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The incidence of ICBs in the cardiac group (23 out of 70) was significantly higher than the control group 4 out of 56 ($\chi^2 = 12.03$, $P<0.001$), when only cardiacs with murmurs of intensity grade III/VI or more were considered. Again age was a factor in determining the prevalence of ICBs in association with cardiac murmurs. Thus 4 out of 40 (10%) infants aged 1 day to 4 months had ICBs compared with 19 out of 30 (63%) children aged 4 months to 3 years ($P<0.01$) (Fisher) $\chi^2 = 22.10$, $P<0.0005$). Since most cases with an ICB in this study had associated cardiac murmurs grade III to V/VI, conduction from the chest along the carotid and vertebral vessels might explain the phenomenon.

The conclusion of this study, in conjunction with some of the reported findings, suggests that further investigation is indicated in infants under the age of 4 months with an ICB of grade III intensity. A computerised axial tomographic scan with contrast injection would be appropriate. If cardiac failure is also present, the first choice of diagnostic procedure might be cerebral angiography to confirm the presence of an intracranial arteriovenous fistula.

Summary

In a control group an intracranial bruit (ICB) was heard in 4 of 13 children aged between 4 months and 3 years, but in none of 43 younger infants between the ages of one day and 4 months. In a group of 70 infants with cardiac murmurs of intensity grade III/VI or more, 19 of 30 aged between 4 months and 3 years had an ICB, compared with 4 of 40 younger infants aged between one day and 4 months ($P < 0.0005$). It is concluded that in infants under the age of 4 months, even in the presence of a loud cardiac murmur, an ICB is rarely heard. The presence of an ICB, with or without signs of cardiac failure, strongly suggests an intracranial arteriovenous fistula.

References


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Propranolol as an antihypertensive agent in children

The antihypertensive effect of propranolol, a β-adrenergic blocking agent, is well established in adults (Holland and Kaplan, 1976), but there is little information on it in children. This report describes the antihypertensive effect of oral propranolol in children with hypertension.

Materials and methods

Nine patients with hypertension were studied. Their diagnoses are given in the Table.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>BP Baseline</th>
<th>BP Post-treatment</th>
<th>BP Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>0.5 mg/kg per day</td>
<td>0–2.5 mg/ml per hour</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blood pressure (BP) was measured in the supine position using a cuff which covered two-thirds of the upper arm. Diastolic BP was recorded as the muffling of the Korotkoff sounds. To test exercise-induced tachycardia, patients were asked to run on the spot for one minute. Heart rate was measured before and after exercise.

Propranolol was started at a dose of 0.5 mg/kg per day divided 3 or 4 times a day. Dosage was increased until BP responded or side effects developed. Patients were on the drug 3–7 days before the effect of the treatment was assessed.

Two patients were on no other drug during the study; 2 received diuretic plus α-methylidopa, and 3 received diuretic plus hydralazine. The dosage of...
other medications was constant beginning 2 weeks before propranolol was started and continuing throughout the study period.

Results

Average BP before propranolol was 152/110 mmHg; average pressure after propranolol was 126/90 (Figure). Systolic BP dropped an average of 26 mmHg (P<0.01). Diastolic BP dropped 20 mmHg (P<0.01). A fall in BP was seen in each patient (Table). The propranolol dose varied between 0.6 and 6.4 mg/kg per day, averaging 2.5 mg/kg per day.

The average heart rate before propranolol was 102 per minute, falling with propranolol treatment to 83 (range 52–120 per minute).

Four patients were tested for exercise-induced tachycardia while taking propranolol: all showed an increase in heart rate after exercise. Mean resting heart rate was 85 per minute, and post-exercise was 106.

There was no correlation between pretreatment plasma renin activity and fall in either systolic (r=0.01) or diastolic (r=0.15) BP during treatment. Similarly there was no correlation between plasma renin activity and dose of propranolol required to lower BP. There was no significant change in weight before or after propranolol. The BP response to propranolol was similar in patients taking or not taking diuretics.

One patient developed a resting bradycardia with heart rate 52 per minute, in association with lethargy; these disappeared when propranolol dosage was decreased and hydralazine was added. Another developed mild anorexia which disappeared without change in dosage.

Discussion

Propranolol is an effective antihypertensive agent in children; it is well tolerated. The most common side effect is bradycardia, which is dose dependent.

Severe bradycardia can be managed by decreasing the dosage and/or adding a vasodilator drug such as hydralazine which tends to produce tachycardia. Patients in this study were able to increase heart rate with exercise while taking propranolol, indicating only partial β-blockade.

