

GENDER DIFFERENCES IN THE DEVELOPMENT OF PULMONARY HYPERTENSION (PH)

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INTRODUCTION

PH is a progressive disease that results in right ventricle failure and death. We investigated the levels of a vasodilator, adrenomedullin (ADM), and response to various dilatory agonists during the development of experimentally induced PH in male and female rats.

METHODS

SD rats of both sexes were injected with 60 mg/kg b wt monocrotaline (MCT) and were terminated after 3 weeks. Plasma ADM (pg/ml) and ET-1 (ng/ml) levels were determined. At the maximal contractile responses to NE or ET-1, the rings were exposed to 5×10^{-6} M ACh or 9×10^{-9} M ADM or 1.3×10^{-8} M calcitonin gene related peptide (CGRP).

RESULTS

MCT at the given dose is highly toxic to male rats when compared to female rats that yielded in high mortality (35% vs. 0.03%, $p = 0.0001$). Vascular endothelial damage caused by MCT triggers 12× more ET-1 synthesis/secretion in male rats whereas only 1.3× increase ADM levels. In the case of female rats, ADM secretion is increased with the increase in ET-1. Relaxation in response to ACh, ADM, and CGRP was endothelium-dependent. All three relaxing agents produced less relaxation of hypertensive pulmonary arterial rings. ADM and CGRP induced relaxation of NE contractions was 2.4× greater in female compared to male control vascular rings ($p < 0.004$) and 5.5× greater in female compared with male hypertensive rings ($p < 0.005$).

CONCLUSION

We conclude that gender plays an important role in the development of PH and that female rats exhibit a protective effect in the disease progression suggesting that sex hormones may influence the pathophysiology of the PH.