Committee News

Low-Flow Sevoflurane is Safe, Economical, and Better for the Environment

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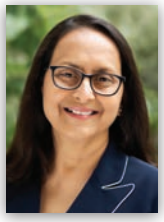
The majority of inhaled anesthetic gases administered to patients are unmetabolized and ultimately vented to the atmosphere. As potent greenhouse gases, these emissions contribute to climate change and negatively impact public health (*BMJ* 2022;377:o1301; *PLoS One* 2016;11:e0157014). Reducing waste is a fundamental strategy to prevent pollution and conserve physical and economic resources (*Anaesthesia* 2022;77:1023-9; asamonitor.pub/40kSYby). One of the most effective strategies for minimizing environmental contamination and waste of inhaled anesthetics is to adopt the practice of low-flow anesthesia. Low-flow anesthesia can be defined as: "*The practice of reducing fresh gas flow (FGF) well below minute ventilation to the lowest level consistent with equipment capabilities… while ensuring safe and effective care for the patient*" (asamonitor.pub/42zlGaD). While this definition allows for a range of FGFs, quite often the minimum effective total FGF is less than 1 L/min. Unfortunately, outdated recommendations to exceed clinical requirements for sevoflurane have been driving avoidable waste and pollution for decades. We must update best practice around FGF management.

The use of low FGF with sevoflurane has been extensively studied, is a safe practice, and has economic and environmental benefits (*Can J Anaesth* 2020;67:1595-23; *Anaesth Intensive Care* 2019;47:223-5; *Anesth Analg* 2012;114:1086-90; *Br J Anaesth* 2020;125:680-92). However, the U.S. Food and Drug Administration (FDA)-approved package insert for sevoflurane, last updated in 2003, recommends "sevoflurane exposure should not exceed 2 MAC [minimum alveolar concentration] hours at flow rates of 1 to < 2 L/min. Fresh gas flow rates < 1 L/min are not recommended" (asamonitor.pub/40lPsyp). This label continues to influence the behavior of anesthesia professionals who may be reluctant to use what constitutes off-label FGF settings when administering lower-flow sevoflurane. As a result, sevoflurane is routinely delivered using FGF rates well above what is needed to safely achieve the desired clinical effect. This contributes to avoidable expense for health care facilities and environmental pollution that harms public health (*Anaesth Intensive Care* 2019;47:235-41). As physicians, we must consider the health and safety of our patients both in the OR and beyond and continuously adopt current scientific evidence to guide our practice.

The manufacturer package insert for sevoflurane cites studies in animal models that showed evidence of renal toxicity due to exposure to Compound A (fluoromethyl-2,2-difluoro-1-(trifluoromethyl)vinyl ether), a degradant formed by the reaction of sevoflurane with strong bases (such as NaOH, KOH) in some CO_2 absorbents (asamonitor.pub/40lPsyp). However, extensive research has failed to find any evidence of harm in humans due to sevoflurane use with low FGFs (*Can J Anaesth* 2020;67:1595-23). While it is unclear how many anesthesiologists abide by this FDA recommendation in the U.S., a review of an anesthesia-focused insurance company's closed-claim database spanning over 20 years did not find any claims relating to allegations of injury or death due to the use of low-flow sevoflurane (asamonitor.pub/3FItu09). Notably, countries of the European Union never introduced minimal FGF restrictions and routinely use low FGFs in practice. Taken together, there is ample scientific and real-world evidence that supports the conclusion that sevoflurane can be administered safely without concern for FGFs of <2 L/min described in the package insert.

Even though Compound A has not been shown to be toxic in humans, carbon dioxide absorbents have been reformulated to eliminate the production of Compound A. Specifically, many cost-competitive CO_2 absorbents currently on the market have a limited concentration of strong base (<2% NaOH) or have eliminated the strong base entirely, reducing Compound A production to negligible amounts even when using low FGFs (*Anesth Analg* 2021;132:993-1002; *APSF Newsletter* 2005;20:25-44). Low-alkalinity absorbent technologies are formulated to optimize CO_2 absorption while minimizing Compound A production. Thus, potential concerns about Compound A toxicity with low FGFs can be addressed with the purposeful selection of CO_2 absorbent. Chemical compositions of CO_2 absorbents, including the percentage of NaOH or KOH, can be easily obtained from the manufacturer or distributor. Of note, as FGFs are lowered, CO_2 absorbents will be consumed more quickly; however, environmental and cost benefits still favor lowest possible FGFs (*Br J Anaesth* 2020;125:680-92; *Anesth Analg* 2020;130:374-81).