The mechanism of the antihypertensive effect of propranolol is currently being debated. Part is related to suppression of renin release (Laragh et al., 1972). However, several investigations have shown that the antihypertensive effect of propranolol (in adults) does not correlate with the decrease in plasma renin levels that occurs with this treatment (Michelakis and McAllister, 1972; Tarazi and Dustan, 1972). Decreased cardiac output and direct CNS effects may also be important mechanisms (Holland and Kaplan, 1976).

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (years)</th>
<th>Blood pressure before propranolol (mmHg)</th>
<th>Propranolol dosage (mg/kg per day)</th>
<th>Plasma renin (ng/ml per hour)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>140/100</td>
<td>1.8</td>
<td>14.2</td>
<td>Renal artery stenosis</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>158/109</td>
<td>4.0</td>
<td>8.7</td>
<td>Post haemolytic uraemic syndrome</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>183/137</td>
<td>6.4</td>
<td>8.2</td>
<td>Interstitial nephritis</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>132/98</td>
<td>3.1</td>
<td>ND</td>
<td>Post-transplant</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>151/98</td>
<td>0.9</td>
<td>8.4</td>
<td>Postrenal trauma</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>190/150</td>
<td>1.0</td>
<td>5.0</td>
<td>Cockayne’s syndrome</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>140/100</td>
<td>1.2</td>
<td>ND</td>
<td>Post-transplant</td>
</tr>
<tr>
<td>8</td>
<td>15</td>
<td>150/104</td>
<td>3.5</td>
<td>4.6</td>
<td>Systemic lupus erythematosus; nephritis</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>126/89</td>
<td>0.6</td>
<td>&gt;10.0</td>
<td>Systemic lupus erythematosus; nephritis</td>
</tr>
<tr>
<td>Mean</td>
<td>9.5</td>
<td>152/110</td>
<td>2.5</td>
<td>8.4</td>
<td></td>
</tr>
</tbody>
</table>

ND = not done.
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The effectiveness of propranolol in our patients may be related to the elevated plasma renin activity, although the degree of plasma renin elevation before treatment did not correlate with the fall in BP. Studies in hypertensive adults have shown that propranolol may be effective even when the renin is not elevated (Holland and Kaplan, 1976). Further data will be needed to determine if plasma renin activity will predict the antihypertensive effect of propranolol in children. The plasma concentration of propranolol varies markedly in adults given the same oral dose (Nies and Shand, 1975), and this probably explains the wide range of dosage found to be effective in this study.

Our arbitrary goal in treating hypertension in children is a diastolic BP of 85–90 mmHg or less. Several patients in this study received additional medications after the propranolol trial period. Using propranolol combined with other agents, a diastolic BP of 85 mmHg or less was achieved in most of the patients.

Theoretically it might be ideal to achieve a normal BP for age in hypertensive children, in whom one must be concerned about a 40–60 year follow-up, but there is no proof that this is essential, while the number of drugs and their side effects multiply when such an attempt is made. Patients who are asked to endure such side effects may stop complying with the treatment. There is also the important and poorly answered question about growth rates in children on large doses of antihypertensive drugs. In view of these considerations we do try to achieve a BP normal for age, but only when it can be done with well tolerated doses of antihypertensive drugs.

We conclude that propranolol is a safe and effective antihypertensive agent in children, which has been effective when other drugs—including α-methyldopa, hydralazine, and diuretics—have been ineffective. Because it blocks β-adrenergic receptors, it is contraindicated in patients with asthma and congestive heart failure. It should not be used in patients with phaeochromocytoma unless an α-adrenergic blocking agent is given simultaneously (Pritchard and Ross, 1966).

Summary

The antihypertensive effect of oral propranolol was studied in 9 children with hypertension. After treatment with propranolol, systolic blood pressure fell by an average of 26 mmHg (P < 0.01). Diastolic pressure decreased by 20 mmHg on average (P < 0.01). The mean propranolol dose was 2.5 mg/kg per day. Side effects included bradycardia and anorexia. There was no correlation between pretreatment plasma renin activity and fall in blood pressure. Propranolol is an effective and well tolerated antihypertensive agent in children.

This work was supported in part by Clinical Investigation Projects Grant number 5–16–445. The opinions expressed are those of the authors and are not to be construed as reflecting the views of the US Navy.

References


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Heights and weights of West Indian children with the sickle cell trait

The sickle cell trait (genotype AS) appears to offer young children some protection from falciparum malaria and, with few exceptions, appears to be benign. A recent report that children in Philadelphia with the sickle cell trait were smaller in size and
Propranolol as an antihypertensive agent in children.

W R Griswold, R McNeal, S A Mendoza, B B Sellers and S Higgins

Arch Dis Child 1978 53: 594-596
doi: 10.1136/adc.53.7.594

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