Acta Anaesth. Bel., 2023, 74 (1): *35-41*

Review

Low Flow Anesthesia – Mission Impossible?

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Unstructured abstract

Because low flow anesthesia reduces waste of environmentally unfriendly inhaled anesthetics, it is coming in the spotlights – again. Despite a detailed theoretical description, considerable teaching efforts of this simple technique have not succeeded in consistently lowering fresh gas flows (FGF) during manual control[1]. Worse, even though technology has solved the hurdles of manual delivery and the technology is widely available, we fail to maximally implement it. The delivery of inhaled anesthetics with high FGF prior to securing the airway remains common practice. We fail to consistently adjust MAC to age and poorly titrate opioids to reduce the fraction of the MAC we administer. We fail to incorporate hysteresis which is reflected in the use of excessively high FGF and vaporizer settings during wash-in and in the failure to maintain low FGF prior to emergence ("coasting"). By failing to fully appreciate the quantitative effects of the delivery if inhaled anesthetics we miss the opportunity to reduce waste to the absolute minimum. Belief and myth are strong when the environmental impact of inhaled anesthetics is considered. We need better, detailed life cycle analyses with low flow data before making claims pro/con inhaled/TIVA. We tend to lose sight of perspective, and have to continue to weigh the impact of drug selection on patient care.

Introduction

Terms like "high", "medium", "low", "minimal", or "metabolic" FGF serve no purpose except for causing confusion. There is no arbitrary "L/min" that defines "low flow". The better term (proposed by Sem Lampotang) would be "lower flow anesthesia", the use of any FGF lower than what *you* are using today. Instead of using confusing terms (like high, medium, minimal, etc.) the exact FGF should be quoted. The use of "definitions", "formulas" and "recipes" detracts from the appeal of lowering FGF - lower flow anesthesia is actually very easy to practice when a few basic concepts are taken into account.

The examples in the text will focus on the use of sevoflurane in O_2/air in an average adult. Amounts of sevoflurane can be expressed in mL of vapor or mL of liquid (1 mL liquid = 181.5 mL vapor at 1 atm and 20°). The concentrations of sevoflurane along its partial pressured cascade will be referred to as the delivered (= vaporizer dial setting), inspired, and end-expired concentration, abbreviated as FDsevo, FIsevo, and FETsevo, respectively.

Teaching lower flow anesthesia

Let us consider what is happening from a quantitative point of view 30 min into an anesthetic during which FETsevo has been maintained at 2% (Figure 1). Based on uptake data in humans[2], we calculated FDsevo (left Y-axis, black line) required to attain the same FETsevo of 2% over a range of FGF (X-axis) and the amount of sevoflurane waste (mL vapor per minute) (right Y-axis, blue line). It is immediately obvious why lowering FGF is advantageous: sevoflurane

Presented at the Annual Meeting of the Belgian Society of BeSARPP, November 19, 2022, The Square, Belgium.

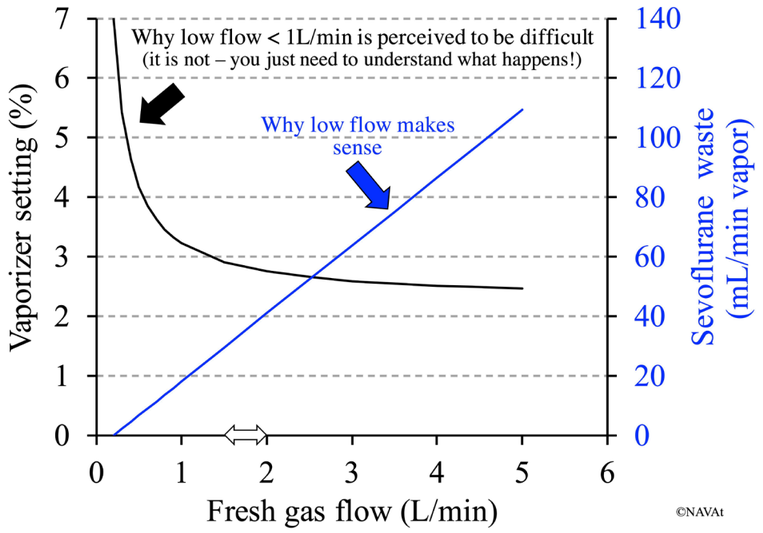

Fig. 1 — Quantitative aspects of low anesthesia.
All possible FDsevo (left Y-axis) - FGF (X-axis) combinations (black line) that attain FETsevo at 2% 30 min into an anesthetic during which FETsevo has been maintained at 2%. Right axis represents corresponding sevoflurane vapor waste (mL/min; blue line). Data based on calculations using published uptake data in humans[2]. See text for details.

