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Stable Ischemic Heart Disease

INTRAVENOUS RANOLAZINE RELIEVES ISCHEMIA BY INCREASING MYOCARDIAL ADENOSINE LEVELS

Moderated Poster Contributions
Stable Ischemic Heart Disease Moderated Poster Theater, Poster Hall B1
Saturday, March 14, 2015, 10:45 a.m.-10:55 a.m.

Session Title: Stable Ischemic Heart Disease: Highlighted Research
Abstract Category: 25. Stable Ischemic Heart Disease: Basic
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Background: The mechanism of action by which ranolazine (RAN) reduces stress-induced myocardial ischemia is not fully understood. We hypothesized that RAN relieves ischemia through the cardioprotective effects of adenosine (ADEN).

Methods: Non-flow limiting stenosis was created in the LAD artery in 17 open-chest dogs. We compared hemodynamic changes, global (peak LV dP/dt) and regional (radial strain) myocardial function, myocardial perfusion, and regional ADEN level in the absence and presence of intravenous RAN at rest and during dobutamine (DOB) stress.

Results: With stenosis, RAN significantly reduced the rate-pressure product, LAD pressure without changing pressure gradient, peak LV dP/dt without changing left atrial pressure, and radial strain. It had no effect on LAD blood flow. DOB produced the opposite effects, which were not altered with the addition of RAN. Blood flow improved and ADEN increased at rest and with DOB in the presence of RAN. Arterial blood volume also increased without change in myocardial blood volume, implying dilatation of intramyocardial vessels.

Conclusion: RAN increased myocardial ADEN levels, which likely is cardioprotective during exercise-induced ischemia. The mechanism of increased ADEN levels induced by RAN is unknown but may be related to increased availability in association with resistance vessel dilatation. This is the first observation of this novel mechanism of action of RAN during intravenous administration.

Table 1. Hemodynamics, Myocardial Function and Blood Flow, and Metabolic Data

Parameter	Stenosis	Stenosis+Ran	Stenosis+Dob	Stenosis+Ran+Dob
HEMODYNAMICS				
Heart Rate (beats/min)	102±2	99±2	158±4	155±4
Mean Aortic Pressure (mmHg)	99±3	83±2 †	153±9	112±7‡
RPP (beats/min•mmHg)	12,070±521	10,580±481 *	30,015±1,989	24,513±1,908
LAD Artery Pressure (mmHg)	81±3	65±3 *	101±6	76±5‡
Aortic-LAD Pressure Gradient (mmHg)	17±3	13±1	50±6	42±6
LAD Blood Flow (mL/min)	20±1	17±1	44±4	36±3
MYOCARDIAL FUNCTION				
Peak LV dP/dt (mmHg/s)	7,400±1,226	6,293±945 *	24,911±3,938	18,784±3,038
Left Atrial Pressure (mmHg)	16±1	15±1	18±1	16±2
LAD Radial Strain (%)	21±3	15±2 *	23±4	25±4
MYOCARDIAL BLOOD FLOW				
LAD Endocardial/Epicardial Ratio	0.85±0.08	1.16±0.15	0.76±0.10	0.89±0.08
Arterial Blood Volume (S/D ratio)	---	0.30±0.02	0.42±0.040 *	---
LAD Myocardial Blood Volume (A)	76.4±4.2	67.1±5.2	69.7±3.9	72.8±4.4
METABOLIC DATA				
LAD Region Adenosine (ng/mL)	10.6±2.1	21.7±4.3 *	20.5±3.2 *	43.1±13.3

Ran = ranolazine; Dob = dobutamine; RPP = rate pressure product; LAD = left anterior descending; S/D = systolic/diastolic
* p<0.05 vs. stenosis; † p<0.001 vs. stenosis;
‡ p<0.05 vs. stenosis+dobutamine