Nitrous Oxide For Anesthesia May Decrease Complications And Death

Giving nitrous oxide as part of general anesthesia for noncardiac surgery doesn't increase the rate of complications and death—and might even decrease the risk of such events, according to a pair of studies in the May issue of *Anesthesia & Analgesia*, official journal of the International Anesthesia Research Society (IARS).

But an accompanying series of editorials points out some important limitations of the two studies—which can't completely overcome previous concerns about the safety of using nitrous oxide (N2O) as a surgical anesthetic.

Is Nitrous Oxide Safe for Surgical Anesthesia?

Nitrous oxide is the world's oldest general anesthetic, but there's a long history of debate regarding its appropriate role in modern surgical anesthesia. Although nitrous oxide provides effective sedation and pain control, it has known disadvantages and side effects. A previous study, called "ENIGMA-I," reported a small but significant increase in myocardial infarction (heart attack) among patients receiving nitrous oxide as part of anesthesia for noncardiac surgery (procedures other than heart surgery).

The two new studies, based on large patient databases, question the harmful effects of nitrous oxide. Dr Kate Leslie of Royal Melbourne Hospital, Australia, and colleagues analyzed data from a previous study of more than 8,300 patients undergoing surgery. That study was designed to assess the effects of giving one type of blood pressure drug (beta-blockers) during surgery, not the effects of nitrous oxide.

Dr Leslie and colleagues compared the risk of death or serious complications after surgery for patients who versus did not receive nitrous oxide as part of anesthesia. Twenty-nine percent of patients in the study received nitrous oxide.

The results showed comparable rates of adverse outcomes between groups. With or without nitrous oxide, the overall rate of death or serious complications was approximately seven percent, including about a six percent rate of myocardial infarction. Risk of death after surgery was about three percent in both groups.

Outcomes remained similar on "propensity score" analysis—a technique accounting for characteristics making patients more or less likely to receive nitrous oxide. Use of nitrous oxide varied widely between the different countries and hospitals participating in the study.

No Increase in Risks with N2O—But 'More Definitive' Studies Needed

Dr Alparslan Turan of the Cleveland Clinic and colleagues outcomes reviewed more than 49,000 patients undergoing noncardiac surgery between 2005 and 2009. In this study, 45 percent of patients received nitrous oxide.

The results suggested a significant reduction in the risk of death after surgery for patients receiving nitrous oxide: about one-third lower than in patients who did not receive nitrous oxide. There was also a significant 17 percent reduction in the combined rate of major complications and death.

Surprisingly, nitrous oxide was specifically associated with a 40 percent reduction in the risk of major lung- and breathing-related complications. However, the authors acknowledge the risk of "selection bias"—anesthesiologists may have avoided using nitrous oxide in patients at risk of lung problems. Again, the findings remained significant on propensity score analysis.

In one of three accompanying editorials, Thomas R. Vetter, MD, MPH, and Gerald McGwin, Jr, MS, PhD, of University of Alabama at Birmingham highlight some important limitations of the study data. They note that, although both studies were large, they were not randomized trials—the strongest type of scientific evidence.

Drs Vetter and McGwin emphasize that even sophisticated techniques like propensity score analysis can't account for all of the differences between groups that may have affected responses to nitrous oxide. They note that a randomized "ENIGMA-II" study is underway, and may provide "additional, perhaps more definitive insight" on the risks and potential benefits of using nitrous oxide as part of general anesthesia.

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