

Title: DOES NITROUS OXIDE INDUCE MYOCARDIAL ISCHEMIA IN PATIENTS WITH POOR VENTRICULAR FUNCTION?

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**Introduction.** In canine models, Philbin *et al.* and Nathan found that nitrous oxide (N<sub>2</sub>O) caused contraction abnormalities of myocardium supplied by a critically stenosed coronary artery.<sup>1,2</sup> Cahalan *et al.* have used transesophageal echocardiography (TEE) and electrocardiography to show that N<sub>2</sub>O does not induce myocardial ischemia when used as an adjunct to fentanyl anesthesia in patients (Pts) who have severe coronary artery disease accompanied by well preserved valvular and left ventricular (LV) function.<sup>3</sup> But the issue of the safe use of N<sub>2</sub>O in Pts with poor LV function remained unresolved.<sup>3</sup> We have extended the study of Cahalan *et al.* to Pts with poor LV function.

**Methods.** With approval from our committee on human studies and informed consent, we studied 46 Pts scheduled for elective coronary artery surgery. Methods were the same as those of Cahalan *et al.* except that Pts with an ejection fraction (EF) by angiography of less than 40% were not excluded. After premedication with lorazepam, Pts were anesthetized with a 15 mcg/kg bolus and 0.2 mcg/kg/min infusion of intravenous fentanyl. Relaxation was provided with 0.1 mg/kg of pancuronium. After endotracheal intubation, a TEE transducer was positioned to obtain a short-axis cross-sectional echocardiogram of the LV at the level of the papillary muscles for detection of segmental wall motion abnormalities (SWMA). Following 20 minutes of ventilation with 100% oxygen, baseline data was collected, then either 60% nitrogen (N<sub>2</sub>) or 60% N<sub>2</sub>O (random assignment) was added to the inspired gas for 10 minutes. Then, 100% oxygen was given for 10 minutes, and finally 60% N<sub>2</sub>O or N<sub>2</sub> (which ever was not previously used) was given for 10 minutes. A diagnostic quality 12-lead electrocardiogram (EKG) and hemodynamics were recorded before induction of anesthesia (awake), and together with the LV short-axis echocardiogram at the end of each treatment period. Surgery did not start until the study was concluded. Myocardial ischemia was diagnosed if two independent observers found ST segment changes of more than 1 mm (0.1mv) or worsening of LV segmental contraction (graded qualitatively).<sup>3</sup> The data reported by Cahalan *et al.* (18 Pts), which was obtained under identical conditions by identical methods, was pooled with the data obtained in this study.

**Results.** Ischemia was diagnosed in 11 of the pooled 64 Pts. Two Pts developed gross ST segment changes while awake, and com-

plained of severe angina. EKG changes did not resolve with induction of anesthesia, the TEE probe was not placed, the study was aborted, and the Pts went directly to surgery. In 8 Pts ischemia was diagnosed by both SWMA and ST segment changes, and in one by SWMA changes alone. Six developed ischemia between awake and baseline data collection periods. In one of these the ischemia resolved before the baseline data collection. In 3 it resolved during the first test gas (N<sub>2</sub>O twice, N<sub>2</sub> once). In one it decreased progressively and almost resolved by the end of the study, and in the last it persisted throughout the study unchanged. In 3 it developed during 100% oxygen and resolved (N<sub>2</sub>O twice) or persisted (N<sub>2</sub>) during the next and final period. Ischemia started more often during baseline (Binomial p=.027) and resolved more often during N<sub>2</sub>O (Binomial p=.037).

There was no difference between EF in ischemic and non-ischemic Pts (t-Test, p=.46). Ischemia was significantly more likely in Pts not on beta blockers preoperatively (Binomial p=.043), but preoperative Calcium channel blockers made no difference (Binomial p=.536). When compared to each previous 100% oxygen period, N<sub>2</sub>O decreased heart rate (HR) by 9% (t-Test p<.001), mean arterial pressure by 5% (p=.002), and cardiac output (CO) by 17% (p<.001) compared to N<sub>2</sub>.

**Discussion.** Neither N<sub>2</sub>O nor N<sub>2</sub> were found to induce ischemia in Pts with coronary artery disease during fentanyl anesthesia, even if ventricular function was poor. Philbin *et al.* found similar decreases in HR 12% and CO 17% compared to N<sub>2</sub>, and Nathan found an 8% increase in HR with N<sub>2</sub>O compared to isoflurane.<sup>1,2</sup> Cason *et al.* controlled HR in pigs and found no induction of ischemia by N<sub>2</sub>O.<sup>4</sup> Other factors in the clinical setting, such as use of preoperative beta blockers or changes in hemodynamics on the order of 10%, may have larger effects on induction of ischemia in Pts than that possibly directly produced by N<sub>2</sub>O.

#### References.

1. Nathan HJ: Anesthesiology 68:407-415, 1988
2. Philbin DM, Foex P, Drummond G, et al.: Anesthesiology 62:166-174, 1985
3. Cahalan MK, Prakash O, Rulf ENR, et al.: Anesthesiology 67:925-929, 1988
4. Cason BA, Mazer CD, Demas KA, Hickey RF: Anesthesiology 67:A46, 1987