Life Cycle Greenhouse Gas Emissions of Anesthetic Drugs

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BACKGROUND: Anesthesiologists must consider the entire life cycle of drugs in order to include environmental impacts into clinical decisions. In the present study we used life cycle assessment to examine the climate change impacts of 5 anesthetic drugs: sevoflurane, desflurane, isoflurane, nitrous oxide, and propofol.

METHODS: A full cradle-to-grave approach was used, encompassing resource extraction, drug manufacturing, transport to health care facilities, drug delivery to the patient, and disposal or emission to the environment. At each stage of the life cycle, energy, material inputs, and emissions were considered, as well as use-specific impacts of each drug. The 4 inhalation anesthetics are greenhouse gases (GHGs), and so life cycle GHG emissions include waste anesthetic gases vented to the atmosphere and emissions (largely carbon dioxide) that arise from other life cycle stages.

RESULTS: Desflurane accounts for the largest life cycle GHG impact among the anesthetic drugs considered here: 15 times that of isoflurane and 20 times that of sevoflurane on a per MAC-hour basis when administered in an O_2/air admixture. GHG emissions increase significantly for all drugs when administered in an N_2O/O_2 admixture. For all of the inhalation anesthetics, GHG impacts are dominated by uncontrolled emissions of waste anesthetic gases. GHG impacts of propofol are comparatively quite small, nearly 4 orders of magnitude lower than those of desflurane or nitrous oxide. Unlike the inhaled drugs, the GHG impacts of propofol primarily stem from the electricity required for the syringe pump and not from drug production or direct release to the environment.

DISCUSSION: Our results reiterate previous published data on the GHG effects of these inhaled drugs, while providing a life cycle context. There are several practical environmental impact mitigation strategies. Desflurane and nitrous oxide should be restricted to cases where they may reduce morbidity and mortality over alternative drugs. Clinicians should avoid unnecessarily high fresh gas flow rates for all inhaled drugs. There are waste anesthetic gas capturing systems, and even in advance of reprocessed gas applications, strong consideration should be given to their use. From our results it appears likely that techniques other than inhalation anesthetics, such as total IV anesthesia, neuraxial, or peripheral nerve blocks, would be least harmful to the environment. (Anesth Analg 2012;114:1086–90)

The World Health Organization recently called climate change the defining issue for health systems in the 21st century, but ironically the health care industry itself is a leading emitter, accounting for >8% of total carbon dioxide (CO_2) emissions in the United States alone.[1] Health sector life cycle assessments reveal 60% of emissions come from procurement, and more than half of this derives from pharmaceuticals and medical equipment.[2] Understandably, the environmental footprint of perioperative services is among the largest in all of health care.[3–7] It therefore benefits anesthesiologists to better understand the ecological consequences of clinical practice and to use this information to minimize negative impacts while maintaining high standards for safe patient care.

Recent publications reported on the global warming potentials (GWP) of inhalation anesthetics[8–10] reflecting a growing concern for the impact of anesthesia practice on the environment. These studies examined the direct climatic effects of inhalation anesthetics, and although modest compared to the cumulative effects of other greenhouse gases (GHG) such as CO_2,[9] the results demonstrated that the majority of impacts are due to desflurane (with the highest heat-trapping effect) and nitrous oxide (N_2O) (with the largest releases), compared to sevoflurane and isoflurane. Based on these findings, clinicians may elect to avoid desflurane and N_2O, or choose to substitute total IV anesthesia instead of general inhaled anesthesia, though this approach appears premature.

For anesthesiologists to begin to factor environmental impacts into clinical decision-making, the entire footprint of drugs requires quantification. Life cycle assessment is a method of evaluating multiple environmental impacts of a product throughout its life cycle and is commonly used to illuminate particular processes or substances in a product that contribute significantly to impacts or to compare

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Accepted for publication February 28, 2012.

This study was funded by the Department of Anesthesiology, Yale School of Medicine.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.anesthesia-analgesia.org).

Conflict of Interest: See Disclosures at the end of the article.

