Discussion

This technique is simple to use, and most of the equipment is commercially available. It is acceptable to patients and enables impotence to be investigated in an ordinary, quiet hospital ward simply by admitting the patient for one or two nights. Direct measurements of penile erections correlate poorly with the presence of decreased libido or loss of morning erections and also with measurements of other aspects of peripheral or autonomic function. We believe that the technique represents a useful advance in the investigation of impotence, and we now use it routinely.

Two-thirds of our diabetic patients had nocturnal erections with an increase in penile circumference and a duration that were within the range shown by the healthy subjects. We cannot imagine an organic lesion that would lead to failure of erection during sexual activity and yet permit normal nocturnal erections, so probably in these patients the impotence was mainly caused by psychological factors. Six diabetics and one healthy subject showed a maximum increase in penile circumference of under 15 mm. The healthy subject, who claimed not to be impotent, was studied only once and on repeated tests might have shown more nocturnal activity, but the diabetics were each studied at least twice. Five of the diabetics complained of total impotence, and all had postural hypotension due to autonomic neuropathy; two also had Charcot’s joints. Impotence in these patients may therefore have had an organic basis.

We suggest that in most diabetic patients who complain of impotence the problem is psychological rather than organic, but why impotence should apparently be so common among diabetics is not clear. Possibly a period of ill health or poor diabetic control causes transient autonomic neuropathy producing reversible organic impotence that might be continued owing to psychological complications. We find that patients are reassured by knowing their impotence does not indicate organic disease, and after this reassurance, or after psychotherapy, some of our patients have reported improved sexual performance.

References


(Accepted 9 September 1979)

Praziquantel: a new schistosomicide against Schistosoma haematobium

J E McMAHON, N KOLSTRUP

British Medical Journal, 1979, 2, 1396-1399

Summary and conclusions

The effectiveness of the new schistosomicide praziquantel was assessed in African schoolchildren infected with Schistosoma haematobium. They were stratified according to the severity of their infection and were then randomly allocated to treatment with two single-dose regimens (30 and 40 mg/kg) and a split regimen of two doses of 20 mg/kg given four hours apart. All three regimens were highly effective and produced few side effects. Children who initially had very high pretreatment egg loads showed a poorer therapeutic response at all dose levels, and further investigations are necessary to find the optimum dose.

Because of its effectiveness in a single dose and lack of toxicity, praziquantel may prove to be the ideal schistosomicide.

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References


(Accepted 9 September 1979)
At 1
Before
At 6
At 3
TABLE
were
*Children
mean
TABLE
after
centrifugation
No
were
fixed and
light
After
counts
in different animals
were
40
in 12 patients with S
haematobium infections given a single dose of 40 mg praziquantel/
kg.

We describe here a study we performed in African school-
children infected with S haematobium to determine the clinical
efficacy and side effects of three regimens of praziquantel.

Patients and methods
One hundred and eighty-three African schoolchildren aged 7-15
and attending a school in Tanga region were studied. Three 10-ml
urine samples were taken at the time of peak egg excretion (1000-1500
h) on three different days and examined. The children were then
divided into three strata according to geometric mean egg load:
stratum I 60-250 eggs, stratum II 251-500 eggs, stratum III >501
eggs. Each stratum was randomly subdivided into four groups
according to previously arranged blocks. Group 1 in each stratum
received praziquantel 30 mg/kg in a single dose, group 2 received
40 mg/kg in a single dose, group 3 received 40 mg/kg in two divided
doses four hours apart, and group 4 received placebo. Altogether
125 children returned for follow-up at one month, 123 at three months,
and 117 at six months.

A school community was selected for the trial because the pupils
were available for a follow-up period of six months and because, in
Tanga region, the prevalence and intensity of S haematobium infection
is much higher in children than in adults. To detect possible seasonal
fluctuations in egg excretion that might confuse therapeutic assessment
a placebo group was included. This group was treated at the end of
the trial.

After urine samples were sedimented in a conical flask for 30
minutes both viable and non-viable eggs were detected in a 10-ml
specimen removed from the bottom of the flask. Briefly, 5 ml of
freshly cooled boiled water was added to the centrifuged deposit.
After thorough shaking hatching was performed under artificial
light at a constant temperature of 22°C for 30 minutes. Miracidia
were fixed and stained with alcohol (2 ml) and eosin (7 drops), and
after centrifugation and withdrawal of supernatant all miracidia
(hatched and non-hatched) in the final 0.1 ml were counted as a cover

Slip preparation under a 16-mm objective lens. In the follow-up
studies the same procedures were used to examine three urine samples
collected on different days during one week.

The drug’s efficacy was evaluated on the basis of a reduction in egg
excretion: cure was considered probable when no eggs or only non-
viable eggs were excreted on three different days.

