Title: NITROUS OXIDE DOES NOT WORSEN ISCHEMIC LEFT VENTRICULAR DYSFUNCTION IN THE PIG

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Introduction. By its direct depressant effects on myocardial contractile function, nitrous oxide (N_2O) can decrease blood pressure, coronary perfusion pressure and oxygen delivery, and can thereby cause regional or global myocardial ischemia. Additionally, a recent study suggests that N_2O, when administered in the presence of critical coronary stenosis, can also cause myocardial ischemia in the absence of hypoxia, tachycardia, or hypotension, and that this ischemia is not always reversible when N_2O is discontinued (1). The purpose of this study was to determine whether N_2O aggravates mild, pre-existing myocardial ischemia in a pig model, in absence of significant hemodynamic changes.

Methods. Six domestic swine were anesthetized by inhalation of isoflurane, intubated and mechanically ventilated with a nitrogen/oxygen mixture, FIO_2=.21. After intravenous access was established, isoflurane was discontinued, and anesthesia was maintained with pentobarbital 25 mg·kg^{-1}, + fentanyl 50 mcg·kg^{-1} followed by a fentanyl infusion, 0.5 mcg·kg^{-1}·min^{-1}. Through a midline sternotomy, the pericardium was opened and a screw-driven pneumatic occluder was placed around the left anterior descending coronary artery (LAD) near its origin. To measure regional systolic shortening (SS), piezoelectric crystals were inserted in the midmyocardium of the LAD and circumflex coronary artery (CX) territories. Catheters were inserted into the aorta, left ventricle, and LAD coronary artery to measure systolic and diastolic blood pressure, left ventricular end-diastolic pressure, and mean LAD coronary artery pressure (SBP,DBP,LVEDP,and CorP, in mmHg). Atrial pacing was instituted at a rate 20% above resting heart rate (HR). Protocol: To induce mild ischemia in the LAD zone, the occluder was inflated until the LAD myocardium showed diminished systolic segment shortening, but not akinesis or bulging. The LAD pressure causing this level of dysfunction was noted, and the occluder was subsequently adjusted as necessary to keep this pressure constant. After the degree of ischemic dysfunction stabilized, measurements of hemodynamics and of LAD and CX segmental function were made every 5 min during 15 min of continued nitrogen administration, FIO_2=.21. N_2O, 79% was then rapidly substituted for nitrogen in the inspired gas, and sequential measurements were again made every 5 min. during 15 min. of N_2O exposure. Then nitrogen 79% was resumed, and final measurements made every 5 min for another 15 min. Regional segmental shortening was calculated as (end-diastolic length - end-systolic length)/end-diastolic length, for both myocardial zones, then was expressed as a percentage of the pre-stenosis value in each zone. Results were analysed by repeated-measures ANOVA, with the Newman-Keuls test used where appropriate.

Results. SBP, DBP, HR, and LVEDP were unchanged by the addition of N_2O. Prestenosis LAD coronary pressure was 91±37 mmHg. Reduction of LAD coronary pressure to 47 mmHg caused decrease in systolic shortening to 62% of control values, whereas shortening in the nonischemic CX zone increased to 123% of control. Substitution of N_2O for nitrogen diminished systolic shortening slightly in the nonischemic CX zone but not in the LAD zone. Resumption of nitrogen increased CX SS.

Hemodynamics and Regional Myocardial Function

(1st) NITROGEN:	5"	10"	15"
SBP	111±21	111±22	112±23
DBP	83±20	83±19	81±18
CorP	47±9	47±9	47±9
HR	108±15	109±13	109±13
LVEDP	6±4	6±3	6±4
LADSS %Control	62±13	62±11	62±15
CXSS %Control	123±32	127±38	126±40
NITROUS OXIDE:	5"	10"	15"
SBP	109±20	110±19	109±17
DBP	79±16	81±16	80±14
CorP	47±9	48±9	47±9
HR	110±11	110±12	111±11
LVEDP	7±6	7±5	7±4
LADSS %Control	56±10	62±14	58±17
CXSS %Control	117±36*	119±33*	115±36*
(2nd) NITROGEN	5"	10"	15"
SBP	109±16	109±19	107±16
DBP	80±14	81±16	80±16
CorP	47±9	47±9	47±9
HR	110±11	109±12	111±11
LVEDP	7±6	7±6	6±3
LADSS %Control	61±17	64±14	67±15
CXSS %Control	135±42	132±41	131±42

Values are mean ± sd, n = 6. *=significantly different than values during nitrogen, $p<0.05$.

Discussion. A prior study (1) has shown that N_2O can cause regional myocardial dysfunction, probably ischemic, distal to a critical coronary stenosis. In that study, coronary perfusion pressure was decreased 4-5 mmHg by the hemodynamic effects of N_2O. In the current study we used a more significant stenosis but held LAD coronary pressure constant, and found N_2O did not worsen pre-existing ischemic dysfunction. However, decreasing LAD coronary pressure 5 mmHg further in this preparation typically decreases LAD SS by an additional 15-20% of control. These findings support the hypothesis that N_2O does not have a direct detrimental effect on ischemic myocardium.

References. 1. Philbin DM, et al., 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.