Editorial

Propranolol in Tetralogy of Fallot

While total surgical correction is the goal for all patients with tetralogy of Fallot, drug therapy is required for emergency treatment of severe dyspneic spells and could be of value in preventing dyspneic spells and exercise hypoxia in children awaiting operation. β-adrenergic inhibition has been of value in the management of patients with functional obstruction to left ventricular outflow. Since there appears to be a functional element to the outflow obstruction in many patients with Fallot's tetralogy, pronethalol and later propranolol have received therapeutic trial. Some experiences with propranolol in the management of patients with Fallot's tetralogy in three situations follow: (1) management of the acute dyspneic attack, (2) prevention of dyspneic spells, and (3) improvement in children 2 to 6 years old while awaiting corrective surgery.

1. Dyspneic attacks in patients with Fallot's tetralogy are a unique phenomenon that may occur in patients who have little or no cyanosis under usual conditions. The attacks, characterized by dyspnea, cyanosis, and limpness, usually occur in such patients between 6 and 30 months of age; they may disappear spontaneously, but if severe, may be fatal. During the attack the right-to-left shunt increases markedly and arterial oxygen saturation drops precipitously. With prolonged attacks, hypoxia leads to lactic acid accumulation and severe acidosis. The time-honored treatment introduced by Taussig is often all that is necessary; namely, knee-chest position, oxygen, maternal comfort, and for severe attacks intramuscular injection of morphine, 0.2 mg/kg. Intravenous administration of sodium bicarbonate is invaluable in severely acidotic infants. In the laboratory, angiotensin will promptly abort the attack by increasing the systemic vascular resistance, and attacks are precipitated by reductions in systemic resistance. There is ample evidence that β-adrenergic blocking drugs can be used to terminate dyspneic spells. Propranolol in a dose of 0.2 mg/kg of body weight has been used in this hospital in the catheterization laboratory and on the wards to abort severe attacks, some of which were resistant to the other therapeutic measures, including morphine. The mechanism of action is not completely worked out, but we have demonstrated a decrease in the right-to-left shunt following propranolol, presumably due to a change in right ventricular contractility.

2. While the spells in an individual patient may follow a set pattern, they often recur with unpredictable frequency and severity. Preventive measures include avoidance of precipitating factors, anticipation of the time of an attack, and sedation with phenobarbital. Continued attacks are a strong indication for surgery. The surgical creation of an adequate pulmonary blood flow usually eliminates the spells. In suitable patients, we and others have been able to prevent the majority of these spells with propranolol in divided oral doses of 20 to 60 mg daily. Most suitable for treatment are infants with mild cyanosis at rest (arterial oxygen saturation of 70 to 85%) whose selective angiograms show marked cyclic changes in the caliber of the right ventricular outflow tract. Infants with severe cyanosis (oxygen saturation, below 60%) and severe hypoplasia of the right ventricular outflow tract and pulmonary arteries are not significantly improved with propranolol and are better managed surgically. We have treated a few patients with propranolol for 2 to 6 months; their dyspneic spells were eliminated and did not recur after discontinuing the drug. One such patient, however, later

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had a severe attack which led to fatal cerebral thrombosis.

In other patients the majority of severe spells were eliminated by propranolol. To prevent the attacks, it was important to give propranolol every 4 or 6 hours. Eventual shunt surgery, however, gave improvement beyond that produced by propranolol with a higher oxygen saturation, greater infant well-being, increased physical activity, and improved temperament.

To cite an example, propranolol was given to one child from age 10 months to 3 years. Dyspneic spells, which had occurred several times a day before treatment, were eliminated. Growth and development were normal, and as long as he received propranolol every 4 to 6 hours he was essentially asymptomatic. His physical activity, however, gradually became curtailed by hypoxia, and he was frequently tired and cranky. He became so dependent on propranolol that if he missed one dose severe cyanosis and lethargy developed. On the drug, resting arterial oxygen saturation gradually decreased from 90% at age 10 months to 60% at age 3 years. An aortopulmonary shunt, created at age 3 years, resulted in marked clinical improvement.

3. Eventually it is hoped that corrective surgery for Fallot's tetralogy will be safely carried out (if required) during early infancy in all centers, but at present the majority of centers prefer to postpone corrective operation at least until age 5 years. The activity of some young children (2 to 6 years old) awaiting surgery is grossly limited because of hypoxia. In the laboratory, intravenously administered propranolol improves oxygen saturation by 3 to 10% at rest, and by 3 to 15% during exercise.8,9 Eriksson and associates8 have been impressed by the improvement in the well-being and activity of their patients with tetralogy treated with propranolol. In our center these children have done better with a shunt operation which allows postponement of corrective surgery until 7 or 8 years of age. Shah and Kidd8 also have not been impressed with the improvement produced by propranolol in these older patients. Propranolol may decrease the volume of an aortopulmonary shunt in patients with a prior palliative operation, and a fall in exercise oxygen saturation after propranolol has been noted in a few such patients.

In summary then, propranolol is of value in the immediate treatment of severe dyspneic spells of patients with Fallot's tetralogy, although standard measures suffice for the majority. Propranolol is worth trying as a preventative measure in patients with dyspneic spells, but the long-term results are not comparable to a good shunt operation. Shunt surgery is postponed rather than eliminated in the majority of infants with severe spells. Propranolol is of no practical value in patients with severe cyanosis. Although the general trend is toward the elimination of palliative procedures in children with Fallot's tetralogy who are over 2 years of age, it is still common practice to avoid open heart repair until the child is at least 5 years old. Propranolol may allow some children to increase their activity while awaiting corrective surgery, although the results are inconsistent. Patients most suitable for treatment have little cyanosis at rest, show marked reduction in arterial oxygen saturation with activity, or during dyspneic spells, and have angiographic evidence of functional stenosis of the right ventricular outflow tract.

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