Losartan for progressive pulmonary vein stenosis: A possible solution?

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Pulmonary venous obstructive disease remains a challenging problem for pediatric cardiac patients. The development of diffuse pulmonary vein obstruction after pulmonary vein repair can be a vexing problem in children with total anomalous pulmonary venous connection. Often, there is no further treatment that can be offered to these patients and eventually, they succumb to progressive pulmonary vein obstruction.

Zhu and colleagues¹ present an article on the use of losartan in a piglet model of pulmonary vein stenosis. Losartan, a drug typically used for hypertension, blocks angiotensin II type 1 receptors and inhibits transforming growth factor- β (TGF- β) activity. Its use is currently being investigated in a variety of conditions other than hypertension, including prevention of aortic root dilatation in patients with Marfan syndrome.

In a previous study by the authors,² an observation of increased TGF- β expression in specimens from their piglet model with pulmonary vein stenosis led the authors to hypothesize what effect losartan might have on preventing the development of pulmonary vein stenosis. Neonatal piglets were divided into 3 groups (pulmonary vein banding, pulmonary vein banding with losartan, and sham banding). After 7 weeks, hemodynamic measurements were made and tissue samples examined. The authors found a reduction in the level of pulmonary vein intimal hyperplasia and a reduction in pulmonary artery/systemic blood pressure ratios in the losartan-treated group. The authors concluded that losartan may have a beneficial prophylactic effect for patients at risk for the development of pulmonary vein stenosis after surgical repair.

The study has several significant limitations that temper realistic expectations about the potential usefulness of the drug in a clinical setting. In this study, losartan is administered in the presence of normal vessels before any intimal proliferation has developed. This is an important distinction from a clinical scenario, where pulmonary vein stenosis and intimal proliferation would have already developed by the time patients came to clinical attention.

The initial premise for the use of the drug (increased levels of TGF- β in the presence of stenotic pulmonary veins) could not be replicated in this follow-up study, which obfuscates the role losartan had in the results and questions its actual usefulness. This brings to light the inconsistencies that can be seen in working with animals such as neonatal piglets, which can be a precarious species to work with. Hemodynamic measurements often need to be carefully controlled as multiple physiologic factors can affect results.

The limitations of this provocative study should not detract from the important overall work the authors are doing in the field of pulmonary vein stenosis. The development of diffuse pulmonary venous obstructive disease after repair of total anomalous pulmonary venous return remains a challenging issue. Further studies like this one are necessary to advance the treatment options in the search for an ultimate solution to this difficult and frustrating problem.

References

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