Title: GRADUAL OR ABRUPT NITROUS OXIDE ADMINISTRATION IN A CANINE MODEL OF CRITICAL CORONARY STENOSIS INDUCES REGIONAL MYOCARDIAL DYSFUNCTION WHICH IS WORSENED BY HALOTHANE

Authors: B. J. Leone, M.D., D. M. Philbin, M.D., J. J. Lehot, M.D. and P. Foëx, M.D., D.Phil.

Affiliation: Nuffield Department of Anaesthetics, University of Oxford, Radcliffe Infirmary, Woodstock Road, Oxford, U.K. OX2 6HE

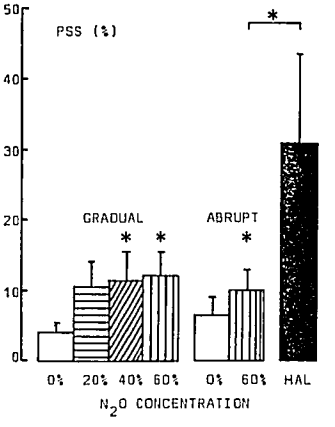
Introduction. The addition of 66% N_2O in a canine model with critical coronary constriction produces contraction abnormalities.[1] Halothane has been suggested to have a beneficial effect on the ischemic heart by decreasing myocardial oxygen demand more than supply.[2] This study was undertaken to see if: 1) the stepwise addition of N_2O would produce dose-related changes in regional function and 2) 0.7% halothane added to narcotic-N_2O would improve oxygen balance and reverse dysfunction in an area of compromised flow.

Methods. Eight mongrel dogs received fentanyl 100 mcg/kg bolus dose followed by infusion of 1.5 mcg/kg/min. Regional ventricular function was measured by recording segment length in areas supplied by the left anterior descending (LAD) and left circumflex (LC) coronary arteries during critical stenosis of the LAD.[1] Inspired O_2 was held at 40% and N_2O was added in a stepwise fashion in increments of 20% and recordings taken at 10 min. Measurements were obtained before N_2O, at 20%, 40%, and 60% inspired N_2O, and after N_2O withdrawal. Then 60% N_2O was abruptly introduced and measurements repeated. After 15 min. halothane, 0.7% inspired, was given to decrease mean arterial pressure (MAP) from 105 to 75 mmHg. The data were analyzed by two-way analysis of variance and Duncan's test or Kruskal-Wallis and Wilcoxon matched pairs tests as appropriate, with $P<0.05$ as a significance level. Data are expressed at % change from control or Mean ± SEM.

Results. Significant reductions in mean arterial pressure (MAP) (8.5% Gradual, 9.4% Abrupt) and peak LV dp/dt (16.1% Gradual, 18.3% Abrupt) occurred with 60% N_2O. Coronary perfusion pressure (CPP) did not decrease; LAD coronary blood flow (CBF) decreased significantly (22.4%) during abrupt 60% N_2O but was no different from values obtained with 60% gradual N_2O (57.0 ± 14.8 vs. 63.4 ± 16.5 ml/100g/min, respectively).

Regional dysfunction, (postsystolic shortening-PSS) appeared with gradual and abrupt N_2O administration. A significant increase in PSS occurred with 60% N_2O whether administered gradually or abruptly (Fig. 1). PSS increased with each increment of N_2O. At 20% this did not achieve statistical significance, but at 40% and 60% N_2O PSS did increase significantly. There was no dysfunction in the LC segment. With the addition of halothane, MAP was decreased from 106.1 ± 4.5 mmHg to 76.1 ± 5.5 mmHg ($P<0.05$) and peak LV dp/dt, decreased from 1681.2 ± 152.3 to 1083.4 ± 80.4 mmHg/s ($P<0.05$). PSS increased from 9.9% ± 3.2 to 30.8% ± 12.6 ($P<0.05$) (Fig. 1).

Discussion. These data demonstrate that the stepwise addition of N_2O produces a substantial increase in PSS in an area of compromised flow comparable to that seen with abrupt N_2O introduction. The increase in PSS with 20% N_2O while not statistically significant was substantial, suggesting that even low concentrations have deleterious effects on compromised myocardium. Since further increases in N_2O did not produce significant further progression in PSS, dysfunction does not appear to be dose-dependent and may occur at very low concentrations. This may be related to changes in regional coronary blood flow though the magnitude of PSS did not appear to relate to the reduction in CBF. The effect of N_2O on the distribution of CBF was not examined and may be a factor. The addition of halothane significantly increased PSS suggesting that although myocardial work decreased, local coronary flow was not preserved or there was an adverse effect on myocardial metabolism. These data suggest that in the compromised myocardium N_2O, even in low concentrations, as well as low concentrations of halothane, may be detrimental.



References. 1) Philbin DM, Foex P, Drummond G, Lowenstein E, Ryder WA, Jones LA: Postsystolic shortening of canine left ventricle supplied by a stenotic coronary artery when nitrous oxide is added in the presence of narcotics. Anesthesiology 62:166-174, 1985.
2) Merin RG: Is anesthesia beneficial to the ischemic heart? II. Anesthesiology 55:341-342, 1981.