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DOI: 10.1213/ANE.0b013e31824f6940

Table 1. Variables for Anesthetic Drugs Required to Provide 1 Minimum Alveolar Concentration (MAC)-hour

Parameter	Desflurane	Isoflurane	Sevoflurane	Propofol
MAC% or equivalent	6.7%	1.2%	2.2%	100 mcg/kg/h
Density (g/mL) (liquid form)	1.47	1.50	1.22	1.03
Fresh gas flow (L/min)	1	1	2	
Molar mass (g/mol)	168	184.5	200.1	178.3
Metabolism (%)	0.02%	0.20%	5%	100%
% MAC-h from agent/N_2O*	37/63	37/63	37/63	0/100
Agent used per MAC-h (g)	10.2	2.0	8.0	0.01
Agent used per MAC-h (mL)	6.9	1.3	6.6	0.01
Agent released per MAC-h (g)	10.2	2.0	7.6	0
GWP_{100} Sulbaek-Andersen et al. (Ref. 9)	2540	510	130	
N_2O used per MAC-h (g)*	71.2	71.2	142.3	

*Modeled as 60/40% fresh gas flow N_2O/O_2; nitrous oxide at 105% MAC, 0.005% metabolism, density of 1.98 g/L (gas), and 100-y GWP (GWP_{100}) of 310.

related products along environmental dimensions.[11] The objective of this study was to perform an initial life cycle assessment on 5 anesthetic drugs—sevoflurane, desflurane, isoflurane, N_2O, and propofol—to inform clinician drug selection on this basis.

METHODS

The present life cycle GHG assessment encompasses 4 inhaled anesthetic drugs: sevoflurane, isoflurane, desflurane, N_2O, and 1 IV drug, propofol. A cradle-to-grave approach was used, encompassing all data pertaining to resource extraction and manufacturing of the anesthetic drugs, transport to health care facilities, clinical use, and disposal or emission to the environment (see Supplemental Figure 1, Supplemental Digital Content 1, http://links.lww.com/AA/A380). At each stage, energy and material inputs were assembled, which were specific to the clinical use requirements of each drug. Emissions were calculated for each stage, including upstream emission (from fuel combustion to produce electricity, for example) as well as direct emission of unmetabolized drug after clinical use. Impacts from each life cycle stage can be compared with one another; for example, the direct effect of the inhaled drugs (which are themselves GHG) can be compared with the indirect effect of emissions (primarily CO_2) from their production. Equivalent GHG impacts were assessed using the most recent 100-year GWP (GWP_{100}) factors from Sulbaek Andersen et al.[10] for the anesthetic drugs and the Intergovernmental Panel on Climate Change 2007 for all other GHG.[12]

In life cycle assessment, the functional unit provides the basis of comparison used to relate all measurements and calculations. The present analysis of the anesthetic drugs was based on a functional unit of 1 minimum alveolar concentration (MAC), or MAC-equivalent for propofol, for maintenance anesthesia for an average 70 kg adult patient for 1 hour (1 MAC-h). This functional unit was related to the physical amount of each drug required according to the factors in Table 1. The carrier gases for the inhalation anesthetics were specified either as O_2/air or a 60/40% admixture of N_2O and oxygen, with 63% of the MAC assigned to the N_2O and the remainder to the halogenated drugs. Data collection was specific to the Yale-New Haven Hospital, including drug transportation, energy requirements, and disposal.

Inventory data were stored and impact assessment performed with SimaPro 7.3.2 Life Cycle Assessment Software,[13] while the life cycle inventory database ecoinvent v2.2 was used as the primary data source.[14] Both of these packages are commercially available and widely used internationally by life cycle assessment practitioners. Where exact matches for the materials, energy, and emissions related to the drugs were unavailable in ecoinvent's chemicals database, proxies that best matched the production characteristics of the target were used, as noted. The sections that follow describe data acquisition and modeling assumptions for each stage of the life cycle of anesthetics (see Supplemental Figure 1, http://link.lww.com/AA/A380).

Mechanisms of Drug Synthesis

With the exception of N_2O, none of the anesthetic drugs had matching records in any available life cycle inventory database, so first we modeled the production of each drug from chemicals that did have associated data. Direct information on the mechanisms of synthesis for each drug was not available from manufacturers; instead each step of the reaction was modeled using SciFinder, a chemistry research platform,[15] resulting in possible pathways. Information on catalysts and reagents used in the synthesis of the drug of interest was gathered from associated patents, and this information was used to narrow the results found in SciFinder. Assumed synthesis routes and proxy data are shown in Supplemental Figure 2 (see Supplemental Digital Content 2, http://links.lww.com/AA/A381).

