

Nitrous oxide use during general anaesthesia for general surgical cases

Nitrous oxide has been used in general anaesthesia for well over a century. However, it still remains one of the most controversial issues within the specialty with many anaesthetists strongly polarised as to whether its use is beneficial or deleterious.

Will the recent publication of the ENIGMA-II trial (Myles et al, 2014) regarding nitrous oxide and adverse cardiovascular events shed new light on this debate?

Nitrous oxide as an addition to inhalational general anaesthesia

Nitrous oxide has many undisputed advantages. It is well known to have a rapid onset of action and use of it as a carrier gas with volatile agents hastens the onset of anaesthesia. One study demonstrated this during inhalational induction with sevoflurane in children (Lee et al, 2013). Patients who had nitrous oxide added to their anaesthetic showed a faster loss of consciousness ($P=0.01$) as well as a reduction in excitatory movements ($P=0.007$).

When used in conjunction with volatile inhalational agents the effects are additive, thus reducing the amount of these drugs required. The marked reduction in minimum alveolar concentration required was noted in the ENIGMA-II study which looked at nitrous oxide usage in patients with proven or suspected cardiovascular disease having major non-cardiac surgery (Myles et al, 2014). Reduction in the use of these expensive agents impacts on the financial cost of delivery of general anaesthesia and may also reduce the incidence of adverse effects associated with use of volatile inhalational agents.

Nitrous oxide is well known for its analgesic properties and these are often used

clinically outside of general anaesthesia. As well as providing perioperative analgesia nitrous oxide may well have persisting effects postoperatively and one follow-up study has shown a reduction in the incidence of chronic pain several years later (Stiglitz et al, 2010).

Disadvantages of use of nitrous oxide

The most commonly mentioned drawback of the usage of nitrous oxide is that of increased postoperative nausea and vomiting. In the ENIGMA-II trial (Myles et al, 2014) 11% of the control group patients

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suffered from severe postoperative nausea and vomiting; however, this was increased to 15% in those receiving nitrous oxide ($P<0.0001$).

Use of nitrous oxide has previously been thought to be associated with increased cardiovascular complications and wound infections. This is thought to be secondary to its effect as an inhibitor of methionine synthase and resulting endothelial damage. The primary outcome for the ENIGMA-II trial (Myles et al, 2014) was death or significant cardiac events. There was no significant increase in death or cardiac events between the two arms of the study ($P=0.64$). As a secondary outcome incidence of surgical site infection was unaffected by nitrous oxide usage perioperatively ($P=0.61$), thus reducing concerns about these complications.

Another issue with nitrous oxide is its ability to diffuse across the materials used to make the cuffs for endotracheal tubes and laryngeal masks. This causes an increase in cuff pressure with possible resulting trauma to the larynx (Braz et al, 2004; Chen et al, 2011).

Prolonged exposure to nitrous oxide may have other damaging effects. A cor-

relation between ambient nitrous oxide levels and markers of oxidative damage to DNA has been shown in nurses working in operating theatres and recovery areas (Wrońska-Nofer et al, 2012).

Conclusions

The ENIGMA-II trial is the largest and most in-depth study into the effects of nitrous oxide in anaesthesia to date. In light of the results we can be confident that the use of nitrous oxide in general surgery is not as dangerous to patients as previously suspected and should not be avoided purely because of concerns regard-

ing safety. However, the link between postoperative nausea and vomiting and nitrous oxide has been confirmed in this trial and this may still be seen as a reason to minimize the use of the gas. **BJHM**

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