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Apoptosis associated Gene Expressions of in Monocrotaline-Induced Pulmonary Hypertension in Rats after Bosentan Treatment

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Purposes :Vascular wall remodeling in pulmonary hypertension is contributed to by an aberration in the normal balance between proliferation and apoptosis of smooth muscle. Endothelin-1 prevents up-regulation of pro-apoptosis and activates caspase-3. Endothelin (ET)-1, a potent endothelium-derived vasoconstrictor peptide, has several properties suggestive of its potential pathophysiological role in pulmonary hypertension.
The objectives of this study were to evaluate the effect of bosentan on bcl2, caspase-3 , vascular endothelial growth factor (VEGF), interlukin(IL) 6 and tumor necrosis factor (TNF)-α in monocrotaline (MCT)-induced pulmonary hypertension and to investigate the correlation between caspase-3 gene expression and other associated genes.
Methods: Sprague-Dawley rats were divided into three groups: control group, MCT group (60 mg/kg), bosentan group (MCT 60 mg/kg plus 20 mg/day bosentan orally). The animals were sacrified after 1 day , 5 day, 1 week, 2 week and 4 week. Gene expressions of bcl2, caspase 3, VEGF, IL-6 and TNF-α were analyzed by real time polymerase chain reaction and westernblot analysis.
Results: The gene expressions of bcl2, caspase 3, VEGF had significantly increased in the MCT group compared with the control group in week 4 by PCR analysis. The gene expressions of caspase and VEGF had significantly decreased in the bosentan group compared with the MCT group in week 4. Bcl2 protein content had significantly increased in the bosentan group in week 4. Gene expressions of IL-6 had significantly increased in week 1, 2 and 4 in the MCT group compared with the control group. Gene expressions of IL-6 had significantly decreased in week 1 , 2 and 4 in the bosentan group compared with the MCT group. Gene expressions of TNF-α had significantly had significantly increased on day 5 in the MCT compared with the control group. Gene expressions of TNF-α had significantly decreased on day 5, in week 1 and 2 in the bosentan group compared with the MCT group. Caspase-3 gene expression significantly correlated with bcl2 and VEGF gene expressions.
Conclusion: Bosentan may hold considerable potential for preventing apoptosis and inflammation.