady state anaesthesia.

**Management of the oxygen and nitrous oxide flow during the maintenance phase:**

The need to discuss the flow rates of N2O and O2 arises specifically because of the possible danger of administration of a hypoxic mixture. Let us analyse the following example. 33% oxygen is set using a flow of 500 ml of O2 and 1000 ml of N2O. Oxygen is taken up from the lungs at a constant rate of about 4 ml/kg/min. N2O is a relatively insoluble gas and after the initial equilibration with the FRC and vessel rich group of tissues, the uptake is considerably reduced. In this situation, there is a constant removal of O2 at a rate of 200 - 250 ml/min, where as the insoluble gas N2O uptake is minimal. Hence the gas that is partly vented and partly returning to the circuit will have more N2O and less of O2. Over a period of time, due to the mixing of fresh gas that has 66% N2O and the expired CO2 free gas that has N2O much higher than that, the percentage of N2O will go up and that of O2 will fall, sometimes dangerously to produce hypoxic mixtures. For most practical purposes, in the absence of oxygen analyser the following technique is safe to use. A high flow of 10 lit/min at the start, for a period of 3 minutes, is followed by a flow of 400 ml of O2 and 600 ml of N2O for the initial 20 minutes and a flow of 500 ml of O2 and 500 ml of N2O thereafter. This has been shown to maintain the oxygen concentration between 33 and 40 % at all times.

**The Gothenburg Technique:**

Initially high flows, oxygen at 1.5 l/min and nitrous oxide at 3.5 l/min had to be used for a period of six minutes after the induction of anaesthesia and this constitutes the loading phase. This is followed by the maintenance phase in which the oxygen flow is reduced to about 4ml/kg and nitrous oxide flow adjusted to maintain a constant oxygen concentration in the circuit. The usual desired oxygen concentration is about 40%. The use of an oxygen analyser is very important since the nitrous oxide added is directly based on its readings and hence any errors would be dangerous.
Other authors have made similar recommendations\textsuperscript{10,11,12,13,14}. Most of the authors opine that the oxygen consumption under anaesthesia is about 200 - 250 ml. However, there is wide disparity in the amount of nitrous oxide to be added into the circuit. This controversy is consistent with the basic controversy surrounding the uptake of the anaesthetic agents and is dealt with in detail in a later stage.

\textbf{Management of the potent anaesthetic agents during maintenance phase.}

This is easily accomplished by dialling in the calculated concentration on the plenum vaporiser for the flow being used. For example, suppose the anaesthetic uptake for a desired concentration of 0.5% halothane is 7.5ml/min (vide infra). If a FGF of 500ml/min is being used, then the dial setting should be 1.5% for at this setting and for the used flow, the total vapour output would be 7.5ml/min. If a flow of 1000ml/min is being used, then the dial setting should be 0.8%. In practice the actual dial setting often over estimates the actual output since the plenum vaporiser underdelivers the agent at low flows. Hence, the dial setting is fine-tuned depending on the endpoints being achieved.

During completely closed circuit anaesthesia, the most popular method of adding agents into the circuit is by the injection technique. This is often used to initiate the closed circuit anaesthesia as described earlier. Later, the same setup is used to continue the anaesthesia by adding either small boluses or by constant infusion into the circuit. The dose to be added depends on the uptake model being used for the conduct of the closed circuit. The endpoint for adding the agent can be the achievement of the desired end tidal agent concentration, measured using an agent analyser. This would be the most accurate method. The end point may also be based on the haemodynamic stability\textsuperscript{15}.

Simple rule of the thumb techniques\textsuperscript{16,17} for adding the anaesthetic agents into the circuit both during the loading phase and the maintenance phase has been suggested.
Weir and Kennedy\textsuperscript{4} recommend infusion of halothane (in liquid ml/hr) at the following rates for a 50 kg adult at different time intervals.

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Rate (ml/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 5 min</td>
<td>27</td>
</tr>
<tr>
<td>5 - 30 min</td>
<td>5.71</td>
</tr>
<tr>
<td>30 - 60 min</td>
<td>3.33</td>
</tr>
<tr>
<td>60 - 120 min</td>
<td>2.36</td>
</tr>
</tbody>
</table>

These infusion rates had been derived from the Lowe's theory of the uptake of anaesthetic agent (vide infra). They had approximated isoflurane infusion (in liquid ml/hr) based on the Lowe's formula as follows:

- 0 - 5 min. \(14 + 0.4X\) wt. ml/hr.
- 5 - 30 min. \(0.2 \times\) initial rate.
- 30 - 60 min. \(0.12 \times\) initial rate.
- 60 - 120 min. \(0.08 \times\) initial rate.