waste (blue line) is reduced proportionally with FGF. That is why lowering FGF makes sense. However, lowering the FGF has practical implications: the lower the FGF, the higher FD has to be (black line). This is caused by rebreathing of exhaled gas in the circle breathing system. The lower the FGF, the more exhaled gas will have to be used instead of fresh gas to fill up the bellows to maintain minute ventilation. In other words, the inspired gas will consist of an increased amount of exhaled gas (minus CO_2 which is removed by the CO_2 absorber). Consequently, more exhaled gas will dilute the fresh gas mixture coming from the common gas outlet of the anesthesia workstation, which will decrease FIsevo and thus FETsevo. The clinician has to compensate for this dilution by increasing the FDsevo. In the average adult, this dilution effect starts to become especially pronounced once the FGF is lowered well below 1 L/min. This is the reason why intuitively many clinicians use a FGF of 1.5 - 2 L/min (white arrow on FGF axis).

While the above calculations are available from the authors upon simple request, it has to be clear one does NOT need complex numbers, models, calculus or formulas to use low flow anesthesia: understanding some basic concepts, having a gas analyzer, and a willingness to reduce FGF is sufficient. The consequences of these basic concepts are presented

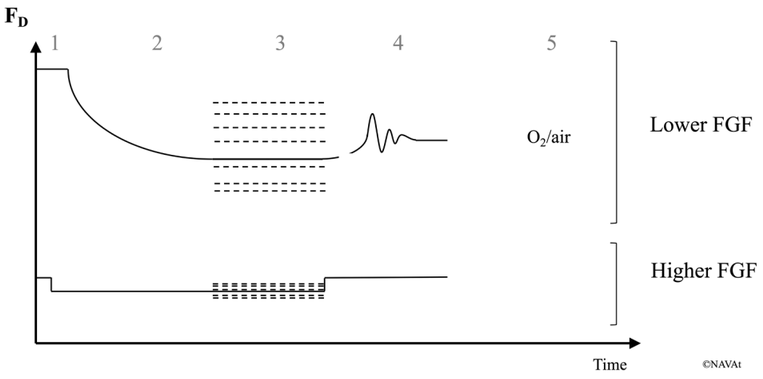

Fig. 2 — Basic concepts of low flow anesthesia.
Basic concepts that apply when lowering fresh gas flows (FGF) during different phases of the anesthetic. Upper line(s) = lower FGF, lower line(s) = higher FGF.

in a slightly different way in Figure 2, comparing FD adjustments (FD, Y-axis) needed to maintain the same FET with high FGF (bottom lines) and low FGF (especially with FGF < 1 L/min) (top lines). Five lessons can be learned, with the following numbers referring to those in Figure 2. One: with low FGF (especially < 1 L/min) it will take longer to wash-in the agent. This can be overcome to a large degree by using the maximum FD. Note that the combination of high FGF and low FD is far more wasteful than the use of low FGF and high FD. This can also be observed in Figure 1: the combination of a lower FGF and higher FD generates less waste than the combination of a high FGF and lower FD. While one may be inclined to use a high FGF and relatively high FD during initial wash-in, this practice should be abandoned as much as possible (see further). Two: especially during the first 10 - 15 min of the anesthetic the FD will have to be higher with lower FGF and more adjustments may be needed because the initial high patient uptake is decreasing rapidly during this period (saturation of the vessel rich group). This can be perceived as distracting because it coincides with the busy post-induction period. Properly managing and maintaining low FGF during this period though is critical to minimize cumulative waste over the entire procedure. Three: FD variability increases when FGF are lowered, especially with FGF well below 1 L/min. This means that it will be difficult to predict what FD to use, not only during the beginning of the anesthetic but also during the maintenance phase when uptake is only decreasing very slowly. For example, during near-closed circuit conditions (FGF range 200 - 400 mL/min), the required FD may differ up to 100% between patients because uptake differs up to 100% between patients (Figure 2)[3]. FET monitoring will guide the clinician. Four: if a new FET target needs to be attained during the maintenance phase, this will occur slowly when a low FGF is used unless the clinician uses a large FD change to speed up the process. This process of adjusting FD up and down to attain the target FET is a feedback system that will cause the FET to oscillate (Figure 2). Five: the dilution of fresh gas by rebreathed gas not only affects the anesthetic agent concentration, but also the O_2 concentration. When the FGF is lowered, the inspired O_2 concentration (FIO_2) will no longer match the FDO_2. This explains why the use of air with a FGF < minute ventilation can cause a hypoxic mixture[4]. To prevent this from happening, the clinician has to increase the proportion of O_2 in the fresh gas, guided by the monitored FIO_2.

