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Sevoflurane for refractory status asthmaticus: balancing bronchodilation with hepatic safety

Patrick M. Honore^{1*}, Yasser Benkaddour², Maryam Erraji Chahid², Sydney Blackman² and Nathan De Lissnyder³

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The recent systematic review by Ho et al. on the use of sevoflurane in refractory status asthmaticus in adults represents a valuable contribution to the literature and provides important clinical insights into this salvage therapeutic option. Nevertheless, several aspects merit further consideration [1].

In their discussion of adverse effects, the authors mainly emphasized hypotension and cases of nephrogenic diabetes insipidus. While these complications may often be clinically manageable, it is critical to underscore the potential for rare but severe, even life-threatening, complications associated with prolonged or repeated sevoflurane administration in the intensive care setting [2–5].

Although sevoflurane is generally regarded as the least hepatotoxic of the halogenated volatile anesthetics, hepatotoxicity remains a potential concern [6, 7]. Unlike other halogenated anesthetics, sevoflurane does not undergo metabolism via cytochrome P450 2E1 to trifluoroacetyl chloride, a metabolite that covalently binds to hepatic proteins and elicits immune-mediated hepatocellular injury. Instead, its principal metabolite,

hexafluoroisopropanol, has minimal protein-binding affinity and is rapidly glucuronidated and excreted in urine [8, 9]. Nevertheless, mechanisms of hepatotoxicity have been proposed, including the generation of compound A, capable of inducing oxidative stress-mediated cellular injury, and perturbations in intracellular calcium homeostasis leading to hepatocellular necrosis [10].

Importantly, repeated exposure to halogenated anesthetics carries the risk of immune sensitization, as reactive acyl metabolites may act as haptens, resulting in idiosyncratic hepatotoxicity upon re-exposure [11]. Identified risk factors for volatile anesthetic-induced hepatic injury include prior exposure, middle age, female sex, obesity, renal impairment, atopy or multiple drug allergies, chronic alcohol or paracetamol use, and cytochrome P450 induction [12]. Beyond direct hepatocellular toxicity, volatile anesthetics also decrease hepatic blood flow secondary to reductions in cardiac output, potentially compounding hepatic injury [13, 14]. Clinically, such complications may range from asymptomatic elevations in aminotransferases to fulminant hepatic failure requiring transplantation [4, 15, 16].

Given the risk profile, we believe it is essential to caution intensivists against the indiscriminate use of sevoflurane in status asthmaticus, particularly in patients with recognized risk factors for hepatotoxicity. While the bronchodilatory properties of sevoflurane render it an attractive therapeutic adjunct in refractory cases, the potential for severe hepatic injury—including fatal necrosis—should not be underestimated.

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*Correspondence:

Patrick M. Honore

patrick.honore@chuucnamur.uclouvain.be

¹ICU Department, CHU UCL Godinne Namur, UCL Louvain Medical School, Campus Godinne Avenue G Thérèse 1, 5530, Yvoir, Belgium

²ULB university, Brussels, Belgium

³Surgery Department, Universitair Ziekenhuis Brussel, Brussels, Belgium



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We therefore recommend that sevoflurane administration for status asthmaticus be avoided in patients with identifiable risk factors for volatile anesthetic-induced liver injury. We suggest this correspondence be viewed as a concise update on key safety considerations that every intensivist should be aware of when contemplating the use of sevoflurane in the management of life-threatening asthma [11].

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Data availability

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

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