Propranolol in supraventricular tachycardias of childhood

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Dworkin, P. H., Bell, B. B., and Mirowski, M. (1973). *Archives of Disease in Childhood*, 48, 382. **Propranolol in supraventricular tachycardias of childhood.** 9 children with supraventricular tachycardias refractory to conventional therapy were treated with propranolol. In 3 children normal sinus rhythm was restored. In 3 others frequency of paroxysmal arrhythmias was decreased. In 1 reduction of ventricular response to the ectopic rhythm was achieved, and in 2 remaining patients, propranolol had no effect. The dosage of propranolol ranged from 0.5 to 4.0 mg/kg per day, given orally, with few side effects. It appears that propranolol can play an important role in treatment of supraventricular arrhythmias of childhood unresponsive to conventional therapy.

Supraventricular tachycardias represent an important management problem in paediatrics. While digoxin is the drug of choice, propranolol has been proposed for arrhythmias refractory to conventional therapy. The mode of action of propranolol is well known (Schamroth, 1966). However, its optimal paediatric dosage, as well as long-term effects and side effects in children, remains to be determined.

In this study, records of 9 children with refractory supraventricular tachycardia treated with propranolol and digoxin have been examined in order to (1) ascertain whether any systematized approach to the use of this drug has been employed; (2) determine the indications for its use in such patients; (3) develop criteria for evaluation of propranolol's effectiveness; and most importantly (4) provide a basis for carefully devised prospective studies and a rational therapeutic approach.

Materials and methods

Between 1961 and 1971, 58 children were primarily treated for supraventricular tachycardias in this institution. Of these, 9 did not respond to conventional therapy and were treated with propranolol. Clinical and ECG records of these children were examined. 8 had idiopathic supraventricular tachycardias without evidence of structural heart disease, confirmed by cardiac catheterization in 3 (Cases 1, 3, and 4). The remaining patient developed the arrhythmia after Mustard procedure for complete transposition of the great vessels

(Case 2). The patients' ages ranged from 9 months to 16 years. There were 7 males and 2 females. All were symptomatic with dyspnoea, dizziness, chest pain, or epigastric distress. In all children, reflex vagal stimulation and sedation were attempted. Previous therapy with digoxin alone, digoxin, and/or cardioversion and/or quinidine had also been unsuccessful in achieving and maintaining a satisfactory ventricular rate. The effectiveness of propranolol was judged by its ability to convert the arrhythmia to sinus rhythm, to slow the ventricular response to physiological values even during exercise if the abnormal rhythm persisted, or to decrease the frequency of paroxysmal attacks. In all patients digoxin was continued. The pertinent clinical and ECG data are summarized in the Table.

Results

Striking clinical improvement was observed in 8 patients. In 3 (Cases 3, 4, and 9) sinus rhythm was restored (Fig. 1). In 1 (Case 9) propranolol was helpful in maintaining sinus rhythm after cardioversion. In another patient with atrial flutter (Case 2) an increase in the degree of AV block established a satisfactory ventricular rate without conversion of the arrhythmia, though sinus rhythm was eventually restored (Fig. 2). In 3 other children, frequency of paroxysmal attacks was reduced from daily to weekly occurrence (Cases 1, 7, and 8). In only 1 child no improvement was observed (Case 6); in another, reversion to sinus rhythm was probably not due to propranolol (Case 5). The dosage of propranolol ranged from 0.5 to 4.0 mg/kg per day by mouth.

FIG. 1.—Conversion of atrial flutter-fibrillation to normal sinus rhythm after addition of propranolol.

The follow-up of these patients ranged from 3½ to 30 months, with a mean of 13 months.

Few side effects were observed. Those noted include the development of sinus bradycardia (Cases 1 and 8), feeding difficulties (Case 3), and aggravation of ketotic hypoglycaemia (Case 2); this led to decrease in dosage in 3 patients (Cases 1, 2, and 3).

Discussion

While the effectiveness of propranolol as an antiarrhythmic agent has been widely documented in the adult population (Wennevold and Sandoe, 1966; Luria, Adelson, and Miller, 1966; Sloman and Stannard, 1967), far less information is available concerning its use in children. By means of β -adrenergic blockade and also through a direct