Transportation

Transportation of drugs to Yale-New Haven Hospital was modeled assuming US diesel trucks. All drugs were assumed to have shipped from their US production locations. The anesthetic gases were transported in lightweight polyvinyl chloride plastic containers while propofol was transported in glass. The volumetric amounts of each drug corresponding to 1 MAC-h were determined and the corresponding amount of packaging was assigned.

Energy and Materials During Drug Delivery

The power ratings of drug delivery machines were obtained from product documentation and supplier information. The baseline energy requirement for the anesthesia

machine (for functions not related to drug delivery, such as lighting, sensors, and displays) was considered to be constant for all of these anesthesia drugs, as would be the case for an intubated patient regardless of whether anesthesia was maintained with an inhaled drug or IV propofol. Basic disposables, such as endotracheal tubes, circuits, and CO_2 absorbents, were considered equivalent and not included in this study.

Only the desflurane vaporizer requires energy for a heating element to keep the drug at the recommended 39°C to ensure controlled titration. The heating element has a power rating of approximately 0.25 kW. The Medfusion 3500 syringe pump (Smiths Medical, St Paul, MN) for propofol delivery has a power rating of 15W. Electricity for all equipment operation was assumed to be provided by Yale natural gas cogeneration facility (40%), and the average eastern US energy mix (60%). Electricity produced 100% from hydropower facilities was modeled in an alternate scenario. Maintaining anesthesia with IV propofol requires additional disposable plastic pieces, modeled as two 60 mL plastic syringes, a 3-way stop cock, and an IV extension tube to supply the 1 MAC-h equivalent. The production, transportation, and disposal of these plastics were included in the life cycle inventory.

Unmetabolized Drugs

Inhaled anesthetic gases undergo little in vivo metabolism. They are either exhaled into the anesthesia machine, from which they are vented into the atmosphere as waste anesthetic gas, or they are exhaled by patients into the indoor atmosphere. In the absence of gas-capturing systems all emissions of unmetabolized drugs were assumed to enter the atmosphere (Table 1). To show the influence of possible gas capture technologies on the final results, an alternate scenario of full gas capture was also modeled. Propofol is rapidly and extensively metabolized, with only trace levels excreted unchanged.[16] Thus, we assumed no unmetabolized propofol entered the environment directly.

Disposal of Accessory Waste and Unused Drugs

Although there are no direct GHG impacts from metabolized propofol, large amounts of unused propofol are routinely found in operating room waste bins. Mankes found that 32% of dispensed propofol was wasted,[17] whereas Gillerman and Browning found that 51% of propofol is wasted.[18] Here we assume 50% wastage rates for the drug. This wasted propofol, along with associated plastics and sharps, is incinerated in accordance with pharmaceutical waste regulations and manufacturer recommendations. This incineration was modeled as unspecified organic chemicals and unspecified plastics in the ecoinvent life cycle inventory database. A small percentage of remaining unprocessed propofol still can make its way into land and water, via quantities remaining in vials, tubing, and syringes that are sent to landfill, through accidental or improper waste handling, and from releases from manufacturing plants, but there are no reliable estimates of this proportion.

RESULTS

Figure 1 shows the life cycle GHG emissions for the inhalation anesthetics and propofol over their complete life cycles. Panel A shows the results for all life cycle stages, whereas panel B depicts nonwaste anesthetic gas emissions from drug manufacturing, transportation, drug delivery, and disposal. For all of the inhalation anesthetics, GHG impacts are dominated by atmospheric waste anesthetic gas emission. The results in panel B correspond to a scenario of complete gas capture and show the relative importance of the remaining life cycle stages.

Desflurane accounts for the largest life cycle GHG emissions among the anesthetic drugs considered here, both in terms of waste anesthetic gas and other life cycle stages. Life cycle GHG emissions of desflurane are 15 times that of isoflurane and 20 times that of sevoflurane on a per MAC-h basis when O_2/air is used, and remain dominant even when N_2O/O_2 is used. Nonwaste anesthetic gas emissions for desflurane are largely due to manufacturing of the drug, the N_2O when given during clinical use, and the electricity required for volatilization during drug delivery.

