Article concludes no reason for laughing gas to be withdrawn from operating theaters

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A debate at this year's Euroanaesthesia meeting in Berlin will focus on whether laughing gas (nitrous oxide) should be banned from the operating room. The debate coincides with an article on the "Current place of nitrous oxide in clinical practice" published in the *European Journal of Anaesthesiology*, that concludes there is "no clinically relevant evidence for the withdrawal of nitrous oxide from the armamentarium of anaesthesia practice or procedural sedation." The article has been prepared by a special taskforce of the European Society of Anaesthesiology (ESA), which organises Euroanaesthesia.

In the debate, Professor Rolf Rossaint, University Hospital Aachen, Germany, will say he believes nitrous oxide should be banned. "Whereas 30 years ago, nearly every general anaesthesia procedure was performed with nitrous oxide as an adjuvant, a steady decline of its use over the last 15 years has been observed. There are several reasons, which caused the reduction of the usage of nitrous oxide," explains Professor Rossaint.

First, today there are new well-tolerated short- to ultra-short acting anaesthetic drugs available and modern anaesthetic machines allowing low-flow anaesthesia with the newer and inexpensive inhalational drugs. It has been repeatedly shown that using nitrous oxide is more expensive than the use of newer, well-tolerated anaesthetics. "These calculations were correct even without including the construction costs of the nitrous oxide pipeline systems in a new hospital or operating theatre, and the technical maintenance costs," says Professor Rossaint.

Professor Rossaint will also say that in the last 15 years we have learned a lot about the possible harmful effects of nitrous oxide. Even when avoiding its contraindications such as presence of closed gas containing cavities or abnormalities of metabolism of vitamin B12, there can be problems related to administration of nitrous oxide (related to the endotracheal tube cuff pressure) which, if not corrected every 15-30 minutes, can cause damage to the throat and/or nerves in patients.

"Furthermore, it has been shown in many large studies that complications such as postoperative nausea and vomiting are increased with the use of nitrous oxide. But not only can there be increased morbidity, there was even a case report series describing technical errors in nitrous oxide delivery causing death in a total of 15 patients," says Professor Rossaint. He concludes: "There are many reasons to stop the use of nitrous oxide."

In the second half of the debate, the arguments against a ban will be put forward by Professor Daniel Sessler, Cleveland Clinic, Ohio, USA, in his talk "nitrous oxide is an effective and safe anaesthetic".

"Nitrous oxide has been used for more than a century and given to about two billion patients," says Professor Sessler. "Its low tissue solubility (and therefore rapid kinetics), low cost, and minimal cardiorespiratory complications have made nitrous oxide by far the most commonly used general anaesthetic in history."

He concedes that there are difficulties associated with use of nitrous oxide, including inactivation of vitamin B12 and potential stiffening of arterial vessel walls. There are thus theoretical biochemical reasons to believe that nitrous oxide may reduce resistance to surgical wound infections and promote myocardial infarctions (heart attacks).

However, Professor Sessler says: "There is, though, no compelling

evidence that nitrous oxide causes important clinical complications. In fact, large randomised trials consistently show that nitrous oxide does not promote complications. For example, an initial study comparing nitrous oxide to supplemental oxygen identified more infections in the nitrous oxide group. But this result is difficult to interpret since oxygen per se may be protective. In fact, large randomised trials comparing nitrous oxide to nitrogen do not demonstrate an increase in infection risk."

He adds that a 7000-patient randomised trial in patients at high risk of cardiovascular events convincingly demonstrates that nitrous oxide does not increase the incidence of postoperative myocardial infarctions. Randomised trials also show that nitrous oxide does not increase the risk of cancer recurrence, and actually reduces the risk of persistent surgical pain.

Regarding clinical complications related to nitrous oxide, Professor Sessler explains that for postoperative nausea and vomiting, a randomised trial with more than 5,000 patients shows that nitrous oxide increases nausea and vomiting only about two-thirds as much as volatile anaesthesia. Clinicians concerned about nausea and vomiting should thus avoid volatile anaesthetics rather than avoiding nitrous oxide. Effects on bowel distention—another often discussed complication—are also minor, he will say.

Professor Sessler concludes: "In summary, nitrous oxide is inexpensive and has favourable kinetics; it does not increase the risk of surgical site infection, postoperative myocardial infarction, or cancer recurrence. The gas may be protective against persistent pain. And the two complications resulting from nitrous oxide administration, nausea and bowel distension, are minor and no worse than complications caused by alternative anaesthetics."

Speaking on behalf of the ESA Taskforce, of which he is a member,

Professor Markus Hollmann, Department of Anaesthesiology, Academic Medical Center, Amsterdam, Netherlands, says: "Members of the task force agreed that, despite its continuously decreasing use in perioperative care, there are no arguments to state that the use of nitrous oxide should be abandoned. There is no evidence indicating that the use of nitrous oxide in a modern clinically relevant setting increases health risk in patients or providers exposed to this drug."

More information: The current place of nitrous oxide in clinical practice, *European Journal of Anaesthesiology*, 2015. DOI: 10.1097/EJA.0000000000000264

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