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_2O) caused contraction abnormalities of myocardium supplied by a critically stenosed coronary artery.[1,2] Cahalan et al. have used transesophageal echocardiography (TEE) and electrocardiography to show that N_2O does not induce myocardial ischemia when used as an adjunct to fentanyl anesthesia in patients (Pts) who have sever coronary artery disease accompanied by well preserved valvular and left ventricular (LV) function.[3] But the issue of the safe use of N_2O in Pts with poor LV function remained unresolved.[3] 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_2) or 60% N_2O (random assignment) was added to the inspired gas for 10 minutes. Then, 100% oxygen was given for 10 minutes, and finally 60% N_2O or N_2 (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).[3] 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 complained of sever 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_2O twice, N_2 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_2O twice) or persisted (N_2) during the next and final period. Ischemia started more often during baseline (Binomial p=.027) and resolved more often during N_2O (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_2O 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_2.

Discussion. Neither N_2O nor N_2 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_2, and Nathan found an 8% increase in HR with N_2O compared to isoflurane.[1,2] Cason et al. controlled HR in pigs and found no induction of ischemia by N_2O.[4] 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_2O.

References.

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