For halothane infusion, they had suggested that the above said rates be multiplied by 0.8 and for enflurane, multiplied by 1.6. These rates had been suggested to produce 1.3 MAC without the use of nitrous oxide. The infusion rates had to be halved if nitrous oxide is used.

The other salient points to be considered during the maintenance phase are the following:

a) Leaks must be meticulously sought for and prevented since they would decrease the efficacy of the system. Flows must be adjusted to compensate for the gas lost in the leaks. b) Most of the gas monitors sample gases at the rate of 200 ml/min, which may be sometimes as high as half the FGF. Hence, care must be taken to return the sample back to the circuit to maximise the economy of FGF utilisation. Some gas analysers like Ohmeda Rascal add air to the sample exhaust. This if returned to the circuit would result in dilution of the anaesthetic mixture and accumulation of nitrogen within the circuit and hence should be vented. This mandates utilisation of a flow adequate to compensate for this loss. Recent studies\textsuperscript{18} have shown that venting of the gas from the analyser does not alter the dynamics to any large extent and can safely be done.
CONTROVERSIES IN THE UPTAKE MODELS OF ANAESTHETIC AGENTS

EXPONENTIAL OR LINEAR?

Knowledge of uptake of anaesthetic agent is very important in the practice of closed and low flow anaesthesia since, the very technique calls for the addition of an amount of anaesthetic agent which is taken up by the body. In fact, mutually contradicting models exist on the uptake of anaesthetic agents. The Lowe's theory \(^{13,14}\) which has wider acceptance ascribes the anaesthetic uptake to an exponential model. It states that the uptake of agent is inversely proportional to the square root of the time, implying that the uptake decreases exponentially with time. It necessitates calculation of unit dose (Appendix 1). This unit dose is the amount of anaesthetic agent to be added to the closed circuit during the time intervals of 0-1 min, 1-4 min, 4-9 min, 9-16 min, and so on. Besides that the circuit and the FRC and the circulating blood of the patient had to be brought to the desired concentration with a prime dose.

Prime dose = \(((\text{circuit volume} + \text{FRC}) + (Q \times \lambda)) \times \text{desired concentration.}\)

This prime dose had to be added into the circuit during the first 9 minutes of closed circuit anaesthesia.

The practical implication of this is that to maintain closed circuit, one must calculate the agent and gases to be added into the circuit using hair-splitting exponential equations, often frightening the anaesthetist. It has been one of the main causes for the reluctance in the widespread usage of the closed circuit anaesthesia.

In total contrast to this exponential theory is the linear model proposed by CY Lin \(^{12,19}\). He states that the uptake of anaesthetic agents is a near constant over the clinically important concentrations. Hence, he advocated adding the anaesthetic agent as a constant rate infusion into the circuit throughout the anaesthetic procedure. Lin had contended that the FRC constituted an extension of the breathing circuit and the washin into it could not be considered as uptake by the body. He had suggested a simple method of conducting the closed circuit anaesthesia: It had
consisted of using a high flow of nitrous oxide and oxygen (6 L/min and 4 L/min respectively) for 3 minutes (three time constants). At the end of 3 minutes, the flows had been reduced to metabolic flows and closed circuit started. Potent agents had been added either through a VOC (like a copper kettle) or by direct injection into the circuit. The anaesthetic agent required to washin the circuit volume and the FRC of the patient had constituted the prime dose and it should be added to the circuit during the first ten minutes, besides the dose required to compensate the uptake of the agent. The formula to calculate the amount of agent to be added into the circuit to equal the uptake had been:

\[
\text{uptake of anaesthetic agent} = \text{desired concentration} \times \text{alveolar ventilation} \times \text{fractional uptake (ml of vapour)}
\]

The fractional uptake (= 1 - \(F_A / F_I\)) for halothane had been calculated as 0.5 and that for enflurane, as 0.4. He had concluded that anaesthesia thus conducted produced a nearly constant inspired and expired concentration implying that the uptake of the anaesthetic agents had been a near constant.