Isoflurane and sevoflurane have similar GHG emission profiles. For both gases, life cycle GHG emissions are dominated by waste anesthetic gas. When O_2/air is used, isoflurane has higher associated emissions than sevoflurane, in large part because its GWP_{100} factor is nearly 4 times as high. When these drugs are administered with N_2O/O_2, emissions increase by 65% for isoflurane and by nearly 900% for sevoflurane, which has higher gas flow requirements. In this scenario, the relative environmental preference of these 2 drugs is reversed, where emissions from sevoflurane are nearly twice as high as those associated with isoflurane. Nonwaste anesthetic gas emissions follow the same pattern: When N_2O/O_2 is used, manufacturing of the N_2O is the largest source of impacts, with nonwaste anesthetic gas emissions increasing by ~200% from the case where O_2/air is used.

GHG impacts of propofol are comparatively quite small, nearly 4 orders of magnitude lower than those of desflurane or N_2O. Unlike the inhaled drugs, the GHG impacts of propofol primarily stem from the energy needed to operate the syringe pump and not from environmental releases of the drug.

Location is an important consideration, because regions have different grid mixes of electricity. If hydroelectricity is the main source of electric power (as is the case in the US Pacific Northwest), then GHG emissions associated with drug delivery decrease nearly to zero, although this stage is not a major driver of life cycle emissions for these drugs. Transportation impacts are also negligible, as are emissions from waste management of accessory materials. Finally, impacts of producing the packaging are typically below 5%.

DISCUSSION

Our results reiterate previous published data on the GHG effects of these inhaled drugs,[8–10] while providing a full life cycle context. In particular, of the inhalation anesthetics, the life cycle GHG effects of desflurane are significantly higher than for isoflurane or sevoflurane, especially when O_2/air is used as the carrier. Desflurane's comparatively high results are a combination of several factors, including a high MAC percentage, a high radiative forcing effect (GWP_{100}), and a low rate of metabolism, which leads in

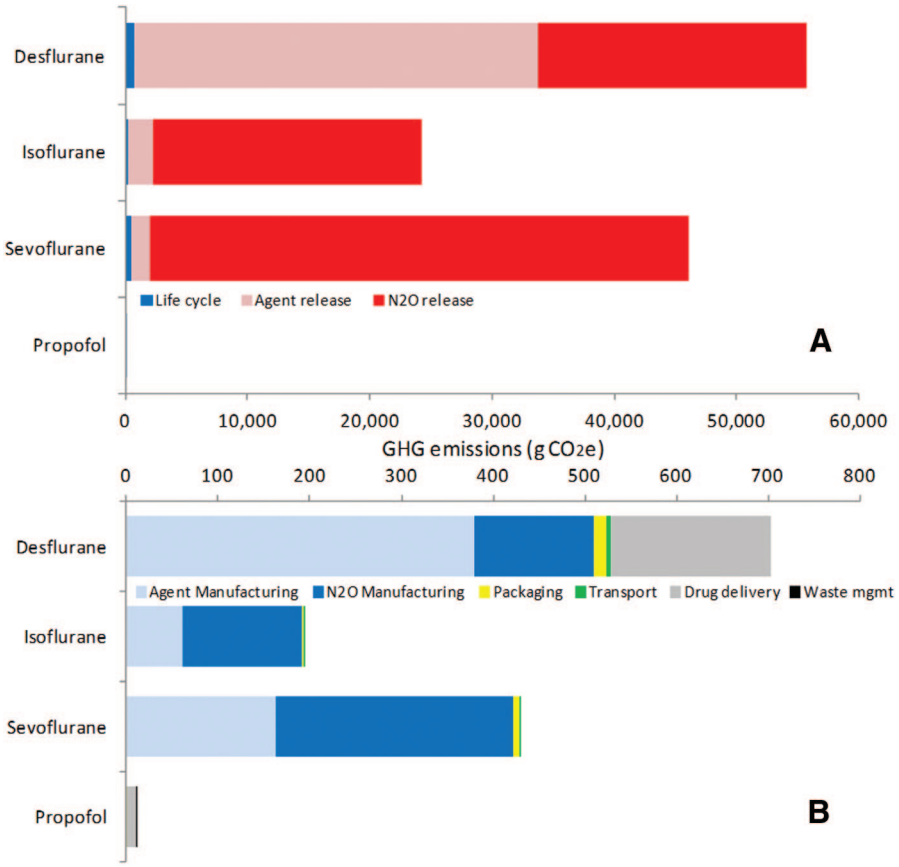

Figure 1. Life cycle greenhouse gas (GHG) emissions of anesthetics, (A) including waste anesthetic gas emissions of halogenated drugs and nitrous oxide (N_2O) and (B) excluding waste anesthetic gas emissions.

turn to a larger proportion of gas that escapes unaltered to the atmosphere. N_2O has low anesthetic potency and therefore a high MAC percentage. This, combined with a GWP_{100} 310 times that of CO_2, makes N_2O a major contributor to GHG emissions when used as a carrier gas.

