Anaesthetic in the garb of a propellant

Sir,

Serendipity is the forerunner of scientific discoveries, and anaesthesia is no exception. Pressurised metered dose inhalers are routinely used for perioperative control of reactive airway disease. They can be mounted on the

proximal aspect of the standard endotracheal tube (ETT) connector for direct drug delivery to the tracheobronchial tree by puffs for treatment of bronchospasm. All these inhalers have a propellant, which aids in drug delivery. One such propellant, HFA 134a (hydrofluoroalkane: 1,1,1,2 tetrafluoroethane), is the prime suspect in our current case scenario, discovered while giving general anaesthesia through our Dragus Primus® workstation (Scio four Oxi-plus module).

An American Society of Anaesthesiologists (ASA) physical status II, asthmatic patient undergoing an oncosurgical procedure developed bronchospasm immediately after endotracheal intubation following standard general anaesthesia. He was given 10–12 puffs of salbutamol inhaler via the ETT. A bright red rectangle with halothane printed in black popped on the monitor screen. Nothing abnormal, except that halothane, is not available in our operation theatre (OT) for a decade now. We use only isoflurane, sevoflurane and desflurane as inhalational anaesthetics yet the machine was falsely reading halothane. This was an extremely surprising observation, which was further investigated upon. We found that after 4–5 min the red rectangle disappeared, only to reappear before extubation seconds after the second dose of salbutamol aerosol puffs. The Drager Primus® workstation flashed a note reading "three mixed agents"(detection of three different inhalational anaesthetic agents simultaneously in the inspiratory gases – nitrous oxide, the inhalational agent being used, which was sevoflurane; and halothane!) after a time lag of approximately 30 s each time after 10–15 puffs of salbutamol aerosol inhaler. It showed inspiratory halothane as 0.5% followed by end-tidal halothane 0.5%, gradually falling to 0 after approximately 5 min depending upon the tidal volume, respiratory rate, fresh gas flow and other ventilatory parameters [Figure 1] irrespective of the inhalational agent being administered. We later found that this time lag was least with desflurane as the inhalational agent and maximum with isoflurane. Occasionally, after three or more doses of 10–12 puffs each, a peach coloured rectangle with "enflurane" printed appeared on the screen when no enflurane was being administered.

Both Drager Primus® workstation and Datex Ohmeda S/5® module workstations in our OT produced bizarrre response to salbutamol aerosol inhaler (Asthalin Cipla®). When salbutamol from an ampoule was given as a nebulisation in the anaesthesia circuit, there were no such observations in the agent gas monitor (AGM) of both these workstations. Hence, we concluded

Figure 1: Drager Primus Anaesthesia workstation showing the halothane red rectangle after asthalin puffs given via the endotracheal tube

that the propellant hydrofluoroalkane (HFA134a), the medium for suspension of salbutamol is responsible for the interaction and not the salbutamol *per se*.

The 134a HFA, propellant in inhalers is chemically 1, 1, 1,2-tetrafluoroethane, also known as norflurane. In 50 vol% concentration, it can induce anaesthesia, but this moderately potent anaesthetic discovered in 1967 never underwent human trials.[1] AGMs use infrared (IR) analysers. Gases with two or more dissimilar atoms in their molecule (nitrous oxide, carbon dioxide and halogenated anaesthetics) have unique IR light absorption spectra. Absorption spectra of HFA134a match with that of halogenated volatile anaesthetics (8–12 μm range).[1,2]

The mechanism of changes produced by HFA 134a-based inhalers in the two anaesthesia workstations mentioned could be as below: In S/5 Datex Ohmeda® anaesthesia workstation, misreading of the propellant as an inhalational anaesthetic so that both the inspiratory as well as expiratory values of the inhalational anaesthetic in use suddenly shoot up without the anesthesiologist changing the dial concentration. In the Drager Primus® workstation, flashing of either halothane or enflurane label (with inspiratory and end tidal concentrations as well) is because of the greater structural similarity between the propellant norflurane and halothane vis a vis the other anaesthetic agents which the workstation is programmed to read though the monitor never mistakes the propellant for isoflurane, desflurane or sevoflurane.

In our institution, we now utilize this peculiar observation as a confirmatory test for two things. Firstly, the correct placement of salbutamol puffs (denoted by

inspiratory halothane concentration) and secondly, of salbutamol having reached the trachea in an adequate dose (denoted by end-tidal halothane concentration). Besides salbutamol sulphate, beclomethasone dipropionate and triamcinolone acetonide aerosol inhalers also use HFA-134a as propellant. HFA-134a is also being used as a preanaesthetic vapocoolant spray. In the 1990s, it began replacing dichlorodifluoromethane (Freon) in domestic refrigerators and automobile air conditioners as a high-temperature refrigerant.[3] It replaced chlorofluorocarbons as a propellant in inhalers in December 2008, in compliance with the United Nations Environment Program protocol on ozone depleting substances.[4,5] This is because it has an insignificant ozone depletion potential and a negligible acid rain potential.[3]

This propellant has been shown to be safe and nonanaesthetic in standard inhaler doses.[4] HFA134a may result in microsomal enzyme induction.[5] Defluorination of HFA134a has been seen in rat hepatocytes.[6] Due to molecular similarity between halothane ($CF_3CHClBr$) and propellant (CF_3CH_2F), further research is warranted into halothane-associated hepatitis due to anti-tri-fluoro-acetyl antibodies after repeated administration or long-term use. Because of its high global warming potential (100 years-GWP equals 1430), HFA-123a has been banned from use in Europe since 2011(starting with cars), to be completely phased out by 2017.[3,7,8] Thus, the quest for the ideal propellant for pressurised metered dose inhalers does not end with HFAs.

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