Unfortunately very little literature exists on the efficacy of either of these models. The study conducted to compare these two models in our Institute, revealed that predictive performance of both the models were statistically similar, and linear uptake model had scope for improvement where as the exponential model had no such scope. Lin's linear model however has a distinct superiority in the form of simplicity.

**Our subsequent experience in simplifying low flow anaesthesia**

100 patients of ASA physical status 1 or 2 undergoing general surgical procedures under general anaesthesia were induced with thiopentone and intubation facilitated with succinylcholine after preoxygenation with 100% oxygen for 3 minutes. Total FGF of 100 ml / kg was used for initial 10 min, \(N_2O\) to \(O_2\) ratio of 60:40 along with 1.5% isoflurane, after connecting patients to the circle breathing system. FGF was reduced to 300ml/min of \(N_2O\) and 300ml/min of \(O_2\) at the end of 10 min but the dial setting of 1.5 % isoflurane was not changed for the rest of the period. In the control
group, after the initial 10 minutes, patients were given a flow of 4L/min in the ratio of 65:35 of N₂O:O₂.

During the course of low flows, inspired O₂ concentration never fell below 0.3(30 v/v %). Initially as N₂O was being used up rapidly, initial inspired O₂ concentration increased and the End tidal O₂ concentration was higher than the inspired O₂ concentration. After a period of 20 minutes, N₂O usage decreased and a period of constant uptake is present. Least value of inspired O₂ concentration recorded was 0.31. After one hour the mean value of FiO₂ was 0.41(41 v/v %) and 0.39(39 v/v %) at the end of 2 hours (fig 3).

For the first five minutes in high flows, the inspired isoflurane concentration was around 1.1 v/v%. This value settled to around 0.7v/v%. This value was more or less constant through out the period. Initially, the concentration of end tidal isoflurane was 0.59±0.027. This value rose during high flow period to 0.78±0.015 v/v%. During low flows the mean concentration was 0.55± 0.007 v/v%.

![Changes in O₂ & N₂O conc over time](image-url)
The combined MAC value computed from the end tidal concentration of N2O and Isoflurane was maintained at 1.1 to 1.2 MAC and this along with IV narcotics provided adequate depth of anaesthesia for all patients (fig 4). N₂ accumulation was found to decrease during the initial high flow period and subsequently in the low flow period, there was a gradual increase in its concentration up to a mean of around 3. But this did not necessitate change in flow rates to wash it off as FiO₂ did not fall below 0.31. Conduct of anaesthesia proved to be safe with no adverse outcome.

Total gases consumed for 120 min were calculated and the usage was 66 L of N₂O, 55 L of O₂ and 9.3 ml of liquid Isoflurane in the low flow group. In the high flow group, 176.5L of O₂ and 320 L of N₂O and 25.83 ml of liquid isoflurane were used. The total cost in high flows was Rs. 532.69 and Rs. 192 in the low flow group leading to a cost reduction of 64%.

**Sevoflurane controversy**

Sevoflurane, like all currently used volatile anaesthetics, is degraded by carbon dioxide absorbents. The most significant degradant is a haloalkene known as "compound A" being nephrotoxic in rats at an exposure of 150 – 340 ppm-h. Applying low-flow sevoflurane in
volunteers one study group found an intact renal function using validated markers of renal function (creatinine clearance, serum BUN and creatinine), but a transient increase of experimental markers of renal function (urine excretion of protein, glucose, and certain tubular enzymes). This “transient renal injury” was attributed to compound A. Additionally, the study group claimed a threshold value of compound A of about 150 ppm-h to induce transient renal injury and postulated a similar renal sensitivity to compound A in humans as in rats.

However, over the years these results and conclusions could not be confirmed by other study groups. Several studies found that the renal uptake and metabolism of the glutathione and cysteine conjugates of compound A are different in rats and humans. Thus, the threshold for nephrotoxicity of compound A in rats does not apply to humans. Furthermore, summarizing all data about protein excretion on postoperative day 3 (as “sensitive marker” of renal dysfunction) after low-flow sevoflurane from surgical patients and volunteers did not show a threshold even though exposures up to almost 500 ppm-h had been documented.

