Treatment of Recurrent Urinary Tract Infections: Efficacy of an Orally Administered Biological Response Modifier

Ch. Frey*, W. Obolensky, H. Wyss

*Urologist, Basel, Switzerland
Key Words. Urinary tract infections · Biological response modifier · Bacterial extract · OM-8930 (Uro-Vaxom)

Abstract. 64 out-patients suffering from recurrent UTI were treated under double-blind conditions with one capsule daily of either the biological response modifier OM-8930 or the placebo for 3 months, followed by a 3-month observation period. Dysuria, bacteriuria, leucocyturia and antibiotic or chemotherapeutic consumption showed a significant reduction under OM-8930 in comparison with the placebo. As to the tolerance, a single case of allergic exanthema on the neck was observed in the OM-8930 group. Both the curative efficacy in the acute crisis and the consolidative efficacy in preventing further recurrences showed a highly significant superior effect of OM-8930 with respect to the placebo.

Introduction

One of the major problems associated with urinary tract infections (UTI) is their risk of becoming recurrent or chronic. Long-term low-dose antibiotics may reduce the recurrence rate of urinary infections, but they rapidly develop after therapy cessation [Fries, 1983]. Another alternative consists in stimulating the body’s own defence mechanisms by the administration of biological response modifiers. One of those is OM-8930 (gelatin capsules containing 6 mg of immunostimulating fractions extracted from Escherichia coli; Uro-Vaxom®, OM Laboratories, Geneva, Switzerland), an orally administered extract from E. coli. Its actions on the immune defence mechanisms involve mainly the stimulation of macrophages, T- and B-lymphocytes and secretory immunoglobulins. Preliminary unpublished open clinical trials have shown the therapeutic efficacy of OM–8930 in UTI, reducing bacteriuria, antibiotic consumption, frequency, duration and severity of recurrences.

The aim of the present study was to reassess these results under double-blind conditions.

Patients and Methods

After giving informed consent, 64 out-patients, mostly women, aged 22–84, with recurrent lower UTI (at least 2 symptomatic episodes per year) were enrolled in this 6-month placebo-controlled double-blind multicentre study of OM–8930 at the time of an acute symptomatic recurrence (at least 10⁴ germs/ml, mid-stream urine sample). Upon reception of the bacteriological results, the patients were given daily for 3 months one capsule of either OM-8930 or the placebo, the following 3 months serving as a supplementary observation period. For the treatment of the initial crisis, antibiotics or chemotherapeutics were administered together with the test product and, when necessary, for later recurrences. Examinations for bacteruria (Urotube®, Roche), dysuria and leucocyturia were performed at study outset, 1 week after the end of the initial treatment with antibiotics or chemotherapeutics, then 3 and 6 months after the study outset, and at any symptomatic recurrence.

Side-effects as well as effectiveness in curing the acute crisis and in preventing further recurrences were assessed by the treating physician.

1 We wish to thank Wirtschaftsmathematik AG, Zurich, for the statistical analysis.
Biological Response Modifier (OM-8930) in Recurrent UTI

Table I. Evolution of urinary parameters and symptoms

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study outset</th>
<th>Week 3–4a</th>
<th>Month 3</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OM-8930</td>
<td>OM-8930</td>
<td>OM-8930</td>
<td>OM-8930</td>
</tr>
<tr>
<td>≥ 10^4 total germs/ml</td>
<td>n1/n2</td>
<td>31/31</td>
<td>8/32</td>
<td>4/25</td>
</tr>
<tr>
<td>%</td>
<td>100</td>
<td>8/30</td>
<td>16</td>
<td>5/27</td>
</tr>
<tr>
<td>p (Wilcoxon)b</td>
<td>n.s.</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>≥ 5 leucocytes/field</td>
<td>n1/n2</td>
<td>29/32</td>
<td>10/28</td>
<td>4/25</td>
</tr>
<tr>
<td>%</td>
<td>91</td>
<td>10/31</td>
<td>11/29</td>
<td>3/26</td>
</tr>
<tr>
<td>p (Wilcoxon)c</td>
<td>n.s.</td>
<td>0.05 &lt; p &lt; 0.10</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Dysuria</td>
<td>n1/n2</td>
<td>23/28</td>
<td>4/26</td>
<td>0/21</td>
</tr>
<tr>
<td>%</td>
<td>82</td>
<td>4/28</td>
<td>15</td>
<td>0/21</td>
</tr>
<tr>
<td>p (χ²)</td>
<td>n.s.</td>
<td>0.05 &lt; p &lt; 0.10</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Results expressed as the number of positive findings (n1) with respect to the number of observations (n2) and as percentages.

a One week after end of initial treatment with antibiotics or chemotherapeutics.
b 5-point scale: ≤ 10^3/10^4/10^5/10^6/10^7.
c 3-point scale: <5/5–10/> 10.

Results

After opening of the randomization code, it was revealed that 32 patients had been treated with OM-8930 (average age: 49.2 ± 15.8 years) and 32 with the placebo (54.2 ± 16.7 years). There were no significant differences between the two groups as regards age, sex, diagnoses, concomitant diseases, incidence of previous recurrences and baseline values of follow-up parameters. The urinary parameters improved more clearly under OM-8930 than under the placebo, with statistically significant differences between the two groups for dysuria and laboratory parameters (table I).

For the initial crisis, the average duration of concomitant treatment with antibiotics (broad-spectrum penicillins, tetracyclines) or with trimethoprim-sulfamethoxazole lasted for 13.2 ± 8.4 days in the group receiving OM-8930 and for 12.5 ± 6.4 days in the placebo group (n.s.; Behrens-Fisher test). Subsequent concomitant treatment for recurrent infections lasted for 2.7 ± 5.9 days in the OM-8930 group and for 12.1 ± 6.9 days in the placebo group (p < 0.01; Behrens-Fisher test). As to the tolerance, a single case of allergic exanthema on the neck was observed in the OM-8930 group. The curative efficacy of the test treatment was evaluated by the physicians as evident or possible in 88% (28/32) of the cases under OM-8930 and in 50% (16/32) of those under the placebo (p < 0.001; Wilcoxon’s rank sum test, 4-point scale). The difference between the overall long-term efficacy assessed at the conclusion of the 6-month study was even greater, being judged as evident or possible in 87% (26/30) of the cases under OM-8930 against 39% (12/31) of those under the placebo (p < 0.001; Wilcoxon’s rank sum test, 4-point scale).

Discussion

This report shows that OM-8930 significantly improved both the laboratory and clinical parameters associated with UTI. Such improvements are certainly the reflection of stimulated or restored cellular and humoral immune mechanisms, which are often impaired in infection-prone subjects [Janas et al., 1979; Riedasch et al., 1983].
Of further interest is the fact that this type of biological response modifier can be prescribed over longer periods, without giving rise to resistant bacterial strains or severe side-effects, which may appear under antibiotic treatment [Hannedouche et al., 1983]. Another noteworthy feature is the persistence of the effect for at least 3 months after therapy cessation.

The administration of OM-8930 started at the time of an acute crisis, together with antibiotics or chemotherapy, and continued after its healing, is therefore effective in treating recurrent UTI.

References


Received: July 2, 1986
Accepted: July 8, 1986

Ch. Frey, MD,
Urologist,
Picassoplatz 8,
CH-4052 Basel (Switzerland)