Oral treatment of subacute bacterial endocarditis in children

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SUMMARY Fourteen episodes of subacute bacterial endocarditis in 11 children were successfully treated with antibiotics, which in 13 cases were given largely by mouth. It is suggested that oral treatment of bacterial endocarditis should be considered for children who are only moderately but not severely ill, and who have sensitive organisms.

Most published reports of subacute bacterial endocarditis have stressed the need for parenteral rather than oral treatment. A few early reports showed successful treatment with oral penicillins (Gray et al., 1964; Gray, 1969), but these regimens have never achieved popularity. We present 14 episodes of subacute bacterial endocarditis in children successfully treated with antibiotics given largely by mouth, and discuss why some patients may be better treated with oral rather than parenteral antibiotics.

Patients and methods

Between 1960 and 1975, 14 episodes of subacute bacterial endocarditis (SBE) in children have been received at this hospital, all but the first 2 being under the care of one of us (G.H.W.). Details of those treated orally are given in the Table. In all 14 cases repeated blood cultures were positive; in 8 cases Streptococcus viridans was cultured, in 3 others streptococci or enterococci, and in 3 staphylococci. In 13 episodes the age and clinical manifestations were characteristic. Case 7 may seem less certain because of the rarity of SBE in infancy (Macaulay, 1954), but there were unexplained fever and persistently positive blood cultures growing Strep. viridans. On admission 4 children had evidence of pulmonary emboli, one had nephropathy, and one developed meningitis with a sterile cerebrospinal fluid a few days after starting treatment. Treatment with an appropriate antibiotic was

Table Details of patients

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (yr)</th>
<th>Underlying lesion</th>
<th>Organism</th>
<th>Treatment</th>
<th>Daily dose (g)</th>
<th>Duration (w)</th>
<th>Bactericidal dilution of serum</th>
<th>Serum levels of drug (µg/ml)</th>
<th>MIC of drug against organism (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>CTGA, VSD, PS</td>
<td>Strep. viridans</td>
<td>Erythromycin</td>
<td>8</td>
<td>1</td>
<td>5 6</td>
<td>3 7</td>
<td>0-05</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>VSD, CTGA, PS</td>
<td></td>
<td>Penicillin V</td>
<td>6</td>
<td>2</td>
<td>10</td>
<td>0-06</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>VSD</td>
<td></td>
<td>Ampicillin</td>
<td>6</td>
<td>4</td>
<td>5 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>VSD</td>
<td></td>
<td></td>
<td>8-16</td>
<td>7</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Tetralogy</td>
<td></td>
<td></td>
<td>8 8</td>
<td>2</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>11</td>
<td>Mitral incompetence</td>
<td></td>
<td></td>
<td>8</td>
<td>2</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>6 m</td>
<td>TGA, small PDA</td>
<td></td>
<td></td>
<td>2</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>VSD, banded</td>
<td></td>
<td></td>
<td>4</td>
<td>6</td>
<td>5 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>7</td>
<td>Staph. aureus</td>
<td>Cloxacillin</td>
<td>7-56</td>
<td>12</td>
<td>3</td>
<td>0-03</td>
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<tr>
<td>10</td>
<td>8</td>
<td>VSD</td>
<td>Ampicillin</td>
<td>2</td>
<td>6</td>
<td>1-6</td>
<td>0-01</td>
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</tr>
<tr>
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<td>6</td>
<td>Tetralogy</td>
<td>Staph. albus</td>
<td>2</td>
<td>5</td>
<td>1/16</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>13</td>
<td>7 f</td>
<td>Microaerophilic streptococcus</td>
<td></td>
<td>2</td>
<td>6</td>
<td>5-0</td>
<td>0-02</td>
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</tr>
</tbody>
</table>

CTGA = congenital corrected transposition of great arteries; VSD = ventricular septal defect; TGA = transposition of great arteries; PS = pulmonary stenosis; PDA = persistent ductus arteriosus. MIC = minimum inhibitory concentration.
started on diagnosis. Case 14, who had very severe
general symptoms and whose illness due to an entero-
ococcus began 6 weeks after a corrective operation for
tetralogy, was given intravenous treatment for 2
months. Case 13 was treated intravenously for 2
weeks because he objected violently to oral medi-
cation, though in the subsequent 6 weeks he was
treated by an indwelling oro gastric tube which he
accepted even while up and about.