There are practical environmental impact mitigation strategies. Desflurane and N_2O should be restricted to cases where they may reduce morbidity and mortality over alternative drugs. Clinicians should avoid unnecessary high fresh gas flow rates for all inhaled drugs. Although reducing fresh gas flow rates increases the requirement for CO_2 absorbent and its concomitant footprint, this is unlikely to offset the benefits of reducing volatile drug and N_2O use. Charcoal absorbers may be placed within the anesthesia circuit to capture volatile waste anesthetic gas. Unfortunately, charcoal does not permanently remove the volatile drug. Volatile anesthetics diffuse into the atmosphere from charcoal absorbers in a matter of days, so they do not prevent emissions.

Inhalation anesthetics are not generally included in climate change mitigation strategies because they are deemed "medically necessary." Current Occupational Safety and Health Administration and Joint Commission regulatory language revolve around protection of worker safety through methods such as prevention of excessive exposure from handling, checking machines for leaks, and fire prevention.[19] The American Society of Anesthesiologists-approved guidelines for waste anesthetic gas management recommend "discharging safely to the outside atmosphere."[20] There is currently no waste anesthetic gas policy limiting discharge of anesthetic gases into the atmosphere.

Technologies on the near horizon include photochemical air purification.[a] This approach can theoretically destroy all waste anesthetic gases. Alternatively, current volatile waste anesthesia gas capturing systems can reclaim volatile gases for reuse rather than discharge waste into the atmosphere. The Dynamic Gas Scavenging System designed at Vanderbilt University is a cryogenic condensing system built into the exhaust system of multiple operating rooms. This system is activated only when the patient exhales. Because the vacuum pump is only intermittently active, the system has minimal impact on heating, ventilation, and air conditioning energy usage.[21] Deltasorb® is an alternative technology consisting of a canister that snaps into existing scavenging circuits. It uses a sieve-like filtering matrix that adsorbs volatile anesthetic gas. The canisters are returned to the vendor where the captured anesthetics can be extracted, liquefied, and processed into medical grade anesthetics (Blue-Zone Technology, Toronto, Canada). The Food and Drug Administration is presently considering approval for reprocessed volatile drugs, which may also find use in veterinary medicine.

Propofol has the least overall impact on GHG emissions, even assuming a 50% wastage rate, disposable plastics for

[a] http://cleantech.ku.dk/airfilter/article/, Copenhagan Centre for Atmospheric Research, University of Copenhagen, last accessed February 1, 2012.

IV administration, and the energy requirements of the infusion pump. The high proportion of wasted propofol may have environmental impacts other than GHG emissions. Some quantity of unprocessed propofol likely makes its way into the environment, where it has moderate persistence.[17,22] It is unknown what course the metabolites take within ecosystems or whether these are harmful.

There is significant uncertainty in this analysis, particularly regarding the synthesis of propofol and the volatile drugs. Our results, therefore, should be interpreted with caution. Future research would benefit from commercial-scale synthesis data from pharmaceutical companies. Nevertheless, from our results it appears likely that techniques other than inhalation anesthetics, such as IV anesthesia, neuraxial, or peripheral nerve blocks, would be least harmful to the climate.

Finally, there are also important human health considerations from reducing GHG emissions. The World Health Organization estimates climate-related mortality at 0.3% of all annual deaths (150,000/year) and expects this number to increase.[23] For example, the incidence of cardiovascular disease and asthma may increase due to the emissions from coal-fired power plants and through temperature changes, and infectious diseases may spread more readily due to altered habitats resulting from climate change. Clinical decisions should consider the full environmental and human health impacts from anesthetic use.

DISCLOSURES

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Conflicts of Interest: This author has no conflicts of interest to declare.
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