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Altered expression of Hsp90 and CAV-1 might affect the failing right ventricle of monocrotaline induced pulmonary hypertension

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BACKGROUND & OBJECTIVE: Pulmonary arterial hypertension can be well studied using the monocrotaline model in rats (1). The mechanism of right ventricular failure in this model is still not completely known. Heat shock protein 90 (Hsp90) seems to play a role in compensating mechanism of the failing heart alongside with caveolin-1 (CAV-1) and its phosphorylated isoform (pTyr14CAV-1). Therefore we hypothesized that levels of these proteins might be changed in right ventricle of experimentally induced pulmonary hypertension.

DESIGN/METHODS: Group of 13 male Wistar rats was subcutaneously (2) injected with monocrotaline (MON; 60 mg/kg) and 7 control rats (CON) received vehicle. Separate group of 20 (MON) and 10 (CON) rats was used for hemodynamic measurements. Animals were weighted frequently and vital functions were measured using MouseOx meter. Rats were sacrificed after 4 weeks or immediately if showing dyspnea, lethargy and significant weight reduction.

RESULTS: MON-treated rats had a decrease in body weight when compared to controls (MON: 312±11 g vs. CON: 358±6, $P<0.01$). Right ventricular systolic pressure was significantly increased (MON: 50.65±6.28 vs. CON: 21.52±2.49, $P<0.01$). Right ventricular weight to body weight ratio was significantly increased (MON: 1±0.07 vs. CON: 0.53±0.02, $P<0.01$), whereas left ventricular weight to body weight ratio was not significantly changed (MON: 1.84±0.35 vs. CON: 2.18±0.04). Expression of Hsp90 in the right ventricle of monocrotaline treated rats was significantly increased (MON: 1317±399 vs. CON: 100±26, $P<0.05$), while in the left ventricle it remained stable (MON: 106±26 vs. CON: 100±4). Expression of caveolin-1 in the right ventricle of MON group was decreased (MON: 66±14 vs. CON: 100±9), as well as in the left ventricle (67±11 vs. CON: 100±23). Expression of pTyr14CAV-1 was significantly decreased in the right ventricle (MON: 48±13 vs. CON: 100±14, $P<0.05$), while in the left ventricle was unchanged (80±24 vs. CON: 100±22).

CONCLUSION: Elevated level of Hsp90 in hypertrophied right ventricle along with altered expression of CAV-1 isomers might contribute to or be a protective mechanism against hypertrophy of the right ventricle and its eventual failure in the monocrotaline-induced pulmonary hypertension model.

1. Hayashi Y**,** Lalich JJ, Proc Soc Exp Biol Med, 124(2): 392-6, 1967

2. Chesney CF, Allen JR, et al., Am J Pathol, 70(3): 489–492, 1973