EFFICACY OF MYRRH IN THE TREATMENT OF HUMAN SCHISTOSOMIASIS MANSONI

RASHIDA BARAKAT,† HALA ELMORSHEDY, AND ALAN FENWICK

High Institute of Public Health, Department of Tropical Health, Alexandria University, Egypt; Imperial College, Department of Infectious Disease Epidemiology, London, United Kingdom

Abstract. Myrrh (Mirazid) has been produced and marketed as an antischistosomal drug since 2001. The current study was designed to assess the efficacy of a commercially available product of myrrh. One hundred four individuals, infected with Schistosoma mansoni, were randomized in two groups, one for myrrh and the second for praziquantel. Treatment—whether myrrh or praziquantel—was given twice with a 3-week interval. The cure rate with myrrh was very low, 15.6% after the first treatment, and 8.9% after the second treatment. Egg reduction among uncured persons was also very low, being 17.2% after the first treatment, and 28% after the second treatment. Praziquantel cure rate was 73.7% and 76.3%, and individuals still passing S. mansoni ova after praziquantel treatment showed a substantial reduction in the geometric mean egg counts (84% and 88.2% after the first and second treatments, respectively). When 34 individuals—uncured after two myrrh treatments—were offered praziquantel in the standard dose, 32 of them stopped passing S. mansoni eggs when tested 4 weeks post-treatment. The results of the current study raise serious doubts about the antischistosomal properties of Mirazid.

INTRODUCTION

For more than two decades, praziquantel has remained the drug of choice for the treatment of the three common schistosome species, Schistosoma mansoni, Schistosoma haematobium, and Schistosoma japonicum. However, reliance on a single drug has raised considerable concern that tolerance or even resistance to the drug might develop.

Recently, a new antischistosomal drug, myrrh (Mirazid), was introduced in the Egyptian market in the form of gelatinous capsules produced by Pharco (Alexandria, Egypt). It is an extract of an oleo-gum resin obtained from the stem of the plant Commiphora molmol (myrrh). It has been used as a safe, natural flavoring substance that has been approved by the U.S. Food and Drug Administration. Studies with hamsters demonstrated that the administration of the resin and the volatile oil obtained from the plant stem by alcohol extraction followed by steam distillation induced parasitological cure of S. mansoni infection. The mechanism of action of myrrh on the schistosome worms, as suggested by the manufacturer, is related to permanent loss of musculature of the worms leading to separation of male and female couples and their shift to the liver where destruction and phagocytosis take place. However, there are no other published data confirming these findings. Furthermore, recently a multicenter investigation of the potential antischistosomal activity of different derivatives of the resin including the commercial preparation Mirazid was tested in mice and hamsters infected with Egyptian, Peurto Rican, or Brazilian S. mansoni strains. The drug was found toxic for mice at high doses and produced modest or no worm reduction at lower doses, and the authors stated that they couldn't recommend the use of this drug in human cases of schistosomiasis.

The only published human study of the effect of myrrh against schistosomiasis mansoni reported that after a single course of myrrh treatment (10 mg kg⁻¹ day⁻¹ for 3 days), the cure rate was 91.7%. When a second course of myrrh (10 mg kg⁻¹ day⁻¹ for 6 days) was offered to the uncured persons, it resulted in an overall cure rate of 98.09%. Cure rate was not influenced by age, sex, body weight, history of treatment with praziquantel, presence of decompensated liver disease, or type of schistosomiasis. With respect to S. haematobium, cure was obtained in 91.5% of treated individuals after 2 months and it increased to reach 95.2% on the third month post-Mirazid treatment.

The marketing of this drug in Egypt prompted a controversy because the published data documenting its antischistosomal properties, whether in experimental animals or in humans, consist of papers written by the discoverers of these properties, and no independent confirmation has appeared, so far, of these antischistosomal effects. In view of the fact that the drug is currently reported to be prescribed on a large scale by Egyptian private physicians, especially in rural areas (Barakat R and others, personal communication), the current study was designed to assess the efficacy of the commercially available product of myrrh and to compare it with praziquantel in the treatment of S. mansoni in a controlled blind trial.

