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EFFECTIVENESS OF BOSENTAN TREATMENT IN MIR-200B NULL MICE AS A MODEL FOR PULMONARY HYPERTENSION IN CONGENITAL DIAPHRAGMATIC HERNIA

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Background:
Congenital diaphragmatic hernia (CDH) is a complex condition where patients suffer from pulmonary hypertension due to abnormal lung development. Effectiveness of current treatments for pulmonary hypertension in CDH patients are unknown. We determined that CDH patients with poor outcomes have decreased levels of a microRNA known as miR-200b, and created a miR-200b null mice. miR-200b null mice have pulmonary hypertension, abnormal lung development, and up regulation of endothelin receptor-A in their lungs similar to that of CDH patients.

Objective:
The objective of our study is to determine the effectiveness of the drug bosentan, an endothelin receptor antagonist, in miR-200b null mice.

Methods:
Following ethical approval, miR-200b null and wildtype mice were treadmill trained underwent baseline graded maximal exercise tests and echocardiographs at 8 weeks of age. Bosentan was administered via gavage at 100mg/kg of body weight/day for three weeks. Weekly graded maximal exercise tests and end of study echocardiographs were performed to evaluate pulmonary hypertension. After three-week treatment lungs were formalin fixed and paraffin embedded. Embedded lungs were then serial sectioned and Verhoeff-van Gieson stained to evaluate vasculature.

Results:
Preliminary results show that miR-200b null mice have improved VO_2 max after bosentan treatment ($p=0.053$, $n=2$) and increased run time to exhaustion. At this time no difference in artery thickness measurements is seen between WT and miR-200b null mice after three week bosentan treatment. We are currently analyzing echocardiographs to determine changes in pulmonary acceleration time.

Conclusion:
These results suggest that Bosentan increases VO_2 max and prevents worsening of pulmonary hypertension. In conclusion, determination of the effectiveness of bosentan in the treatment of pulmonary hypertension could lead to better treatment options for patients suffering from pulmonary hypertension in CDH.