TABLE
Clinical features and response to therapy

Case no. and sex	Age (yr)	ECG	Rate/min	Unsuccessful therapy	Weight (kg)	Propranolol		Results§	Side effects
						Dose (oral) (mg/kg per day)	Duration (mth)		
1 M	12 2/12	Atrial flutter; junctional rhythm	280	Digoxin	40	*0.3 to 3 then to 0.5	13	+	Bradycardia
2 M	2 6/12	Atrial flutter	160	Digoxin; cardioversion; quinidine	12.5	*1.5 to 4	7	++	Aggravation of ketotic hypoglycaemia
3 M	8/12	Atrial flutter-fibrillation	140–240	Digoxin; cardioversion	8.3	*3.6 to 1.2	5.5	+++	Feeding difficulties
4 F	9/12	Atrial flutter-fibrillation	140	Digoxin; cardioversion; quinidine	5.5	†1.5	4	+++	
5 M	10 6/12	Junctional rhythm; left atrial rhythm	110		30	*2 to 4	30	0	
6 M	17	Paroxysmal atrial tachycardia; left atrial rhythm	130	Oubain digitalis	66	*1.2 to 1.8	3.5	0	
7 M	9 6/12	Paroxysmal atrial tachycardia; junctional rhythm; A–V dissociation	160	Quinidine	29	*1.4 to 1.7	6	+	
8 M	16 2/12	Junctional rhythm; ectopic atrial activity	40–130	Digoxin	50	*0.8	30	+	
9 F	8 1/12	Paroxysmal atrial tachycardia; Wolff-Parkinson-White Type B	240	Digoxin	25	‡0.8	18	+++	Bradycardia

*With digoxin. †With digoxin and quinidine. ‡Maintenance after cardioversion. § + + +, return to normal sinus rhythm; + +, establishment of physiological ventricular rate; +, reduction in frequency of episodes of tachycardia; 0, no effect.

FIG. 2.—Increase in degree of AV block with decrease in ventricular rate upon addition of propranolol. Normal sinus rhythm was eventually restored.

'quinidine-like action' on myocardial cells, the drug depresses the automaticity of the sinus and subsidiary pacemakers, slows the conductivity of the sinoatrial and atrioventricular junctions, and increases the refractory period of the atrioventricular node (Schamroth, 1966).

The drug of choice in treatment of supraventricular tachycardias of childhood is digoxin. Approximately 15% of patients, however, are refractory to it as well as to quinidine, cardioversion, and other modes of therapy (Linde, 1971; Nadas *et al.*, 1952; Simcha and Bonham-Carter, 1971). Though only a minority, these patients present a serious therapeutic problem. Our experience and that of others in adults indicate that propranolol can be useful in this situation. The prime aim of treatment in these patients is the restoration of a physiological ventricular rate, rather than suppression of the ectopic rhythm (Fidelle, Cloup, and Nouaille, 1969.)

Our study indicates that in these patients with refractory supraventricular arrhythmias, significant decreases in ventricular response can be achieved by addition of propranolol. The drug was useful in a wide range of rhythm disturbances, including atrial flutter, paroxysmal atrial tachycardia, flutter-fibrillation, and less defined supraventricular ectopic activity, including junctional rhythms and left atrial ectopic activity (Mirowski, 1966).

Optimal paediatric dosage of propranolol is

unknown. There have been no adequate studies concerning dosage in treatment of supraventricular tachycardias in children. Amounts ranging from 20 to 120 mg/day have been reported (Luria *et al.*, 1966; Walters *et al.*, 1968). Prophylaxis against return of atrial fibrillation after cardioversion was achieved with 80 to 180 mg/day (Escudero, Martinez, and Cuan, 1969). Dosage per kg was not reported in these studies.

In our patients the amounts successfully employed ranged from 0.5 (Case 1) to 4 mg/kg per day (Cases 2 and 5). No optimal therapeutic dosage for all patients could be ascertained. The dosage must be individually adjusted in each patient. It appears that a rational therapeutic approach is an initial dosage of 1 mg/kg per day, gradually increasing to as high as 4 mg/kg per day until satisfactory results are obtained.

Major contraindications to the use of propranolol include cardiac failure unrelated to haemodynamic consequences of the arrhythmia, sinus bradycardia and complete heart block, pulmonary hypertension resulting in right ventricular failure (cor pulmonale), and cardiogenic shock.

In our series, propranolol has been used for up to 2½ years with very few side effects observed. No patient required discontinuation of the drug. Undesirable side-effects reported by others include (1) light-headedness, rashes, visual disturbances, purpura, and paraesthesiae; (2) those due to

specific pharmacological action of the drug, such as hypotension, bradycardia, cardiac failure, dyspnoea, and wheezing; and (3) biochemical abnormalities including a rise in BUN, SGOT, sodium retention, and aggravation of hypoglycaemia (Stephen, 1966). When propranolol is administered intravenously, an isoprenaline drip should be available to overcome β -adrenergic blocking effects if necessary.

Positive conclusions based upon our study must be made with caution. Ideally, our patient population would be more homogeneous with respect to age, arrhythmia, and management before propranolol therapy. Precise and quantitative evaluation of efficacy of propranolol is made difficult by concomitant use of digoxin, though digoxin alone was clearly ineffective in controlling ventricular rate. Encouraging results from this study indicate, however, that propranolol is a useful adjunct in the treatment of childhood supraventricular arrhythmias refractory to conventional therapy.

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