The above five basic concepts should guide the clinician seeking to lower FGF. Translating it into practice is simple: after having secured the airway, start with 1 L/min FGF, set FDsevo at 8%, and lower FGF more after wash-in. Next, adjust the vaporizer and O_2 settings guided by gas analyzer readings. Just apply the above principles. It is really that simple. With experience, every clinician will develop one's own FGF - FD sequence. Welcome to the green operating room!

Target controlled low flow delivery

Alas, teaching alone does not help to consistently and persistently lower fresh gas flows during manual control[5]. In addition, only a handful of "closed circuit enthusiasts" will consistently reduce waste to the absolute minimum. Fortunately, technology has solved the hurdles of manual agent and O_2 delivery, putting us on the road to consistently minimize waste. Figure 3 again illustrates the rationale for reducing FGF for a procedure during which FETsevo has been maintained at 2%: cumulative sevoflurane waste decreases proportionally with FGF[2,6,7]. But how low can we go? The minimum amount of liquid sevoflurane needed to maintain FETsevo at 2% for 1h in the average adult is ~ 7 mL (6 mL body uptake, 1 mL to prime lungs and circuit (Figure 3)[2]. The minimum O_2 FGF that has to be used is the patient's O_2 consumption, assuming no circle breathing system leaks are present.

The algorithms used by the workstations in target controlled low flow mode seek to attain the target concentrations in a timely manner while simultaneously seeking to minimize waste. The different workstations handle agent and carrier gas delivery in a different manner, resulting in small differences in how the target agent and O_2 concentrations are reached (Figure 4). All anesthesia workstations consistently reduce agent and carrier gas waste. Their target maintenance FGF ranges from closed (average 180 ml/min) to 500 mL/min, resulting in a cumulative sevoflurane consumption of 6.8 to 10.9 mL needed to maintain a 2% FETsevo for 1h.

Unfortunately, the ingenuity with which engineers have conceived these systems is sometimes surpassed by the "creativity" with which some clinicians defeat the purpose of these systems. Some clinicians simply fail to use the feature and do not activate the target control mode. Some only activate the target control mode 5 to 10 min into the anesthetic in the mistaken belief that the oscillating FGF (Figure 4, left upper pane) or exponential decreasing FGF (Figure 4 right upper pane) represents a failure of the workstation to adequately reduce waste. In proceeding to manage the FGF and vaporizer settings themselves they are actually failing to realize this constitutes normal functional behavior of the workstation. Others limit the lowest FGF they allow the workstation to use to

