ABSTRACTS

AM WALTON MD; Wladyslaw Pluta, MD; Bertram Pitt, MD; Values are mean ± standard error (SEM).

MECHANISM OF OPIATE MEDIATED SYSTEMIC AND CORONARY RESISTANCE

Administration of the Opiate fentanyl (F) 1.3 μg/kg, measured along with plasma arginine vasopression (AVP) left circumflex coronary blood flow (CBF) ml/min were measured along with plasma arginine vasopression (AVP) and coronary resistance (CVR) were measured in 10 animals heart rate (HR), beats/min; aortic pressure (MAP) mm Hg; left atrial pressure (LAP) mm Hg; cardiac output (CO) ml/kg/min.

F 0.027 2.6 5.9
N 0.032 3.1 6.27
f 0.027 2.6 5.9

SEM 0.01 0.3 1.19

Naloxone (N) and the competitive AVP antagonist—L-1 Tyr (Me) AVP (AAVP) were studied in 6 conscious dogs. After N 0.10 mg/kg IV, F i.c. failed to significantly increase SVR, CVR and AVP despite an increase in AVP from 5.0 to 32.9 after F i.c. This effect of N is unrelated to its beta-adrenergic blocking activity and is not mediated through action on alpha-adrenergic receptors. The P-induced contraction appears to be associated predominantly with an influx of calcium ions across the vascular smooth muscle-cell membrane.

CONTRACTILE ACTIONS OF RACEMIC AND D-PROPRANOLOL ON ISOLATED CANINE MESENTERIC AND CORONARY ARTERIES

Robert Forman, MD, FACC; Calvin Eng, MD; Edward Kirk, PhD, Albert Einstein College of Medicine, Bronx, New York

This study was undertaken to compare the effects of verapamil (V) and nitroglycerin (TNG) on the collateral blood flow to the central and border zones of ischemic myocardial areas. In 12 dogs the left main and left anterior descending (LAD) coronary arteries were separately cannulated and perfused at constant rates into the left main coronary artery to increase the monitored collateral blood flow by approximately 25-50%. The order of V and TNG administration were alternated. Regional myocardial blood flows, in ml/min/g, were measured with each intervention using microspheres and compared by analyses of variance. The LAD and left main arteries were injected with different colored gelatin and the central-ischemic, border and normal zones excised for counting. The flows in the normal tissue increased from 0.380 to 0.561 for V (p < .025). Flows in the border region increased from 0.380 to 0.561 for V (p < .025).

Thus TNG increases collateral blood flow in both central ischemic and border zone tissues. V does not increase flow to either of these regions. The mechanism of action of V in relief of angina is presumably due to an increase in collateral blood flow.

V Tuesday, April 27, 1982

DRUG EFFECTS ON BLOOD VESSELS

8:30-10:00

MECHANISM OF OPIATE MEDIATED SYSTEMIC AND CORONARY RESISTANCE

Stanislaw Pasyk, MD; Roger J. Grekin, MD; Joseph A. Walton MD; Wladyslaw Pluta, MD; Bertram Pitt, MD; University of Michigan, Ann Arbor.

The differentiation of monoaminergic receptors depends upon the availability of selective antagonists. Most agents antagonizing serotonin (5-HT) in vascular smooth muscle lack specificity and block other monoamines including o-agonists, histamine, and dopamine. The selectivity of Ketanserin (KS) was tested in isolated rabbit aorta. Arterial ring preparations were mounted in a myograph for the recording of isometric tension, and equilibrated with oxygenated Krebs buffer containing propranolol (10^-6 M) and inhibitors of monoamine uptake (10^-5 M cocaine; 10^-6 M fluoxetine). Concentration-response experiments (n = 36) for 5-HT in the presence of varying KS concentrations revealed competitive antagonism. Schild plots showed an apparent dissociation constant (KD) for KS of 3.10^-8 M. KS did not attenuate contractions elicited by 5-HT in the presence of varying 5-HT concentrations. Schild plots showed an apparent dissociation constant (KD) for KS of 3.10^-8 M. KS did not attenuate contractions elicited by 5-HT in the presence of varying 5-HT concentrations. Schild plots showed an apparent dissociation constant (KD) of 3.10^-8 M. KS did not attenuate contractions elicited by 5-HT in the presence of varying 5-HT concentrations.