Considering all of the studies published to date in patients or volunteers (other than that reported by Eger et al.), and even using proteinuria as a so-called “sensitive” (albeit unvalidated and experimental) marker of renal dysfunction, there is no difference between the renal effects of low-flow sevoflurane and other anaesthetics (isoflurane, desflurane, enflurane and propofol). This also applies to patients with preexisting renal impairment. Furthermore, there have been no case reports of compound A-associated renal injury reported in humans so far. Thus, low-flow, minimal-flow and closed-loop anaesthesia with sevoflurane is as safe as anaesthesia with other anaesthetics. In conclusion, compound A is no longer a matter of concern.

Compound A is produced by degradation of sevoflurane in the presence of soda lime or Baralyme. As such, it is not a metabolite produced by biotransformation of sevoflurane in the body, but is rather a degradation product generated in the anaesthesia circuit. Changing the composition of the absorbent by eliminating the potassium hydroxide has reduced the formation of compound A to a large extent. Eliminating the NaOH also has made it safer. Amsorb® plus is now available in India.
<table>
<thead>
<tr>
<th>Absorbent</th>
<th>Hydroxide content</th>
<th>Compound A</th>
<th>Menthol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baralime</td>
<td>KOH 4.7%</td>
<td>64.6</td>
<td>373</td>
</tr>
<tr>
<td></td>
<td>Ba(OH)₂ 7.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodalime</td>
<td>KOH 2.9%</td>
<td>56.4</td>
<td>606</td>
</tr>
<tr>
<td></td>
<td>NaOH 1.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofnolime</td>
<td>NaOH 2.6%</td>
<td>2.2</td>
<td>91</td>
</tr>
<tr>
<td>Amsorb® plus</td>
<td>Ca(OH)₂</td>
<td>Negligible</td>
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<tr>
<td></td>
<td>CaCl₂</td>
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**TERMINATION OF LOW FLOW ANAESTHESIA.**

Unlike the initiation or the maintenance of the closed circuit, termination is less controversial. There are only two recognised methods of termination of the closed circuit. They are as follows:

Towards the end of the anaesthesia, the circuit is opened and a high flow of gas is used to flush out the anaesthetic agents which accelerates the washout of the anaesthetic agents. This has the obvious advantage of simplicity but would result in wastage of gases.

The second method is the use of activated charcoal⁸. Activated charcoal when heated to 220°C adsorbs the potent vapours almost completely. Hence, a charcoal-containing canister with a bypass is placed in the circuit. Towards the end of the anaesthesia, the gas is directed through the activated charcoal canister. This results in the activated charcoal adsorbing the anaesthetic agent resulting in rapid recovery and at the same time, reducing theatre pollution. Nitrous oxide, due to its low solubility is washed off towards the end by using 100% oxygen.

To conclude the low flow closed circuit anaesthesia has many advantages to offer. To list a few,

1. Enormous financial savings due to use of low fresh gas flows as well as the agent.
2. High humidity in the system leads to fewer post anaesthetic complications.
3. Maintenance of body temperature during prolonged procedures due to conservation of heat.

4. Reduction in the theatre pollution.

The perceived disadvantages are not real:

1. The need to accurately adjust the flows of gases. The system is inherently stable once a steady state is reached and small errors in the dosage of the agents or the gases would be of no concern.

2. Accumulation of trace gases$^{20}$. It has, however, been often overestimated$^{21}$.

3. Need for monitoring equipment. Oxygen monitor is necessary but not mandatory if the recommended flowrates are used. EtCO2 monitor is indicated to ensure satisfactory CO₂ absorption and maintenance of normocarbia.

With a proper understanding of the concepts of practice, the low flow anaesthesia technique can safely be used in all surgical procedures lasting more than an hour.

APPENDIX

<table>
<thead>
<tr>
<th>Company</th>
<th>Product Name</th>
<th>H₂O%</th>
<th>NaOH%</th>
<th>KOH%</th>
<th>Ca(OH)₂%</th>
<th>Significant Other</th>
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<tbody>
<tr>
<td>Allied Healthcare/Chemetron</td>
<td>Baralyme®</td>
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<td>&lt;5</td>
<td>73</td>
<td>Ba(OH)₂</td>
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<td>Allied Healthcare</td>
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<td>3</td>
<td>0.0</td>
<td>&gt;75</td>
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<td>W.R. Grace and Company</td>
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<td>3.7</td>
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<td>0.0</td>
<td>79 – 82</td>
<td>CaCl₂</td>
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<td>~3</td>
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<td>1 – 3</td>
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<td>Sodalime</td>
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REFERENCES


