Nebulized Nitroglycerin in Children with Pulmonary Hypertension Secondary to Congenital Heart Disease

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Nebulized nitroglycerin in children with pulmonary hypertension secondary to congenital heart disease

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Abstract

Pulmonary hypertension continues to be a major cause of morbidity and mortality, despite new treatments. Since inhaled nitric oxide has been reported to be effective in some cases, we investigated using nebulized nitroglycerin to treat pulmonary hypertension in children with congenital heart disease. Four children (ages 6-72 months) with severe pulmonary hypertension secondary to congenital heart disease (all with membranous ventricular septal defect, undergoing cardiac catheterization) were given 3 cc of nebulized normal saline over 10 min as placebo control, followed by nebulized nitroglycerin (20 μg/Kg in 3cc normal saline). Normal saline administration did not elicit any change, but nitroglycerin administration resulted in the following changes (mean ±SE, paired statistics): systolic pulmonary artery pressure from 68±8 to 53±6 at 10 min into treatment (P 0.006), mean pulmonary artery pressure 47±4 to 38±4 (P 0.005), heart rate 131±8 to 127±7 (P 0.13), systolic blood pressure 85±8 to 88±3 (P 0.7), mean blood pressure 59±6 to 63±4 (P 0.5). These results indicate that nebulized nitroglycerin may be an effective, easy to administer, inexpensive, and safe alternative for treatment of severe pulmonary hypertension in children with congenital heart disease, especially in areas where other treatments such as extracorporeal membrane oxygenation or inhaled nitric oxide are inaccessible.

Methods

This study was approved by the Research Administration at Zhejiang Medical University Children's Hospital and consent was obtained for each of the four children, ages 6 months to six years. These children were spontaneously breathing with uncorrected ventricular septal defect and severe PHT undergoing diagnostic cardiac catheterization. Severe pulmonary hypertension was defined as pulmonary artery pressure at least half of systemic blood pressure (Table 1). Baseline pulmonary artery pressure, systemic blood pressure, oxygen saturation, and heart rate were measured. Each patient received 3 cc of nebulized normal saline (NS) as placebo control and these vital signs were recorded at 5 min intervals.
Next, each patient received a dose of 20 g per kilogram body weight of NTG in total volume of 3 cc NS nebulized and their vital signs were recorded at 5 min intervals.

**Results**

Nebulized NS failed to produce any changes in any of the patients. Nebulized NTG, on the other hand, significantly reduced pulmonary artery pressure without changing the systemic BP or heart rate (Table 2). This study was terminated at the end of the catheterization procedure with no long-term follow-up.

**Discussion**

Treatment for severe PHT continues to be difficult and often is not successful, despite the promising role of nebulized NO and ECMO as well as other treatment modalities. The fact that the mechanism of action of nitrovasodilators involves metabolism to NO led us to investigate of their potential. To study the potential benefits of nebulized NTG on PHT, we selected four stable patients undergoing a diagnostic procedure. The lack of effect of NS eliminated the possibility of a placebo effect when using NTG. The significant reduction of both systolic and mean pulmonary artery pressures is encouraging, knowing that patients with uncorrected VSD tend to have sustained high diastolic pressure which would not respond well to any treatment.

Administering nebulized NTG had no effect on systemic BP or heart rate, presumably because of the fast local metabolism and short half-life. This finding is also promising because of the limitations of any treatments associated with systemic effects.

**Conclusion**

Nebulized NTG appears to be an effective, easy to administer, inexpensive and safe alternative for treatment of severe PHT in children with CHD, especially in areas where other treatment modalities such as ECMO or inhaled NO are inaccessible.

Larger studies on similar patients and also on patients with different etiologies are needed to confirm our preliminary findings.

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**References**