In 6 cases treatment was entirely oral, and in
another 6, including the more severely ill as well as
Case 6 with rheumatic heart disease, medication was
given parenterally for the first 2 or 3 days. However,
when no severe general or abdominal symptoms were
present which would suggest inadequate absorption,
drugs were given only by mouth. In 2 cases dilutions of
serum up to 1/16 and 1/64 killed the cultured
organisms; in others serum antibiotic levels 3 to 4
hours after the previous dose exceeded the median
inhibitory concentration (MIC) of the drug for the
cultured organism by factors of 30–250. Treatment
was given for 6 to 8 weeks in most cases, but was
longer in 2 cases because of the nature of the organism
or previous surgery. Some children who
seemed physically well and whose erythrocyte
sedimentation rate had fallen were allowed home
for the latter part of their treatment, with frequent
supervision.

Results

The 10 children treated orally recovered from their
attacks of SBE with no permanent sequels or change in
cardiac status or signs, and all have been
followed up for periods of 1 to 15 years. Case 14,
treated intravenously, also recovered from SBE but
died later from mechanical causes. 3 children treated
orally had second attacks of SBE; we feel that
these were not relapses following inadequate treat-
ment because in 2 cases a different organism was
cultured 9 months and 2 years, respectively, after
the first episode, while in the third child the attacks
were 4 years apart.

No significant complications of treatment were
encountered and in particular no child had vomiting,
troublesome anorexia, or diarrhoea, or 'super-
infection' with other organisms.

Discussion

The clinical and bacteriological spectrum of infective
endocarditis has changed over the last 20 years. From
a predominant involvement of young adults with
rheumatic heart disease emphasis has passed to
older adults, unusual and opportunist organisms,
and association of the disease with invasive pro-
cedures. In children there is now found, as in this
series, an underlying congenital cardiovascular
lesion in 90% of the cases; however, the commonest
organism is still Strep. viridans, the next common
being staphylococci and enterococci (Nadas and
Fyler, 1972).

Despite much discussion no final conclusion has
been reached about the optimum duration of treat-
ment. In cases due to penicillin-sensitive Strep.
viridans short courses (e.g. 2 weeks) have been effec-
tive (Tan et al., 1971), but though there is evidence
that larger doses of antibiotics permit a shorter
period of treatment than the 6 or 8 weeks used 25
years ago, in general 4 weeks' treatment is advised
for such cases (Hayward, 1973; Weinstein, 1970).
Longer periods (4 to 6 weeks) have been advised
for more resistant streptococci and other organisms
There is anecdotal evidence for occasional super-
infection with Gram-negative organisms when oral
treatment is continued for even as short a time as
5 or 6 weeks (Weinstein and Schlesinger, 1973),
but there is also similar evidence that occasional
patients with apparently sensitive organisms need
much longer courses for cure (Hayward, 1973).
We have felt that there is little hazard in extending
oral medication for 2 or more weeks, when no
clinical symptoms have been caused, even though in
some cases it may be unnecessary.

Oral treatment has been and still is regarded as
unsatisfactory (Hayward, 1973; Kaye, 1973), most
physicians preferring to use parenteral treatment,
probably for the following reasons (Weinstein and
Schlesinger, 1973). (1) Extensive past experience
has shown good results using parenteral antibiotics.
(2) Infection may be caused by an organism for which
the best antibiotic may be available only in parent-
eral form. (3) Oral antibiotics may lead to gastro-
testinal irritation. (4) Patients may fail to take the
drugs prescribed unless under observation. (5)
Antibiotics may be irregularly absorbed from the gut.
On the other hand, recommendations for the use
of oral antibiotics spring from the desire to avoid
pain and anxiety, especially in children with chronic
disease who know they may have to return to hospital,
and also to reduce the chances of complications,
such as abscesses, thrombophlebitis, or septicemia,
arising from injections or indwelling cannulae.

We feel that the contraindications to oral treat-
ment listed above can be circumvented in most
children with SBE. Most organisms which cause
SBE are treatable by antibiotics which can be given
by mouth; gastrointestinal symptoms have not been
a problem, and oral treatment can be adequately
supervised and safely left to a certain number of
parents to continue at home. Absorption from the
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gut has led to adequate serum levels of antibiotics and effective treatment, but may be unreliable in those with severe general or abdominal symptoms. The semisynthetic penicillins are especially reliable, and serum levels after oral doses of these drugs exceed many-fold the median inhibitory concentrations for pathogens commonly found in SBE (Knudsen et al., 1961). Various authors recommend that the serum should be bactericidal in dilutions varying from 1 in 2 (Hayward, 1973) to 1 in 20 (Nadas and Fyler, 1972), and these levels are also possible to achieve.

We feel that if the organism is appropriately sensitive, and if attention is paid to the attainment and maintenance of adequate serum levels and to the response to treatment, most children with bacterial endocarditis may be treated effectively with predominantly oral antibiotics, enabling some of them to be managed at home for the latter part of their treatment, and avoiding the discomfort and complications of long-term parenteral treatment.

References


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