

Title : N₂O ADDITION TO HALOTHANE AND ENFLURANE: DEPRESSANT OR STIMULANT IN CORONARY ARTERY DISEASE?

Authors : S.T. Hanowell, M.D., Y.D. Kim, M.D., M. Jones, M.D., E. Pierce, R.N., B.S.N. and
and T.E. Macnamara, M.B., Ch.B.

Affiliation: Anesthesia Section, Clinical Center, NIH, Clinic of Surgery, National Heart, Lung and Blood Institute, Bethesda, Maryland 20205 and the Department of Anesthesia, Georgetown University School of Medicine, Washington, D.C. 20007

Introduction: Nitrous oxide (N₂O) 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 N₂O 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 N₂O 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 N₂O and not with Enflurane supplemented with N₂O, 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 PaCO₂ 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% N₂O 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 Student's 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 N₂O. With Enflurane, the addition of N₂O 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-N₂O, and Group II, comparing Enflurane and Enflurane-N₂O did not change with N₂O addition (Table 2). However, the NE levels of Group I were almost

double those of Group II.

Discussion: With Halothane, the addition of N₂O did not change the measured cardiovascular parameters. N₂O 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 N₂O 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 N₂O. Nitrous oxide supplement to Enflurane anesthesia produced myocardial depression as evidenced by a decrease in CO and an increase in SVR. The absence of a sympathetic response with a raised plasma NE level after N₂O addition suggests that this is a direct effect of N₂O on systemic arterioles and/or left ventricular function. Previously, myocardial depression was noted after N₂O 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 N₂O. These results indicate that N₂O addition to Halothane is better tolerated than to Enflurane in the patient with CAD.

TABLE 1
EFFECT OF ADDITION OF N₂O ON HEMODYNAMIC DATA

	Group I		Group II	
	Halothane	Halothane + N ₂ O	Ethrane	Ethrane + N ₂ O
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 ₂ O	Ethrane	Ethrane + N ₂ O
E (pg/ml)	29.1	27.7	35.6	42.0
NE (pg/ml)	405.1	456.6	273.3	272

References: 1. Smith NT, Calverly RK, Prys-Roberts C, et al: Impact of nitrous oxide on the circulation during enflurane anesthesia in man. *Anesthesiology* 48: 345-349, 1978
2. Eiscle JH, Reitan JA, Massumi MD, et al: Myocardial performance and N₂O analgesia in coronary-artery disease. *Anesthesiology* 44:16-20, 1976
3. Smith NT, Eger EI, Stoelting KK, et al: The cardiovascular-sympathomimetic responses to the addition of nitrous oxide to halothane in man. *Anesthesiology* 32:410-421, 1970