The effect of Captopril treatment on chronic hypoxia induced pulmonary vascular remodeling in the Fawn-Hooded, Sprague-Dawley, and Brown-Norway rat

Robert C. Molthen1,2,3, Amy E. Heinrich1, Steve T. Haworth1, Gary S. Krenz3,4, and John B. Gordon5

1 Department of Medicine – Pulmonary and Critical Care, Medical College of Wisconsin, Milwaukee, WI 53226
2 Research Service, Department of Veterans Affairs, Zablocki VAMC, Milwaukee, WI 53295
3 Department of Biomedical Engineering, Marquette University, Milwaukee, WI 53201-1881
4 Department of Mathematics, Statistics and Computer Science, Marquette University, Milwaukee, WI 53201-1881
5 Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI 53226

Abstract

Remodeling in the Fawn-Hooded, Sprague-Dawley, and Brown-Norway rat hypoxia in the rat model of pulmonary hypertension (PH). Neither the etiology nor the structural and functional consequences of this remodeling are well understood. It is known that chronic treatment with Captopril reduces pulmonary hypertension in the Fawn-Hooded rat lung. This study examines effects of Captopril in the Fawn-Hooded, Sprague-Dawley, and Brown-Norway strain, respectively. Department of Medicine – Pulmonary and Critical Care, Medical College of Wisconsin, Milwaukee, WI 53226

Introduction

Remodeling in the lungs is a well established stimulus for remodeling pulmonary, arterial hypertension and vascular remodeling in the lung. There is no known difference in PH susceptibility among the different rat strains. In this study, the Fawn-Hooded, Sprague-Dawley, and Brown-Norway strain were exposed to chronic hypoxia (10% O2) to examine the structural and functional consequences of this remodeling. We examined consequences of chronic hypoxic exposure (10% O2) using standard hemodynamic analysis and x-ray micro-CT imaging and morphometric models to analyze arterial diameter changes.

Methods

Fawn-Hooded (FH), Sprague-Dawley (SD), and Brown-Norway (BN) rats were exposed to 10% hypoxia for 6 weeks in metabolism cages, with drinking water containing or lacking Captopril. The lungs were excised, placed in an imaging chamber, and the airway pressure replaced by perfluorooctyl bromide, to provide x-ray contrast. The arterial pressure was set to 30 mmHg and the lungs rotated in an x-ray beam at 1° increments. Images were obtained at each pressure and analyzed for arterial diameter changes. Principal pathway models were fit to the data and arterial distensibility was calculated. Hemodynamic analysis was performed in isolated FH, SD, and BN rat lungs using physiologic salt solution, 5% BSA. Parameters were estimated using standard least squares techniques. Parameter estimates were compared among groups.

Conclusion

Captopril treatment reduced the vascular remodeling significantly in SD rats. Measurements were not available for FH rat lungs. No Captopril data is presented for the FH strain and N = 2 for the BN strain.

Results

The results of this study are shown in the tables and figures. Hemodynamic analysis performed in isolated FH, SD, and BN rat lungs using physiologic salt solution, 5% BSA. Pressure data is equal to arterial pressure, Pa, minus partial pressure of oxygen, PaO2.

Significant pulmonary hypertension (P<0.001) at a flow rate of 110 ml/(min•kg), as evident in the perfusion studies, was observed in FH lungs treated with Captopril. Measurements were not available for FH rat lungs. No Captopril data is presented for the FH strain and N = 2 for the BN strain.

Vascular resistance:

Hematocrit in FH, SD, and BN rats, exposed to chronic hypoxia or normoxia and given drinking water with or without Captopril.

Hematocrit: FH, SD, and BN rats, exposed to chronic hypoxia or normoxia and given drinking water with or without Captopril.

Right ventricular hypertrophy:

Heart weight: FH, SD, and BN rats, exposed to chronic hypoxia or normoxia and given drinking water with or without Captopril.

Determining arterial distensibility:

The arterial distensibility, D, is defined as the fractional change in arterial diameter, D, divided by the pressure change, P, as shown in equation 1.

Arterial distensibility: FH, SD, and BN rats, exposed to chronic hypoxia or normoxia and given drinking water with or without Captopril.

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