Title: THE EFFECTS OF NITROUS OXIDE ON THE PULMONARY CIRCULATION AND RIGHT VENTRICULAR FUNCTION IN PATIENTS WITH PULMONARY HYPERTENSION

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Introduction Though nitrous oxide (N_2O) may be a useful adjunct to narcotic anesthesia, its use has been restricted in patients with pulmonary hypertension (PHT) because it may increase pulmonary vascular resistance (PVR). In a previous study of patients with PHT, N_2O resulted in a marked increase in PVR without any significant change in central venous pressure (CVP).[1] However, the compliant right ventricle might have dilated significantly without a significant change in CVP. Thus the clinical significance of this observed increase in PVR is unclear. The purpose of this study was to reexamine the effects of N_2O on the pulmonary circulation using the rapid-response pulmonary artery catheter (RRPAC), and to determine if significant changes in right ventricular function occur as a result of N_2O.

Methods Ten patients with PHT secondary to mitral valvular disease presenting for mitral valve repair or replacement surgery were studied. All patients were in normal sinus rhythm. Written informed consent was obtained and the study protocol was approved by the institutional human investigations committee. A radial arterial catheter and RRPAC were inserted and connected to aneroid-calibrated transducers placed at the level of the right atrium. Patients were anesthetized with fentanyl 50-75 mcg/kg, pancuronium 0.1 mg/kg, and oxygen 100%. Baseline measurements were obtained 10 minutes after the induction of anesthesia and consisted of heart rate (HR), mean arterial pressure (MAP), pulmonary capillary wedge pressure (PCWP), mean pulmonary arterial pressure (MPAP), CVP, cardiac output (CO), right ventricular ejection fraction (RVEF), right ventricular end-systolic volume (RVESV), and right ventricular end-diastolic volume (RVEDV). Right ventricular stroke work (RVSW), and PVR were calculated using standard formulae. 70% N_2O / 30% oxygen was then administered, and the measurements were repeated when a stable end-tidal N_2O concentration had been reached. A "return to baseline" measurement was obtained on 100% oxygen after the N_2O had been eliminated. Thermodilution measurements were performed in triplicate using an REF-1[R] American Edwards computer with iced D5W and averaged. Data were analyzed using repeated-measures ANOVA and paired Student's t-test with Bonferroni's modification. Significance was defined as $p < 0.05$.

Results Nitrous oxide resulted in statistically significant decreases in PAP, PCWP, CO, RVEF, and RVSW (see Table). There were no other significant changes. Return to 100% oxygen resulted in significant decreases in PAP, PCWP, CO, RVEF, and RVSW compared to the baseline measurements. There were no clinically significant reactions to N_2O requiring pharmacologic intervention. No significant differences were observed between the N_2O and "return to baseline" groups.

Discussion Nitrous oxide has several desirable anesthetic properties: hypnosis, amnesia, analgesia, and rapid onset and elimination. A previous study demonstrated that, in patients with PHT, N_2O increased PVR. The anesthetic techniques in that study were either low-dose fentanyl (10 mcg/kg) or halothane. The current study used additional measurements of right ventricular function to examine the effects of N_2O in patients anesthetized with a high-dose fentanyl (50-75 mcg/kg) technique. The results indicate that N_2O did not significantly change PVR and actually decreased PAP and RVSW. The observed changes during N_2O administration in PAP, PCWP, CO, RVEF, and RVSW were similar in magnitude and direction to those observed during the "return to baseline" measurement and were not clinically significant. The similarity in the N_2O and "return to baseline" data suggest that a gradual decrease in sympathetic tone occurred over time which did not return following the elimination of N_2O. The small increase in RVESV at the "return to baseline" is statistically significant, but of doubtful clinical significance. It is concluded that N_2O may be used safely in conjunction with high-dose fentanyl in patients with PHT secondary to mitral valvular disease.

Reference

1. Schulte-Sasse U, Hess W, Tarnow J: Pulmonary Vascular Responses to Nitrous Oxide in Patients with Normal and High Pulmonary Vascular Resistance. Anesthesiology 57:9-13, 1982.

TABLE Means ± S.D. n = 10

	BASELINE	N_2O	RTB
HR (bpm)	77±20	72±17	69±19
MAP (mm Hg)	76±14	67±12	71±13
PAP (mm Hg)	37±15	33±14*	31±14*
PCWP (mm Hg)	27±10	25±10*	24±10*
CVP (mm Hg)	13±4	12±4	11±4
CO (l/min)	3.7±1.4	3.2±1.1*	3.2±1.1*
RVEF	0.31±.09	0.30±.09*	0.29±.10*
RVESV (ml)	110±35	112±34	120±45*
RVEDV (ml)	158±38	158±34	167±45
PVR (d*s/cm^5)	247±191	230±135	206±130
RVSW (gm-m)	17±11	13±9*	13±9*
PCO_2 (torr)	39±15	37±14	----

RTB = RETURN TO BASELINE
*P < 0.05 compared to baseline