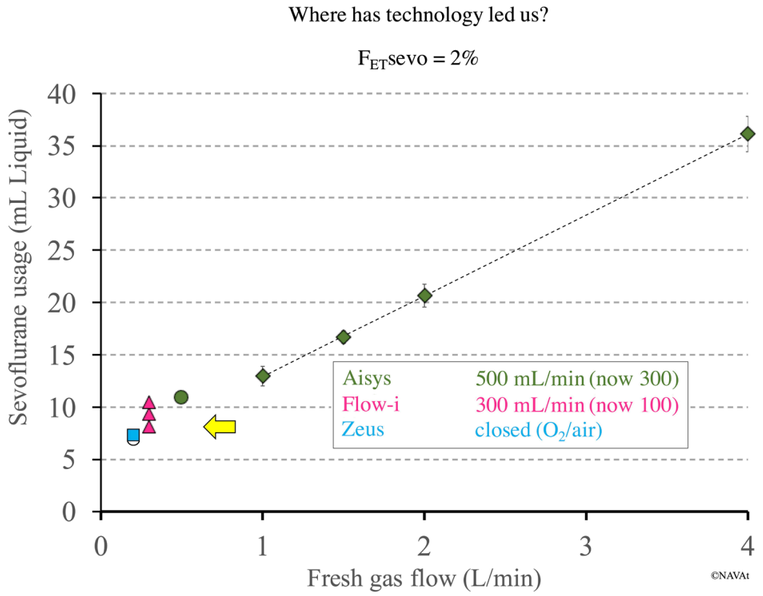

Fig. 3 — How much can target controlled delivery reduce waste?
Lowering FGF with the Aisys (dashed line) proportionally reduces the cumulative amount of sevoflurane (mL liquid) needed to maintain 2% FETsevo for the first hour. The minimum amount of liquid sevoflurane that is needed to maintain 2% FETsevo for 1 hour is 7 mL (6 mL body uptake, 1 mL to prime lungs and circuit), and the minimum O_2 needed is the patient's O_2 consumption. All modern anesthesia workstations consistently reduce agent and carrier gas waste when used in target controlled low flow mode: Aisys (yellow circle), Flow-I (pink triangles), and Zeus (blue diamond). The Zeus can work truly closed (i.e. the amount of liquid sevoflurane that is needed to maintain 2% FETsevo for 1 hour is 7 mL). See text for details.

2 L/min in the mistaken belief of achieving faster target changes, because of a vague notion of safety, or because of the completely outdated concern of compound A toxicity[8]. Occasionally the lowest possible default FGF setting was found not to have been installed, leaving it up to the clinician to lower it at the start of every new case.

Unfamiliarity with the features a work station has to offer is another impediment. For example, one workstation offers a selection of different wash-in rates, which helps to reduce waste during wash-in. Selecting the fastest rate, however, prompts the workstation to increase to FGF at or above minute ventilation. If always used in the fastest mode, the tool will not serve the purpose for which it was designed in the first place. The desired FET does not have to be achieved within one minute!

The use of inhaled agents with high FGF prior to securing the airway

The single most wasteful technique that one can use is that of delivering inhaled anesthetics with a high FGF in the period between intravenous induction of anesthesia and securing the airway. DO NOT TURN ON THE VAPORIZER PRIOR TO SECURING THE AIRWAY. With the use of for example 8 L/min FGF and a FDsevo of 4% for 3 min, approximately 960 mL sevoflurane vapor or 5.3 mL liquid sevoflurane will have been consumed. To put this in perspective, one only has to consider that the amount needed to prime the circuit and lung and provide for patient uptake to maintain a 1.5% end- expired sevoflurane concentration for 1 hour is only ~ 5.25 mL sevo liquid: in just 3 minutes one will waste as much anesthetic agent as is used during entire case managed with the lowest possible FGF (closed circuit delivery). The first five minutes of an anesthetic are crucial to minimize waste if one manually controls the flow meters and vaporizer settings[9]. If anesthetic depth is judged inadequate during this period, an additional propofol bolus (often left over after induction) is a better choice. Next, first secure the airway, start ventilation, and only then start agent delivery, either manually controlled (e.g. with 1 L/min FGF) or target controlled (by activating target controlled delivery).

Which concentration to target?

