

Title: SHOULD NITROUS OXIDE BE USED FOR PATIENTS WITH ISCHEMIC HEART DISEASE?
EVIDENCE OF SAFETY FROM A LABORATORY INVESTIGATION.

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INTRODUCTION

Recently evidence has been presented that nitrous oxide (N₂O) may have adverse cardiac effects in patients with coronary disease as well as in animal models of coronary stenosis. A previous study from this laboratory (1) compared two equipotent anesthetics in the dog; 50% nitrogen with 1.8% isoflurane (ISF) and 50% N₂O with 1.4% ISF. The use of N₂O resulted in increases of 5% in HR and 8% in systolic BP. There were no changes in systolic shortening (SS) or subendocardial/subepicardial blood flow (I/O) ratio in a normally perfused region of the heart whereas in an adjacent ischemic region of the left ventricle SS was diminished by 19% and I/O ratio fell by 30%. The present study was designed to determine the mechanism whereby N₂O worsened ischemia during isoflurane anesthesia.

METHODS

In twelve open-chest ISF anesthetized dogs the proximal LAD coronary artery was cannulated and connected to an autoperfusion circuit on which an artificial coronary stenosis could be imposed. Subendocardial SS in the LAD and CCx regions was measured with a sonomicrometer. Regional myocardial blood flow was measured by injecting radiolabelled microspheres into the left atrium. Measurements were made during the imposition of a stenosis sufficient to decrease SS by 30 - 50%. The identical stenosis was imposed during three treatments (50% Nitrogen + 1.8% ISF, 50% N₂O + 1.4% ISF, 50% N₂O + 1.8% ISF) in a randomized and balanced design. Heart rate, systolic BP and left atrial pressure were held constant to match myocardial oxygen demand during the three anesthetic regimens. This was accomplished using atrial pacing, a Fogarty catheter in the aorta, a femoral arterio-venous fistula, and a pressurized blood reservoir.

RESULTS

In the absence of significant changes in HR, systolic BP and LA pressure there was no change in SS or I/O ratio comparing the equipotent anesthetics 50% nitrogen with 1.8% ISF and 50% N₂O with 1.4% ISF (see TABLE, A-B). The effect of adding 50% N₂O to 1.8% ISF (TABLE, A-C) was to decrease SS

in both the ischemic and normally perfused region. There was no change in I/O ratio in either region.

TABLE: EFFECT OF N₂O WITH HR AND BP CONSTANT

| TREATMENT | CCx SS | LAD SS | CCx I/O | LAD I/O |
|------------------------|----------|----------|----------|----------|
| | normal | ischemic | normal | ischemic |
| A N ₂ +1.8 | 18.1±8.3 | 11.8±7.2 | 1.08±.13 | .46±.20 |
| B N ₂ O+1.4 | 18.5±8.0 | 11.8±7.5 | 1.02±.17 | .45±.18 |
| C N ₂ O+1.8 | 14.4±8.4 | 8.4±5.9 | 1.07±.14 | .46±.18 |
| A-B %DIFF | 2% | 0% | 6% | 2% |
| A-C %DIFF | 23%*** | 34%** | 1% | 0% |

Values are mean±SD. See text for abbrev.
** P<.01, *** P<.001 by paired t-test.

DISCUSSION

In the earlier study (1) the substitution of 50% N₂O for .4% ISF resulted in small increases in HR and BP and worsened myocardial ischemia. In the present study, where HR, systolic BP, and LA pressure were held constant, there was no change in SS or I/O ratio comparing the same two treatments; 50% nitrogen with 1.8% ISF and 50% N₂O with 1.4% ISF. This indicates that the worsening of ischemia previously observed was caused by increased myocardial oxygen demand.

When N₂O was added to 1.8% ISF there was a decrease in SS of similar magnitude in both ischemic and normally perfused myocardium with no change in I/O ratio. This indicates that, at a constant level of ISF, the addition of N₂O caused myocardial depression not specific to ischemic myocardium and without adverse effect on myocardial blood flow distribution.

If extrapolated to humans these findings suggest that, so long as blood pressure and heart rate are maintained at an appropriate level, nitrous oxide can safely be used for patients with coronary artery disease.

REFERENCE

Nathan HJ: Nitrous Oxide Worsens Myocardial Ischemia in Isoflurane Anesthetized Dogs. Anesthesiology 68:407-415, 1988.