All children were examined clinically before and four and 24 hours
after treatment. Symptoms were recorded after both general and
specific queries and included anorexia, nausea, vomiting, abdominal
pain, diarrhoea, giddiness, tiredness, weakness, body pain, headache,
and fever.

Results
The probable-cure rates and reduction in egg excretion in each of
the groups (table I) showed that all treatment regimens were highly
effective. Although group 3 (20 mg) had an apparently higher cure
rate, the application of a t test showed no significant difference
between this regimen and those given to groups 1 and 2 (at one month’s follow-
up t = 0.36660 (DF = 64) and 0.85496 (DF = 63) respectively).

Both the cure rate and the pronounced reduction in egg count at
one month were maintained at three and six months follow-up. At
six months, as well as the 117 children who had three urine samples
examined another 14 provided one or two specimens. Counts on these
additional samples were also consistent with the pattern shown in
the earlier follow-up examinations.

Analysis of results according to pretreatment egg loads (table II)
showed that children with the heaviest infections (stratum III) had
the lowest cure rate. But even in stratum III there was a considerable
reduction in the number of children infected. The child with the most
unfavourable parasitological response still showed an 89-9% reduction
in egg excretion.

Side effects—No side effects attributable to the drug or related
to intensity of infection occurred on any drug regimen. There were no
significant effects on respiration, pulse rate, or blood pressure.
Complaints of nausea, abdominal pain, weakness, headache, dizziness,
tiredness, and pain in the limbs are relatively common in the school-
children in this area, and they occurred with equal frequency before
and after treatment and in treated and placebo groups (table III).
Seventeen children failed to report for clinical examination 24
hours after treatment. All were traced and found to be working in
the rice fields.

Discussion
The introduction of a drug combining effectiveness and lack of
toxicity on oral administration of a single dose represents a

<table>
<thead>
<tr>
<th>Group 1 (30 mg)</th>
<th>Group 2 (40 mg)</th>
<th>Group 3 (2 x 20 mg)</th>
<th>Group 4 (placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients examined:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 month</td>
<td>32</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>At 3 months</td>
<td>31</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>At 6 months</td>
<td>28</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>No (%)*</td>
<td>22 (71)</td>
<td>25 (83)</td>
<td>30 (86)</td>
</tr>
<tr>
<td>At 1 month</td>
<td>22 (71)</td>
<td>22 (76)</td>
<td>28 (82)</td>
</tr>
<tr>
<td>At 6 months</td>
<td>22 (79)</td>
<td>20 (71)</td>
<td>25 (81)</td>
</tr>
</tbody>
</table>

| Geometric mean egg count (and 95% confidence limits) of mean: | |
| Before treatment | 308.5 (31.4-3034.7) | 208.4 (33.2-2506.9) | 352.8 (37.0-3361.6) | 324.9 (22.1-4783.3) |
| At 1 month | 1.2 (0.15-4) | 1.1 (0.8-3) | 0.8 (0.6-2) | 1.87 (6.5-5601.5) |
| At 3 months | 0.9 (0.5-3) | 1.1 (0.9-3) | 0.5 (0.3-1.9) | 140 (6.3-3956.4) |
| At 6 months | 1.4 (0.3-9) | 1.1 (0.9-3) | 0.6 (0.4-1.5) | 156 (13.9-2563.9) |

*Children were considered to be probably cured when they excreted only dead eggs (or none at all).

<table>
<thead>
<tr>
<th>STRATUM I</th>
<th>STRATUM II</th>
<th>STRATUM III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probable cure rate (%)</td>
<td>Geometric mean egg count (and 95% confidence limits)</td>
<td>Probable cure rate (%)</td>
</tr>
<tr>
<td>Before treatment</td>
<td>86.4</td>
<td>0.6 (0.2-2.6)</td>
</tr>
<tr>
<td>At 1 month</td>
<td>84.1</td>
<td>0.6 (0.4-0.9)</td>
</tr>
<tr>
<td>At 3 months</td>
<td>81.4</td>
<td>0.8 (0.1-17.3)</td>
</tr>
<tr>
<td>At 6 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
major advance in the treatment of schistosomiasis, both for individuals and potentially for mass chemotherapy in control schemes.

In the area where these investigations were conducted, where schistosomiasis is endemic, a comparative trial of niridazole (150 mg/kg administered over five days) and hycanthone (2.5 mg/kg single injection) was carried out. At two to three months’ follow-up niridazole and hycanthone treatment resulted in overall cure rates of 61.1% and 56.5% respectively compared with a rate of 76.6% in this trial. Praziquantel also produced a greater reduction in egg load in patients who were not cured. Although the groups treated by these drugs were homogeneous in age, sex, and egg loads and the same techniques were used to evaluate drug effectiveness, transmission may vary greatly from year to year even in the same seasons. Because the level of transmission may affect the parasitological results after treatment, we recommend that a comparative trial of these three drugs should be conducted concurrently before conclusions are reached about the relative efficacy of each drug.

