Short-course Chemotherapy for Cervical Lymph Node Tuberculosis


Sixty-seven patients with tuberculous cervical lymphadenitis were randomized into two treatment groups: Group (A) (33 patients) received isoniazid and rifampicin for 12 months supplemented with ethambutol (or streptomycin) in the first 2 months (S2 or E2H12R12). Group (B) (34 patients) received isoniazid and rifampicin for 9 months plus pyrazinamide and ethambutol (or streptomycin) in the initial intensive phase (S2 or E2Z2H9R9). At 36 month follow-up, 62 patients (92%) remained cured, 30 in Group A and 32 in Group B. The main reason for withdrawal from the study was drug toxicity, two in Group A and one in Group B. The relapse rate after the end of chemotherapy was 3%, one in each group. Nausea, vomiting and epigastric pain were noted but did not alter the final outcome of chemotherapy. It is concluded that a 9-month drug regimen (S2 or E2Z2H9R9) is as effective as a 12-month regimen (S2 or E2H12R12) in treatment of tuberculous cervical lymphadenitis.

The present status of chemotherapy for tuberculosis has been recently reviewed by Grosset. Effective and relatively safe regimens for 6-9 months are now widely used instead of the standard 18-24 months regimens for the treatment of pulmonary tuberculosis. The treatment of lymph node tuberculosis, however, has not been systematically studied and different treatment modalities are still practised including surgical excision, chemotherapy of variable duration or a combination of both. Satisfactory results have been reported with the standard 18 months regimen for the treatment of lymph node tuberculosis.

The 9 months drug regimen of isoniazid and rifampicin with ethambutol in the initial 2 months was used by the British Thoracic Society—concluding
a satisfactory result at the end of a 5-year follow-up period. However, such a successful outcome was not duplicated by Malik et al. who reported a 32% relapse rate using a similar 9-month regimen. Such short courses of chemotherapy are not widely reported. The present study was started shortly after the initial report of the British Thoracic Society and to our knowledge is the first from Saudi Arabia. The aims of this trial were to study the chemotherapy of tuberculous lymphadenopathy in a prospective manner comparing two regimens of rifampicin and isoniazid administered for 9 or 12 months respectively.

**Patients and Methods**

Patients with cervical lymphadenitis attending either the Chest Hospital or King Khalid University Hospital in Riyadh between 1985 and 1986 were enrolled into the study. In addition to physical and ophthalmic examinations, investigations including complete blood count, liver and renal function tests, chest radiograph and tuberculin test were performed. Aspiration or biopsy of lymph nodes were carried out on all patients, and only patients with microbiologically or histologically proven tuberculous lymphadenitis were included in the study. Patients with active pulmonary tuberculosis and pregnant women were excluded. Drug sensitivity tests were performed on culture-positive specimens.

Patients were randomly allocated into two treatment groups. Group A received rifampicin (10 mg/kg) and isoniazid (5–10 mg/kg) for 12 months supplemented with ethambutol (20 mg/kg) or streptomycin (1 g) in the initial 2 months. Group B received rifampicin (10 mg/kg) and isoniazid (5–10 mg/kg) for 9 months with pyrazinamide (30 mg/kg) and ethambutol (20 mg/kg) or streptomycin (1 g) in the initial 2 months. All drugs were administered on an outpatient basis. Patients were assessed every month for the first 3 months and every third month thereafter, over a total of 33 months for the behaviour of lymph nodes and drug toxicity. Enlargement of lymph nodes with positive culture for mycobacterial tuberculosis after finishing treatment was considered a relapse. Fisher’s exact probability test was applied to assess the statistical significance of the differences in responses between the two groups of patients.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics</th>
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<tbody>
<tr>
<td></td>
<td>Group A</td>
</tr>
<tr>
<td>No. of patients</td>
<td>33</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>13–47</td>
</tr>
<tr>
<td>Male:Female ratio</td>
<td>1:2:1</td>
</tr>
<tr>
<td>Unilateral lymphadenitis</td>
<td>27</td>
</tr>
<tr>
<td>Bilateral lymphadenitis</td>
<td>6</td>
</tr>
<tr>
<td>Tuberculin positivity</td>
<td>26</td>
</tr>
<tr>
<td>Paradoxical lymph node enlargement</td>
<td>1</td>
</tr>
</tbody>
</table>

**Results**

The general characteristics of 67 patients, who were eligible for the study, are presented in Table 1; 33 and 34 patients received the 12-month and the 9-month drug regimens respectively. There were no statistically significant differences in the patient characteristics of the two groups (p > 0.3). The diagnosis was established historically for all the patients. Mycobacteria were isolated from 38 patients (56.7%). In *vitro* drug susceptibility testing showed resistance in three (8%) isolates, one to isoniazid, one to rifampicin and one to both.

Three (4.5%) patients developed drug-related jaundice during chemotherapy and they were excluded during the study. They received different treatment regimens and thus were excluded from the final analysis. Paradoxical node enlargement occurred within the first 6 months chemotherapy in four (6%) patients, one in Group A and three in Group B. Patients were followed up for a minimum of 36 months. During this period two (3%) patients had relapses and were successfully retreated. At the end of the follow-up period, 62 (92%) patients were considered cured. There was no difference between the two drug regimens in terms of efficacy (p < 0.4).

**Discussion**

The main goal in the treatment of tuberculosis is to adopt the shortest effective course with minimum drug toxicity, lowest relapse rate and high patient compliance. Unlike pulmonary tuberculosis, progress in chemotherapy seems to be slow in extrapulmonary tuberculosis, because of difficulties in diagnosis or in the assessment of response to therapy. This is reflected in previous reports in which only 30–50% of the patients with lymph node tuberculosis could be diagnosed bacteriologically. Almost similar findings were found in the present study; tubercle bacilli were isolated from 56.7% of our patients.

There was no difference between the 9-month and the 12-month chemotherapy employed in the present study in terms of safety and efficacy. Hepatotoxicity was the major drug-related side-effect encountered in our series, and occurred in three patients (4.5%), one in the 9-month and two in the 12-month regimen. The frequency of adverse hepatic reactions reported by other centres ranged between 1% and 13%. A favourable outcome at
36 months was achieved in 91% of patients in Group A and 94% in Group B. The British Thoracic Society Research Committee reported comparable results in a 3-year follow-up period of 56 patients with lymph node tuberculosis treated for 9 months with ethambutol in the first 2 months. This study also showed that lymph nodes can enlarge during and after treatment without implying a relapse. In contrast, Malik and co-investigators encountered a relapse rate of 32% with 9-months regimen for the treatment of lymph node tuberculosis. However, infection with atypical mycobacteria or non-compliance might have contributed to their poor response.

The results of the present study indicate that short-course chemotherapy with isoniazid and rifampicin for 9 months with an initial four drugs regimen in the first 2 months is highly effective in the treatment of cervical lymph node tuberculosis. The alternative 12-month regimen tested was equally successful.

References