Comparative Effect of Verapamil and Nitroglycerin on Collateral Blood Flow in the Dog

Robert Forman, MD, FACC; Calvin Eng, MD; Edward Kirk, PhD, Albert Einstein College of Medicine, Bronx, New York

This study was undertaken to compare the effects of verapamil (V) and nitroglycerin (TNG) on the collateral blood flow to the central and border zones of ischemic myocardial areas. In 12 dogs the left main and left anterior descending (LAD) coronary arteries were separately cannulated and perfused at constant rates into the left main coronary artery to increase the monitored collateral blood flow by approximately 25-50%. The order of V and TNG administration were alternated. Regional myocardial blood flows, in ml/min/g, were measured with each intervention using microspheres. The LAD was then occluded and the circumflex perfusion pressure kept constant using a servo-pump. V and TNG were infused at constant rates into the left main coronary artery to increase the monitored coronary blood flow by approximately 25-50%. The order of V and TNG administration were alternated. Regional myocardial blood flows, in ml/min/g, were measured with each intervention using microspheres and compared by analyses of variance. The LAD and left main arteries were injected with different colored gelatin and the central-ischemic, border and normal zones excised for counting. The flows in the normal tissue increased from 0.380 to 0.561 with TNG and to 1.232 with V. The control flow in the central ischemic tissue was 0.091 and did not significantly increase with TNG (0.093, p < .001). Flows in the border region increased from control 0.380 to 0.561 for V (p < .025).

However, these were corrected for interdigititation with normal tissue only TNG increased flow in this region. Thus TNG increases collateral blood flow in both central ischemic and border zone tissues. V does not increase flow to either of these regions. The mechanism of action of V in relief of angina is presumably due to an increase in collateral blood flow.

KETANSERIN -- A SELECTIVE SEROTONERGIC BLOCKING AGENT IN VASCULAR SMOOTH MUSCLE

Philip D. Henry, MD, FACC, Malcolm Clark, Cynthia Lucas, Karen T. Bentley, Washington University, St. Louis, MO.

The differentiation of monoaminergic receptors depends upon the availability of selective antagonists. Most agents antagonizing serotonin (5-HT) in vascular smooth muscle lack specificity and block other monoamines including o-agonists, histamine, and dopamine. The selectivity of Ketanserin (KS) was tested in isolated rabbit aorta. Arterial ring preparations were mounted in a myograph for the recording of isometric tension, and equilibrated with oxygenated Krebs buffer containing propranolol (10^-6 M) and inhibitors of monoamine uptake (10^-5 M cocaine; 10^-6 M fluoxetine). Concentration-response experiments (n = 36) for 5-HT in the presence of varying KS concentrations revealed competitive antagonism. Schild plots showed an apparent dissociation constant (KD) for KS of 3.10^-8 M. KS did not attenuate contractions elicited by 5-HT in the presence of varying 5-HT concentrations. Schild plots showed an apparent dissociation constant (KD) of 3.10^-8 M. KS did not attenuate contractions elicited by 5-HT in the presence of varying 5-HT concentrations.

COMPARATIVE EFFECT OF VERAPAMIL AND NITROGLYCERIN ON COLLATERAL BLOOD FLOW IN THE DOG

Robert Forman, MD, FACC; Calvin Eng, MD; Edward Kirk, PhD, Albert Einstein College of Medicine, Bronx, New York

This study was undertaken to compare the effects of verapamil (V) and nitroglycerin (TNG) on the collateral blood flow to the central and border zones of ischemic myocardial areas. In 12 dogs the left main and left anterior descending (LAD) coronary arteries were separately cannulated and perfused at constant rates into the left main coronary artery to increase the monitored collateral blood flow by approximately 25-50%. The order of V and TNG administration were alternated. Regional myocardial blood flows, in ml/min/g, were measured with each intervention using microspheres. The LAD was then occluded and the circumflex perfusion pressure kept constant using a servo-pump. V and TNG were infused at constant rates into the left main coronary artery to increase the monitored coronary blood flow by approximately 25-50%. The order of V and TNG administration were alternated. Regional myocardial blood flows, in ml/min/g, were measured with each intervention using microspheres and compared by analyses of variance. The LAD and left main arteries were injected with different colored gelatin and the central-ischemic, border and normal zones excised for counting. The flows in the normal tissue increased from 0.380 to 1.010 with TNG and to 1.232 with V. The control flow in the central ischemic tissue was 0.091 and did not significantly increase with V (0.093, p < .001). Flows in the border region increased from control 0.380 to 0.561 for V (p < .025).

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