Further investigations using praziquantel against S. haematobium in adults have also shown a favourable parasitological response with low toxicity. Further investigations are needed to establish an optimum dose. The three treatment regimens that we used showed no toxic effects. The increased doses given to groups 2 and 3 did not affect the poorer therapeutic response in children with large egg loads (> 501). But as there was no increase in toxicity at this dose (40 mg/kg) a further trial of even higher doses in people with high egg loads seems to be warranted.

Cure rates of schistosomicides are greatly influenced by pretreatment egg loads. Our finding that children with very heavy infections (stratum III) had the lowest cure rate is similar to the results of a trial of niridazole against S. mansoni. But people with increased intensities of infection do not always respond more poorly to treatment. For example, a group of adolescents gave a more favourable parasitological response to treatment with hycanthone than a group of children, even though their initial egg loads were much higher than those of the children. Here increased immunity in the older children may have influenced the result.

The excretion of a few viable eggs in 19 out of 96 pupils (19.8%) one month after praziquantel treatment may have been due to failure of the drug to kill some adult female schistosomes or to developing worms being present at the time of treatment. Schistosomicides tend to be ineffective against immature worms, and juvenile schistosomes in hamsters with S. japonicum infections were less susceptible to praziquantel than mature forms.

During the past 20 years there have been many attempts to standardise methods for evaluating the effectiveness of schistosomicides. It was considered important to express the results of therapeutic trials as a reduction in the egg count because this is regarded as a far less variable measure of drug effectiveness than the cure rate.

At one month’s follow-up in our trial 48.4% of children in group 1, 33.3% of those in group 2, and 45.7% of those in group 3 were “definitely” cured—that is, they had stopped excreting eggs completely. Opaque and calcified eggs occur rarely in intestinal schistosomiasis. But in urinary schistosomiasis such eggs may be excreted for months, or even years, after successful treatment, and the probable-cure rate (nil or non-viable eggs being excreted) is a truer reflection of the actual condition.

The mode of action of praziquantel is not known. In vitro drug concentrations as low as 0.3 μg/ml serum are rapidly schistosomicidal. No drug that is truly egg suppressant in the sense of inhibiting only the egg laying of the schistosome has yet been identified, and in our trial the maintenance of a favourable parasitological response after the first follow-up examination suggested that the drug killed female schistosomes rather than suppressed oviposition. As with many schistosomicides hepatic shift of adult schistosomes followed praziquantel treatment in baboons (Papio anubus) infected with S. haematobium and vervet monkeys (Cercopithecus aethiops) infected with S. japonicum, but histopathological studies showed that many worms also died in situ.

The control of schistosomiasis remains a major public health problem. In many areas where the disease is endemic children are the main group responsible for transmission. In the area where this trial was conducted children swim and play in water habitats containing the snail intermediate hosts (Bulinus (Physopsis) nasutus and B (P) globosus) of schistosomiasis. Before treatment these children were potentially capable of extruding, into the habitats, millions of viable eggs daily. After treatment this potential was reduced to a few thousand per day. Treating populations with praziquantel before the transmission season combined with taking measures against the snail intermediate hosts might in certain epidemiological situations break transmission in a relatively short time.

Praziquantel, hycanthone, and metrifonate are the only schistosomicides known to be effective in a single-dose treatment against S. haematobium in man. Praziquantel is more effective than metrifonate. It is less toxic than hycanthone, and in the regimen described here it seems to be more effective than the optimum dose of hycanthone. We therefore conclude that praziquantel, because of its effectiveness against the three main schistosomes harboured by humans, its low toxicity, and its ease of administration and stability, seems to be approaching the ideal schistosomicide.

We thank A Mwakanayamle, J Tao, and D Mwakanganga for technical help and Dr D Wegner for his advice and co-operation. Praziquantel was supplied by Bayer AG.

Requests for reprints to: Dr J E McMahon, Karpassi, Burrington, Avon BS18 7AA, UK.

References


TABLE III—Frequency of symptoms (expressed as percentages) before and after treatment