While there is no scientific evidence to support a specific lower FGF limit when using sevoflurane, or any inhaled anesthetic, equipment capabilities can influence the minimum safe FGF. Equipment features favoring lower FGFs include return of gas sampled for CO_2 and agent concentration monitoring to the breathing circuit and a circuit with minimal intrinsic leak. The anesthesia professional should determine the optimal low-flow rate to avoid unnecessary waste, costs, and pollution, while ensuring safe and effective care for the patient. Most adult patients under anesthesia can be managed with a FGF of 0.5 L/min without adding significant burden to the anesthesia professional. With vigilance, flows can often be decreased further to approach "closed-circuit" conditions, where the anesthetic and fresh gas supplied equal the amounts consumed by the patient (*Anesth Analg* 2021;132:993-1002). Since the closed-circuit FGF threshold in adults is typically less than 0.5 L/min, any amount of gas flow above that threshold results in excessive anesthetic lost through the waste anesthetic gas management system. It is important to understand the tools and concepts underlying the safe and effective practice of low-flow anesthesia. Provider-



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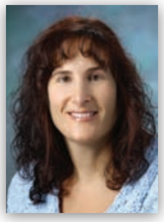

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targeted education on low-flow sevoflurane use will increase comfort in reducing FGFs, and a free course is offered through the Anesthesia Patient Safety Foundation (asamonitor.pub/42zlGaD). Continuing education credits are available, including safety credits for those involved in the MOCA process (apsf.org/tei/lfa).

Once the anesthetic gas is vented to the atmosphere, sevoflurane acts as a greenhouse gas, trapping heat in the atmosphere and contributing to a rapidly changing climate (*J Phys Chem A* 2012;116:5806-20; *Anesth Analg* 2010;111:92-8; *Environ Sci Technol* 2021;55:10189-91). Climate change is a threat multiplier, exacerbating underlying social and physical vulnerabilities, worsening human health, and disrupting health systems' abilities to deliver high-quality continuous care (*Annu Rev Public Health* January 2023). The impacts of climate change on human health are predicted to increase within the coming years and decades, leading to calls to urgently halve emissions by 2030 and reach "net zero" by 2050 to avert the worst predicted harms to civilization (*Annu Rev Public Health* January 2023; *Lancet* 2022;400:1766). Reducing inhaled anesthetic waste through optimizing low flows is one important strategy for anesthesiologists to do their part. It is important for anesthesiologists to be versed in the public health impacts of their practices. The ASA Committee on Environmental Health provides additional resources (asamonitor.pub/40kSYby).

The benefits of reducing sevoflurane waste are not, however, limited to mitigating environmental pollution. Economic benefits from avoiding unnecessary anesthetic waste are well documented (*Anesthesiology* 2013;118:874-84; *Br J Anaesth* 2001;87:559-63). Notably, when using inhaled anesthetics, the FGF rate is the most important determinant of agent consumption, and therefore opportunity for cost savings. Clinical decision support (CDS) tools and best practice alerts can be integrated into anesthesia information management systems to alert anesthesia professionals when FGFs exceed a set threshold during maintenance. For example, implementing real-time high fresh gas flow alerts encouraged resource conservation that led to cost savings of over $100,000/year in two separate studies conducted at large academic hospitals: University of Washington Medical Center and University of California, San Francisco (UCSF) Health (*Anesth Analg* 2023;136:327-37). At UCSF, the cost savings realized were $2.10/MAC-hour for sevoflurane and $3.22/MAC-hour for desflurane (*Anesth Analg* 2023;136:327-37). In addition to cost savings, decreasing unnecessary waste wherever possible will help make health care facilities more resilient to supply chain interruptions and economic swings. Health care institutions and anesthesia departments are encouraged to implement such CDS tools to nudge resource conservation practices.

The sevoflurane FDA package insert is outdated and contributes to harmful, unnecessary pollution, secondary health damages, and costs. While the FDA package insert should be updated to reflect the current scientific evidence, this process requires leadership and initiative by manufacturers. However, manufacturers have little motivation to remove the unsupported warnings against low FGFs, which would result in less product consumption and reduced sales. Given that many anesthesiologists' sevoflurane FGF practices are influenced by minimizing regulatory risks, ASA should make a statement that low-flow sevoflurane is safe and should be determined by the clinical needs of the patient, and not by the outdated FDA package insert. Decades of targeted research and actual clinical use have not linked sevoflurane use with low FGF to patient harm. As volatile anesthetics are costly environmental pollutants, anesthetic waste should be minimized by reducing FGFs whenever possible. ■

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