MATERIALS AND METHODS

The study was carried out in El Zawrat village, Nile Delta, Egypt. The village is located 1 km to the east of the Rosetta branch of the River Nile (geographical coordinates: 31°23’ N and 30°27’ E). It is inhabited by 2,065 individuals. Screening for S. mansoni infection was done through collection of stool samples and examination of two Kato slides (41.7 mg) from each sample. The overall prevalence of S. mansoni infection was 14.5%. Of the infected persons, 104 individuals were randomized in two groups, the first for Myrrh and the second for praziquantel. The characteristics of the two groups being comparable. All adult patients gave informed consent prior to participating in the study, and consent and assent forms were obtained from all children and their parents who agreed to participate in the study. The protocol was reviewed and approved by the ethical committee of the High Institute of Public Health, Alexandria University, Egypt.

Diagnosis of S. mansoni infection and cure assessment was based on examination of two Kato slides (41.7 mg) prepared from each of two stool samples collected in consecutive days. Treatment—whether myrrh or praziquantel—was given twice with a 3-week interval. Myrrh was given, in the form of...
Mirazid capsules, in a dose of 2 capsules on an empty stomach for 3 consecutive days regardless of the age or weight of the treated person (as indicated by the manufacturer), whereas praziquantel was given in a dose of 40 mg/kg body weight after breakfast.

For cure assessment, two consecutive stool samples were collected from each individual 3 weeks after the first treatment and 4 weeks after the second treatment. In both groups, any individual who was still passing eggs 4 weeks after the second treatment received praziquantel in a dose of 40 mg/kg body weight, and final stool samples were collected 4 weeks later from these individuals to determine their infection status.

RESULTS

Of the 104 selected patients, 7 of the myrrh group and 14 of the praziquantel group who did not fully comply during follow-up were considered as lost and therefore eliminated from the results. However, the equivalent status of the two groups was maintained (Table 1).

**Myrrh (Mirazid).** Stool examination 3 weeks after the first myrrh treatment revealed that *S. mansoni* ova could not be detected in the stools of 74 of 45 individuals, indicating a cure rate of 15.6%. All 45 individuals—whether passing eggs or not—were given a second myrrh treatment, and the subsequent cure rate was 8.9%. However, from the seven persons cured after the first myrrh treatment, only four remained negative on a second examination, whereas the other three resumed passing *S. mansoni* ova in their stools. The pretreatment intensity of infection was not a factor determining the outcome of treatment. The reduction in the geometric mean egg count (GMEC) as compared with baseline among uncured patients was just 17.2% after the first Mirazid treatment and 28% after the second treatment (Table 2).

**Praziquantel.** A cure rate of 73.7% was observed after the first treatment and of 76.3% after the second treatment, with cure rate not being correlated with pretreatment GMEC. Individuals still passing *S. mansoni* ova after receiving treatment showed a reduction in their GMEC, as compared with baseline data, of 84% and 88.2% after the first and second treatments, respectively (Table 2).

The difference between cure rate of praziquantel and Mirazid was significant both after one and two treatments (after one treatment: $Z = 6.49, P < 0.05$; after second treatment: $Z = 8.33, P < 0.05$).

**Effect of the final praziquantel treatment.** Praziquantel was offered to all 43 individuals uncured after receiving two treatments (34 of the myrrh group and 9 of the praziquantel group). Examination of stool samples collected 4 weeks after this third treatment showed that 41 (95.3%) of them stopped passing eggs, and the uncured two cases showed 75.4% egg reduction (Table 2).

DISCUSSION

Myrrh (Mirazid) has been produced and marketed as an antischistosomal drug since 2001. Most of the published data documenting its antischistosomal efficacy, whether in experimental animals or in humans, consist of papers written by the discoverers of these properties, and no independent confirmation has appeared so far of these antischistosomal effects. Indeed, a multicenter investigation of the potential antischistosomal activity of different derivatives of the resin including the commercial preparation Mirazid was tested in experimental animals. The drug was found toxic for mice at high doses and produced modest or no worm reduction at lower doses. However, the drug is currently reported to be prescribed on a large scale by Egyptian private physicians, especially in rural areas (Barakat R and others, personal communication).

In the current study, the efficacy of myrrh in treating *S. mansoni* infections was tested, and as a control it was compared with praziquantel. Because the study was conducted during the schistosomiasis transmission season in Egypt—the summer months—two doses of myrrh and praziquantel,

<table>
<thead>
<tr>
<th>Number of individuals</th>
<th>Mirazid</th>
<th>Praziquantel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>15 ± 9.5</td>
<td>13.9 ± 7.8</td>
</tr>
<tr>
<td>Range</td>
<td>5–44</td>
<td>5–39</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mirazid</th>
<th>Praziquantel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric mean egg count</td>
<td>133.1</td>
<td>109.9</td>
</tr>
<tr>
<td>Range</td>
<td>36–1,560</td>
<td>36–1,524</td>
</tr>
<tr>
<td>Low (&lt;100 epg)</td>
<td>48.9%</td>
<td>57.9%</td>
</tr>
<tr>
<td>Moderate (100–400)</td>
<td>35.6%</td>
<td>26.3%</td>
</tr>
<tr>
<td>High (400+)</td>
<td>15.5%</td>
<td>15.8%</td>
</tr>
</tbody>
</table>