Having secured the airway and activate target control low flow delivery, a target FETagent has to be

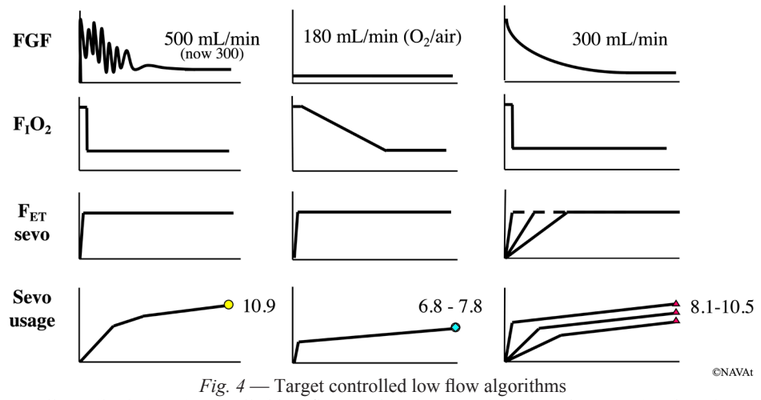

Fig. 4 — Target controlled low flow algorithms
All anesthesia target controlled low flow workstations consistently reduce agent and carrier gas waste but do so in a slightly differently manner: Aisys (GE) (left column), Zeus (Drager) (middle column) or Flow-i (Getinge) (right column). FGF = fresh gas flow (FGF, top line); FIO_2 = inspired O_2 concentration; FET sevo = end-expired sevoflurane concentration; sevo use = mL of liquid sevoflurane (relevant for conditions described in text).

entered. Choosing this number has a direct impact on anesthetic agent use and/or waste: lowering the target FETagent by 50% will lower use and/or waste by 50%. Age and drug interaction affect this number.

We need to properly adjust the target FETagent to the age adjusted fMAC (fraction of the median end-expired concentration). For example, MAC for sevoflurane is 2% for a 25 year old but only 1.4% for a 75 year old person, a 30% reduction. Modern machines calculate MAC - provided you have entered the patient age!

The target FETsesvo also has to take into account drug synergies, especially those of opioids. Intraoperatively, opioids are still the most widely used adjunct agents administered concomitantly with inhaled anesthetics[10,11]. Figure 5 displays all possible combinations of FETsevo (Y-axis,) and fentanyl

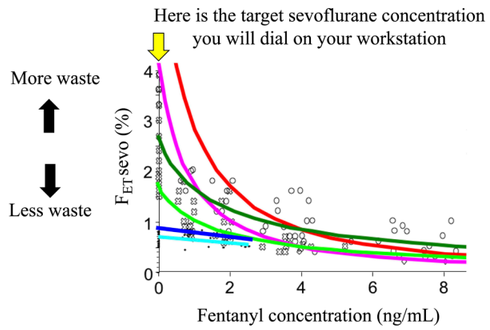

Fig. 5 — Opioid – inhaled agent synergy
Isoboles describing all possible combinations of sevoflurane end-expired (steady-state) concentrations and fentanyl (steady-state) plasma concentrations that result in the same likelihood of unconsciousness (light blue 50% probability, dark blue 95% probability), immobility (light green 50% probability, dark green 95% probability) and lack of autonomic response (pink 50% probability, red 95% probability). See text for details.

effect site concentrations (X-axis) that ensure a similar probability of unconsciousness (light blue 50% probability, dark blue 95% probability), immobility after incision (light green 50% probability, dark green 95% probability), and autonomic reflex response suppression after laryngoscopy (pink 50% probability, red 95% probability). Because of their pronounced synergistic effect on inhaled anesthetics, proper opioid dosing can significantly reduce inhaled agent use and waste. The combination of a fentanyl effect site concentration of 2 ng/mL (attained after a 100 microg fentanyl bolus) with 0.7 fMAC sevoflurane (= 1.5% FETsevo in a 40 year old) ensures unconsciousness, immobility after incision and autonomic reflex response suppression with a probability of >99%, ≈95% and ≈85%, respectively. Opioids can be titrated in such a manner that there rarely is a need for > 0.7 fMAC, certainly in the presence of muscle relaxants[10]. It is important to re-dose opioids (if not using a continuous infusion) because waning effects of opioids will prompt the clinician to increase fMAC, which only serves to increase agent use and waste, and prolong emergence. Tools like the SmartPilot (Dräger, Lübeck, Germany) or possibly nociception/antinociception monitors can help the clinician titrate opioids.

