Direct Healthcare Professional Communication

June 2022

Cardiac events, hepatic, blood, kidney side effects and contraindication in specific population associated with Halothane containing products

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following:

Summary:

- The following undesirable effects have been reported following the use of halothane:
  - Hepatic necrosis, also known as "Halothane hepatitis" occurs rarely but fatalities have been reported. Severe hepatotoxicity occurs more frequently after repeated exposure to halothane.
  - Eosinophilia has been reported in conjunction with halothane induced hepatotoxicity.
  - Malignant hyperpyrexia has occasionally been reported with halothane, as with other halogenated anaesthetics.
  - Cardiac arrhythmias are very common during halothane anaesthesia. Ventricular arrhythmias occur more frequently than with other volatile anaesthetic agents . There have been instances of cardiac arrest.
- As with other halogenated anaesthetics, halothane has a depressant effect on the respiratory and cardiovascular systems and the following undesirable effects have been reported:
  - Respiratory depression, Hypotension , Bradycardia , Skeletal muscle relaxation, Post-operative nausea, vomiting and shivering. Renal failure, sometimes with concurrent liver failure
  - Adverse reactions have been spontaneously reported during post-approval use of Halothane. These events are reported voluntarily from a population with an unknown rate of exposure. Therefore it is not possible to estimate the true incidence of adverse events.

Further information:

Cardiac

The incidence of cardiac arrhythmias may be increased when adrenaline, most other sympathomimetics (e.g. methylphenidate), and theophylline are used concurrently with halothane. Cardiac arrhythmias are very common during halothane anaesthesia. Ventricular arrhythmias occur more frequently than with other volatile anaesthetic agents (see 4.4). There have been instances of cardiac arrest. Bradycardia Intraoperative, Cardiac arrest in patient with extraocular cystices, Ventricular extrasystole, Idioventricular rhythm

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Hepatic

The incidence of severe liver damage (jaundice, which may lead to hepatic failure as a consequence of Page 2 of 3 massive hepatic cell necrosis) is much rarer but cases requiring liver transplants and fatalities have been reported. The risk of developing hepatic failure appears to be greatly increased by repeated exposure to halothane. Although short intervals of time between exposures are likely to increase the risk of hepatotoxicity, even long intervals between exposure may not reduce the risks, since some patients have developed severe reactions to halothane given many years after the previous exposure. Hepatic necrosis, also known as "Halothane hepatitis" (see section 4.4) occurs rarely but fatalities have been reported. Severe hepatotoxicity occurs more frequently after repeated exposure to halothane. Eosinophilia has been reported in conjunction with halothane induced hepatotoxicity. Fulminant Hepatic, Failure Acute toxic hepatitis. During the induction of halothane anaesthesia, a moderate fall in blood pressure commonly occurs. (Halothane lowers arterial blood pressure in a dose-dependent manner). The pressure tends to rise when the vapour concentration is reduced to maintenance levels, but it usually remains steady below the pre-operative level. This hypotensive effect is useful in providing a clear operating field and a reduction in haemorrhage. However, if necessary, intravenous doses of methoxamine (5 mg are usually adequate) can be given to counteract the fall in blood pressure.

Renal

The following undesirable effects have been reported: Renal failure, sometimes with concurrent liver failure

Paediatric population

Children anaesthetised with halothane should have ECG, blood pressure, oxygen saturation and end tidal CO2 monitoring in a setting where full resuscitative equipment is available and with staff fully trained in the resuscitation of children. The presence of additional arrhythmogenic factors especially hypoxia and carbon dioxide retention, use of sympathomimetics (see 4.5), and other factors which may stimulate the sympathetic nervous system should also be taken into account. Thus, to prevent hypoxia, inhalational anaesthetics are given with concentrations of oxygen greater than 21%. Use of inhaled anaesthetic agents has been associated with very rare increases in serum potassium levels that have resulted in cardiac arrhythmias and death in children during the postoperative period. The condition has been described in patients with latent as well as overt neuromuscular disease, particularly Duchenne muscular dystrophy. Use of suxamethonium has been associated with most, but not all of these cases. These patients showed evidence of muscle damage with increased serum creatine kinase concentration and myoglobinuria. These patients did NOT have classical signs of malignant hyperthermia such as muscle rigidity, rapid increase in body temperature, or increased oxygen uptake and carbon dioxide production. Prompt and vigorous treatment for hyperkalaemia and arrhythmias is recommended. Subsequent evaluation for latent neuromuscular disease is indicated

References

EMC https://www.medicines.org.uk/emc/product/13105/smpc#gref

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Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: https://primaryreporting.who-umc.org/EG
QR Code:

Hotline: 15301

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