**TABLE 2**

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. treated</th>
<th>No.</th>
<th>Percent (%)</th>
<th>Baseline GMEC</th>
<th>No.</th>
<th>Percent (%)</th>
<th>Baseline GMEC</th>
<th>GMEC after treatment</th>
<th>Percent reduction in GMEC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirazid</td>
<td>45</td>
<td>7</td>
<td>15.6*</td>
<td>105.4</td>
<td>38</td>
<td>84.4</td>
<td>139</td>
<td>115.1</td>
<td>17.2</td>
</tr>
<tr>
<td>Praziquantel</td>
<td>38</td>
<td>28</td>
<td>73.7</td>
<td>117.5</td>
<td>10</td>
<td>26.3</td>
<td>91.4</td>
<td>14.6</td>
<td>84.0</td>
</tr>
<tr>
<td><strong>Second treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirazid</td>
<td>45</td>
<td>4</td>
<td>8.9†</td>
<td>141.3</td>
<td>41†</td>
<td>91.1</td>
<td>132.1</td>
<td>95.1</td>
<td>28.0</td>
</tr>
<tr>
<td>Praziquantel</td>
<td>38</td>
<td>29</td>
<td>76.3</td>
<td>115.3</td>
<td>9§</td>
<td>23.7</td>
<td>94</td>
<td>11.0</td>
<td>88.2</td>
</tr>
</tbody>
</table>
3 weeks apart, were offered to the randomized groups in an attempt to eliminate any immature worms that might have escaped the action of the first treatment. Cure was based on the absence of *S. mansoni* ova from the stools.

The cure rate with myrrh was very low, not only after one but also after two treatments. The effect in individuals who stopped passing *S. mansoni* ova could be attributed to the reversion rate recorded in several studies even in the absence of antischistosomal chemotherapy. Cure rate of Mirazid was significantly lower than that of praziquantel both after the first and the second treatments.

Administration of the second dose of Mirazid did not succeed in curing any of the cases who were not cured after the first treatment. Furthermore, 3 of the 7 cases apparently cured after the first treatment started to pass *S. mansoni* ova again, which might be attributed to reinfestation as the study was carried out during schistosomiasis transmission season. Egg reduction among uncured persons was also very low, being 17.2% and 28% after the first and second treatment, respectively. These results suggest that the antischistosomal properties of myrrh are at best negligible. The same negligible cure rate was also reported when myrrh was tested in mice.

The discrepancy between our data and those reported by Sheir and his group cannot be easily explained. However, they did not mention in detail their criteria for cure assessment as the number and frequency of collected stool and urine samples or the technique used for preparation of the samples. Furthermore, no data are available about egg counts before or after treatment, a parameter that is considered crucial for cure assessment.

With respect to praziquantel, the cure rates after the first and second treatments (73.7% and 76.3%, respectively) were slightly lower than those obtained in the same area of Egypt during a previous study (Barakat R and others, unpublished data), but they are still within the range reported for praziquantel. Reduction in GMEC among uncured individuals (84% and 88.2% after the first and the second praziquantel treatment, respectively) was as high as in other studies.

The conclusion that Mirazid is not in fact antischistosomal was confirmed by the fact that when 34 individuals uncured after two Mirazid treatments were offered praziquantel in the standard dose, 32 of them stopped passing *S. mansoni* eggs when tested 4 weeks post-treatment, and the remaining 2 showed a 75.4% egg reduction.

The results of the current study raise serious doubts about the antischistosomal properties of Mirazid and about the correctness of its use by schistosomiasis patients. It is mandatory to reassess its efficacy and efficiency through further independent multicenter investigations under standard conditions.

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Authors’ addresses: Rashida Barakat and Hala Elmorshedy, High Institute of Public Health, Department of Tropical Health, Alexandria, Egypt. E-mail: barakat@dataxprs.com; elmorshedy@dataxprs.com. Alan Fenwick, SCI, Imperial College, Department of Infectious Disease Epidemiology, St. Mary’s Campus, Norfolk Place, London, W2 1PG, United Kingdom. E-mail: a.fenwick@ic.ac.uk.

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