Hysteresis

The rate of rise or decay with which the clinician likes to see the target FETagent change has a direct impact on waste because a fast change implies the use of a high FGF. A fast rise is often desired immediately after intravenous induction, a fast decay just prior to emergence. It is important to realize that there is a delay between the course of the measurable concentration of a drug (in exhaled

gas or in blood) and the effect of the drug. The relationship between these two is embedded in the effect-site concentration concept. The effect site concentration takes the delay into account between measurable concentrations and clinical effect. This delay is called hysteresis.

So how is hysteresis relevant to low flow anesthesia? A rapid rise of the desired FETagent involves the need for an increased FGF (even when FD is increased) which causes waste. However, often there is no need for a fast wash-in to high FETagent because the combination of the effects of the decreasing propofol concentration with the still low but increasing FETagent suffices to ensure unconsciousness. This "cross-over process" between decreasing propofol concentration and rising FETagent in the presence of opioids (which act synergistically to ensure hypnosis) obviates the need of a high FGF – high FDagent combination. One workstation explicitly offers such a slow wash-in mode[12]. Towards the end of the case, the reverse applies: the vaporizer can be stopped a while before the end of surgery if low FGF is maintained (coasting). Tools to help titrate inhaled agents during these transition periods are the processed EEG, Smart Pilot, and MAC Brain (Flow-i, Getinge, Solna, Sweden) which takes the hysteresis into account. Summarized, slow alveolar wash-in and wash-out supplement our low flow armamentarium.

Adding it up

Abandoning the use of desflurane and using sevoflurane instead reduces the environmental impact of inhaled anesthesia (expressed as global warming potential) by a factor 60. The impact of sevoflurane can still be further reduced by (1) avoiding the administration of sevoflurane with high FGF before securing the airway; (2) target controlled low flow delivery; (3) proper age correction of MAC; (4) proper opioid titration (synergy) to limit fMAC to ~ 0.7; and (5) slow wash-in and wash-out. The combined environmental effect of these actions needs to be incorporated in any life cycle analysis pertaining to the use of inhaled agents. Only such an analysis can serve as the basis for a rational discussion about their use, including a comparison of their environmental impact with that of propofol. Finally, conclusions based on such environmental analyses should continue to take into account the impact on patient care. Perspective remains key.

Conclusion

Low flow anesthesia reduces the environmental impact of inhaled anesthetics. Understanding the effects of lowering FGF on the difference between the dialed and end-expired agent concentration empowers the clinician to lower FGF. It also provides the rationale for the further development and use of target controlled low flow delivery. To maximally reduce agent use with automated target controlled low flow delivery systems, one further has to consider the factors affecting target selection (patient age, opioid use) and hysteresis (slow wash-in, slow wash-out). The combined use of these factors can have a pronounced effect on agent use and waste. Lowering FGF is only one part of a larger puzzle to reduce the environmental impact of inhaled anesthetic agents. The quantitative aspects outlined in this manuscript should be part of any life cycle analysis of inhaled anesthetic agents.

Acknowledgment statements relating to this article:
1. Assistance with this article: None.
2. Financial support and sponsorship: None.
3. Conflict of interest: Dr. Hendrickx has received lecture support, travel reimbursements,equipment loans, consulting fees, and/or meeting organizational support from AbbVie (North Chicago, Illinois, USA), Acertys (Aartselaar, Belgium), Air Liquide (Paris,France), Allied Healthcare (St. Louis, Missouri, USA), ArmstrongMedical (Coleraine, United Kingdom), Baxter (Deerfield, Illinois, USA), Dräger (Lübeck, Germany), General ElectricHealthcare (Madison, Wisconsin, USA), Getinge (Gothenburg, Sweden), Hospithera (Anderlecht, Belgium), Heinen und Lowenstein (Bad Ems, Germany),Intersurgical (Wokingham, United Kingdom), MDoloris Medical Systems (Loos, France),MEDEC (Aalst, Belgium), Micropore (Elkton, Maryland, USA), Molecular Products (Harlow, United Kingdom), Philips (Brussels, Belgium), Piramal (Mumbai, India), and Quantium Medical (Barcelona, Spain). Dr. Hendrickx is the current chair of the Industry Liaison Task Force of the European Society of Anaesthesiology and Intensive Care (Brussels,Belgium). The other authors declare no competing interests.

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doi.org/10.56126/74.1.05