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Group 1 Before treatment</th>
<th>Group 1 24 h after treatment</th>
<th>Group 2 Before treatment</th>
<th>Group 2 24 h after treatment</th>
<th>Group 3 Before treatment</th>
<th>Group 3 24 h after treatment</th>
<th>Group 4 Before treatment</th>
<th>Group 4 24 h after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>6.2</td>
<td>6.2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.2</td>
<td>6.2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3.4</td>
<td>3.4</td>
<td>18.2</td>
<td>18.2</td>
<td>18.2</td>
<td>18.2</td>
<td>18.2</td>
<td>18.2</td>
</tr>
<tr>
<td>Nausea</td>
<td>15.6</td>
<td>15.6</td>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
<td>8.1</td>
</tr>
<tr>
<td>Tiredness</td>
<td>12.5</td>
<td>12.5</td>
<td>20.2</td>
<td>20.2</td>
<td>20.2</td>
<td>20.2</td>
<td>20.2</td>
<td>20.2</td>
</tr>
<tr>
<td>Weakness</td>
<td>9.4</td>
<td>9.4</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
</tr>
<tr>
<td>Pain in limbs</td>
<td>9.4</td>
<td>9.4</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
<td>15.6</td>
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<tr>
<td>Headache</td>
<td>25.0</td>
<td>25.0</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
<td>18.7</td>
</tr>
<tr>
<td>Fever</td>
<td>12.5</td>
<td>12.5</td>
<td>9.4</td>
<td>9.4</td>
<td>9.4</td>
<td>9.4</td>
<td>9.4</td>
<td>9.4</td>
</tr>
</tbody>
</table>

Before treatment | 32 | 32 | 33 | 29 | 36 | 30 | 37 | 30

24 h after treatment | 32 | 32 | 33 | 29 | 36 | 30 | 37 | 30

No of patients % with symptoms
Boy or girl—parental choice?

G A DOVE, CAROL BLOW

British Medical Journal, 1979, 2, 1399-1400

Historical and archaeological evidence\(^1\) confirms that all ages and all societies have coped with the problem of selective preference for boys, and the need to limit their populations, by strategies that include simple infanticide, abortion, abstinence, adoption, and neglect. The practice of exposing alive the unexpected or unwanted child is a subject of considerable interest and controversy which recurs in the myths and legends of most, perhaps all, peoples.\(^2\)

The following case history reveals and examines this phenomenon and the controversy it caused, initially among medical students at a general practice seminar and later among the medical staff who became involved.

Case report

A 30-year-old married Englishwoman (an only child) pregnant for the sixth time (para 3 + 3) threatened to kill both herself and the child of this pregnancy if the child was another daughter. The problem was presented to the general practitioner by her husband (also English), whose dilemma was how to deal with his wife’s threat. The woman herself had agreed to the first two abortions and concurred in the need for the third—her husband wanted to buy a car. All three abortions had occurred before the “normal” birth of their two live girls, both now under 5 years old.

At a subsequent interview between the general practitioner and the wife she admitted to her feelings and requested an amniocentesis to determine the sex of the child, and an abortion if the fetus was not male. It was thought that the husband, despite his obvious dilemma, might also wish for a boy and thus be colluding with his wife. Whatever happened, it seemed likely that the woman would continue to get pregnant until a male child was born to them, thus sterilisation or contraception was out of the question.

The patient was introduced by the general practitioner to a “sympathetic” gynaecologist, who, after consultation with his colleagues, agreed to have an amniocentesis performed providing the patient undertook psychiatric treatment. To this both husband and wife readily agreed. The result of the amniocentesis, performed at the 21st week of the pregnancy, showed that the fetus was female.

The prevailing medical opinion was that her request for an abortion on these grounds should be refused but that considerable support should be given to the continuation of the pregnancy together with an undefined offer of some help should a subsequent pregnancy occur.

She was delivered of a normal female child at 40 weeks by a caesarean section. Three months after the delivery mother and child are alive and well and the mother continues to receive psychiatric support.

Discussion

The demands that this woman and her family made on our medical expertise led us to question the basic social and biological factors which operate in our society and which provoked a seemingly intelligent woman to want to terminate a pregnancy for this reason. Furthermore, her demands led us to question her ability to care for her progeny of either sex now or in the future: do her live children require surrogate support? Nevertheless, the evidence is that she is an exemplary wife and mother.

A recent global review of the subject\(^3\) found that despite the emergence of female emancipation and the need to limit family size a preference for boys remains. In all communities “economic considerations for sex preference are minimal while psychological and emotional considerations have come to the fore”\(^4\) — that is, anxiety about not having sons is evident. The review concluded that sex preference simply reflects the roles women and men have in society and conflicts with the humanitarian notion that every child is a wanted child and it questioned the status of women in society.\(^5\) Milton Freeman\(^6\) in his comments on the prestige, ethos, and economics of the practice of infanticide in primitive Eskimos regarded it as an evaluation of adult sex roles rather than a primary means of population control.

One must ask whether this woman’s need for a son represented a similar interpretation of sex roles in our supposedly emancipated society or whether it was the surfacing of other primitive, complex feelings\(^7\) that men have about pregnancy and which should be looked for in counselling before and after termination of pregnancy and in antenatal care. It is interesting that such strong feelings, expressed by an articulate, aggressive woman who was diagnosed as requiring psychiatric care, were not only listened to but acted on.

New techniques for diagnosing fetal abnormality by amniocentesis may create entirely new attitudes. There is certainly