TITLE : ALVEOLAR HYPOXIA INCREASES PLASMA ENDOTHELIN-1 LEVEL IN CONSCIOUS RATS

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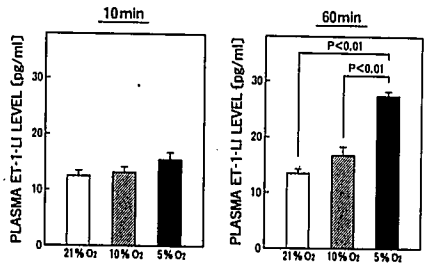
Introduction: Endothelin-1 (ET-1) is a novel vasoconstrictor peptide purified from the culture medium of porcine aortic endothelial cells (1). To investigate the effect of alveolar hypoxia on ET-1 secretion, we measured the plasma ET-1 level in conscious unrestrained rats under hypoxic conditions.
Methods: Male Wistar rats were exposed to 21 %, 10 % or 5 % O_2 for 10 min or 60 min. Arterial blood was obtained through the femoral arterial catheters. The plasma ET-1 level was measured by radioimmunoassay, as previously reported (2).
Results: PaO_2 and $PaCO_2$ decreased in hypoxic rats. The plasma ET-1-like immunoreactivity (ET-1-LI) level of rats exposed to 5 % O_2 for 60 min was significantly higher than that of rats exposed to 21 % or 10 % O_2 for 60 min (Fig.). The plasma ET-1-LI level was parallel to the severity of hypoxemia. The plasma ET-1-LI level was not different among 3 groups exposed for 10 min.
Discussion: These results indicate that alveolar hypoxia stimulates ET-1 release and suggest a possible pathophysiological significance of ET-1 in hypoxia. Endothelium-dependent vasoconstriction is demonstrated in isolated vessels including pulmonary arteries in vitro under hypoxic or anoxic condition (3,4). This contraction, explained by the release of endothelium-dependent contracting factor (EDCF1), is very rapid and poorly sustained (3,4). Considering the slow increase of plasma ET-1-LI level under hypoxic condition and the long-lasting effect of ET-1 (1), it is unlikely that ET-1 itself is EDCF1.
References: 1) Nature 332, 411, 1988. 2) Biochem. Biophys. Res. Commun. 163, 1512, 1989. 3) Hypertension 13, 658, 1989. 4) Exp. Lung. Res. 7, 101, 1984.

Fig. EFFECT OF ALVEOLAR HYPOXIA ON PLASMA ET-1 LEVEL



Values are means ± SEM from 5-8 separate experiments. Statistical analysis was performed by Duncan's multiple range test.

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TITLE:EFFECTS OF BUNAZOSIN, A NEW ALPHA-1 BLOCKER ON REGIONAL MYOCARDIAL FUNCTION IN THE ISCHEMIC CANINE HEART.

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Introduction. Evidence for a significant contribution of alpha adrenergic coronary vasoconstriction to experimental and clinical myocardial ischemia has recently been suggested. Regional myocardial function(RMF) has been highlighted as a sensitive indicator of myocardial ischemia. We examined the effects of bunazosin, a newly-synthetized alpha-1 blocker of IV use on regional myocardial function in the ischemic canine heart. We used systolic shortening(%SS), percentage of end-diastolic length as a parameter of regional myocardial function.
Methods. Twelve mongrel dogs were anesthetized with pentobarbital(30mg/kg) and artificially ventilated. They were instrumented to measure heart rates(HR), left ventricular pressure(LVP), arterial pressure(AP), left circumflex coronary blood flow(CBF) and LVdp/dt. Cardiac index(CI) and stroke volume index(SVI) were calculated. Two pairs of 5 MHz sonomicrometry microcrystals were implanted along the short axis of the left ventricle to measure the segment length(SL). One pair was implanted within the area supplied by the left anterior descending coronary artery (LAD) and the other within the area supplied by the left circumflex artery (LCX). An adjustable screw clamp was applied to the LCX to reduce CBF by 50%-70% until RMF was impaired. Then, bunazosin hydrochloride 0.05mg/kg/min was given intravenously over 20 min. The hemodynamic parameters were recorded during the experiment. The student t test was utilized for statistical significance. A p value of less than 0.05 was considered significant.
Results. The decreased LCX flow by tightening the screw clamp significantly decreased the %SS of the myocardium supplied by the stenosed LCX. Bunazosin decreased AP, LVP and increased %SS significantly. No significant changes were observed in CI, SVI, CBF or LVdp/dt. The HR and LVEDP tended to decrease but not significantly.
Discussion. Even when critical coronary stenosis was made to reduce coronary flow to a point of regional myocardial dysfunction, the alpha receptors were considered to be active. We conclude that the alpha-1 blocker may be beneficial for jeopardized ischemic myocardium to improve RMF.
Reference. Circulation 81:1-13, 1990.