Title : N_2O ADDITION TO HALOTHANE AND ENFLURANE: DEPRESSANT OR STIMULANT IN CORONARY ARTERY DISEASE?

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Introduction: Nitrous oxide (N_2O) is commonly used as a supplement to potent halogenated inhalation anesthetics to reduce their MAC and thus limit their cardiovascular effects. However, in normal volunteers, the addition of N_2O to halothane results in a different cardiovascular response than with Enflurane. A sympathomimetic response is seen with Halothane and the lack of such a response is seen with Enflurane.[1] The hemodynamic changes following the combination of N_2O with halogenated agents has not been determined for patients with coronary-artery disease (CAD). Nitrous oxide, alone, has been administered to these patients and myocardial performance is significantly depressed.[2] To investigate if the cardiovascular system of a patient with CAD is stimulated by Halothane supplemented with N_2O and not with Enflurane supplemented with N_2O, the following study was done.

Method: Fifteen patients undergoing coronary artery bypass surgery were studied after informed consent and institutional approval. All patients had 2 to 5 coronary artery lesions and normal left ventricular (LV) function with a LV end-diastolic pressure less than 15 torr. Propranolol was tapered prior to operation and all medications discontinued except nitrates. Premedication was morphine (7.5-10 mg) and scopolamine. Incremental doses of sodium thiopental was used to achieve unconsciousness and succinylcholine was administered to facilitate tracheal intubation. Pavulon was given and respiration was controlled to result in a $PaCO_2$ between 35-40 torr. Radial arterial pressure, EKG and Swan Ganz catheter were monitored. The patients were divided into two groups following loss of consciousness. Group I (7 patients) received an inflow concentration of 2-3% Halothane for 5 minutes and then 1% Halothane for 10 minutes. After this equilibration period, heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), and cardiac output (CO) were recorded and an arterial blood sample drawn for plasma epinephrine (E) and norepinephrine (NE) levels. The Halothane concentration was then lowered to 0.5% and 50% N_2O added. After 15 minutes stabilization, hemodynamic parameters were again measured and a blood sample taken. For Group II (8 patients), Enflurane was used instead of Halothane. All data were analyzed with Students t-test for paired data and a level of significance of 0.05 was chosen.

Results: The hemodynamic data is summarized in Table I. There was no significant change in HR, MAP, CVP, CO and SVR between Halothane alone and equianesthetic levels of Halothane and N_2O. With Enflurane, the addition of N_2O did significantly decrease CO and increase SVR while HR, MAP, and CVP were not altered. The plasma E and NE levels of Group I, comparing Halothane and Halothane-N_2O, and Group II, comparing Enflurane and Enflurane-N_2O did not change with N_2O addition (Table 2). However, the NE levels of Group I were almost double those of Group II.

Discussion: With Halothane, the addition of N_2O did not change the measured cardiovascular parameters. N_2O addition to a steady-state Halothane concentration in normal volunteers was reported to increase MAP, CVP and SVR.[3] This was attributed to sympathetic activation though plasma NE levels were not measured. In our study the NE level was unchanged with N_2O addition. The NE levels, however, were elevated for Halothane throughout the study period of 30 minutes following induction. This suggests that Halothane results in an increase in sympathetic activity and prevents depression of myocardial performance by N_2O. Nitrous oxide supplement to Enflurane anesthesia produced myocardial depression as evidenced by a decrease in CO and an increased in SVR. The absence of a sympathetic response with a raised plasma NE level after N_2O addition suggests that this is a direct effect of N_2O on systemic arterioles and/or left ventricular function. Previously, myocardial depression was not noted after N_2O addition to Enflurane in volunteers with normal LV function.[1] In patients with CAD, there may be little myocardial reserve and a more dramatic change will be seen if contractility or SVR is altered by N_2O. These results indicate that N_2O addition to Halothane is better tolerated than to Enflurane in the patient with CAD.

TABLE 1
EFFECT OF ADDITION OF N_2O ON HEMODYNAMIC DATA

	Group I		Group II	
	Halothane	Halothane + N_2O	Ethrane	Ethrane + N_2O
HR (bpm)	72 ± 15	76 ± 14	70 ± 10	65 ± 10
MAP (torr)	87 ± 11	79 ± 12	75 ± 7	82 ± 15
CVP (torr)	18.0 ± 4.4	13.2 ± 3.1	10.6 ± 2.4	9.3 ± 3.9
CO (L/min)	6.1 ± 3.5	5.4 ± 2.4	4.4 ± .9	3.7 ± .5*
SVR (dynes·sec·cm^{-5})	1213 ± 826	1272 ± 738	1258 ± 272	1556 ± 328*

*Significant change within group, $p<0.05$

TABLE 2
CHANGES IN PLASMA CATECHOLAMINE LEVELS

	Group I		Group II	
	Halothane	Halothane + N_2O	Ethrane	Ethrane + N_2O
E (pg/ml)	29.1	27.7	35.6	42.0
NE (pg/ml)	405.1	456.6	273.3	272

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