WFSA warning communication on cessation of halothane production and the imminent shortage of the volatile anaesthetic agent

Target Audience

Ministries of Health, Drug and Medical Devices Regulatory Bodies, National Medical Store Departments, Societies of Anaesthesiologists, the Anaesthesia Provider Community**,** and other stakeholders interested in the topic.

Executive summary

WFSA regrets to inform the healthcare community that the foremost manufacturer of halothane has ceased production of the volatile anaesthetic agent; clarification is still needed as to whether there are alternative producers. This communication provides insight into the challenges posed by this situation, its impact on access to safe surgery in resource-constrained settings, and possible strategies for adaptation and a smooth transition to alternative anaesthesia techniques not using halothane. While this transition may present challenges, it also offers an opportunity for innovation and improvement in anaesthesia practices.

Introduction

Halothane was officially introduced into clinical practice in 1958 after its approval by the FDA in the USA. It has been widely used for inhalational induction of anaesthesia in paediatrics and maintenance of general anaesthesia in many surgical cases, particularly in resource-constrained environments. However, its use is associated with a higher degree of metabolism (25%) and potential adverse effects, such as "halothane hepatitis," a lethal condition, as well as a high incidence (20%) of arrhythmias, which can be exacerbated by the use of catecholamines and the presence of hypoxia and hypercapnia. Due to these concerns, newer inhalational anaesthetic agents, such as enflurane, isoflurane, sevoflurane, and desflurane, have been developed with better safety profiles.

Current need for halothane in clinical practice

While halothane's clinical use has declined in high-income countries (HIC) and has been replaced by safer agents like isoflurane and sevoflurane, it has yet to disappear completely from global clinical practice. In lower-resource countries, especially in rural areas, halothane continues to be used due to its cost-effectiveness and suitability for the inhalational induction of children. This is particularly true in some African countries, where halothane is the only available inhaled agent. As a result, halothane remains on the World Health Organization (WHO) Essential Medicines List (EML). A survey by the World Federation of Societies of Anaesthesiologists (WFSA) revealed that more than 26 African countries still rely on halothane due to limited access to other inhalational agents and the necessary infrastructure for their

administration. Therefore, the continued availability and access to halothane is essential for African countries and other parts of the world with similar resource constraints.

Impact of halting production and impending shortage of halothane

The advent of safer inhalation agents, their preferential use in most HIC, and increasing production costs for halothane led to a continued decrease of both production and halothane manufacturers. The few remaining manufacturers only produced for the local markets of low- and middle-income countries (LMICs), especially in Africa. One of India's manufacturers and the largest supplier to Sub-Saharan Africa, Piramal Pharma Ltd (https://www.piramalpharma.com/), ceased production of halothane at the end of 2023. This has raised many concerns regarding sustaining the improvement in access to safer anaesthesia and surgical services in LMICs' healthcare systems.

Smaller urban and rural facilities in resource-constrained countries are primarily dependent on halothane use. The shortage of halothane will leave most providers, some trained in and practicing only halothane-based anaesthesia, with only isoflurane, which is unsuitable and not recommended for inhalational induction in children. This will pose potential risks for higher morbidity and mortality from incidents of unsafe anaesthesia and its complications in these settings. These halothane-dependent facilities will most likely need to be better equipped and staffed in the future, which will increase the cost burden in places already resource-limited.

Challenges to a timely, smooth transition to alternative anaesthetic techniques

- Low halothane stocks/reserves (<24 months) available in the concerned countries.
- Urgency of the transition to alternative anaesthesia techniques to ensure continuity of surgical care.
- Urgent budgetary allocation needed for infrastructure changes (e.g., upgrades of vaporizers and/or machines) and consumables.
- Need for customized learning resource packages and providers capacity building interventions to facilitate adaptation and safe implementation of alternative anaesthesia techniques.

Recommended strategic approaches for a smooth transition to alternative safe anaesthesia practices

- Awareness of the impending halothane shortage and its impact.
- Advocacy for resource mobilization to ensure a smooth transition and continuity of access to safer surgical interventions.
- Capacity building for providers on other safe approaches, including the clinical use of alternative inhalational agents, i.e., sevoflurane and isoflurane, and management of associated complications, application of low flow anaesthesia techniques for cost containment.
- Acquire and fit isoflurane and sevoflurane vaporizers on current anaesthesia machines with halothane vaporizers or outright procurement of modern anaesthesia machines fitted with isoflurane and sevoflurane vaporizers for all operating rooms.
- Ensure adequate budget allocation for procurement of needed anaesthetic agents, factoring in the increased cost of the inhalation agents.

- Scale up the positioning of sevoflurane on the EML ladder for equitable access.
- Manufacturers of inhalational agents to facilitate the exchange of halothane vaporizers with sevoflurane vaporizers.
- Request the manufacturers to continue production and distribution so that countries can transition safely over a year or two.

WFSA remains committed to supporting and working closely with Health Ministries through Societies of Anaesthesiologists to ensure a smooth transition period.

Issued 9 Aug 2024

1. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=011338
2. GW Black. A review of the pharmacology of halothane. Br J Anaesth. 1965 Sep;37(9):688-705. doi: 10.1093/bja/37.9.688.