Methisoprinol* in the Treatment of Non-bacterial Pharyngitis

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(*The trade name of Methisoprinol is Isoprinosine, supplied by Newport Pharmaceuticals International)

SUMMARY

In thirty patients with non-bacterial pharyngitis, methisoprinol was administered orally on a dose of 1-3 grams three times daily. The treatment was started on the first day of illness in 15 patients, on the second day of illness in 7 patients, and on the third day of illness in 8 patients. There was a difference in the clinical response depending on how soon treatment was given. In the first group, the fever and upper respiratory symptoms were relieved after only 2 or 3 doses of methisoprinol and the drug was discontinued after a total dose of 2 grams to 3 grams. In the second and third group, results were less satisfactory and the patient still had fever, signs and symptoms of sore throat at the end of the course of treatment which was terminated at 72 hours. [Phil J Microbiol Infect Dis 1972; 1(1):36-39]

Key Words: methisoprinol, pharyngitis, viral infection, upper respiratory infections

INTRODUCTION

The treatment of non-bacterial or viral sore throat has been essentially symptomatic or non-specific in the absence of specific antiviral agents effective against common causes of pharyngitis or tonsillitis such as the adenovirus, coxsackie, myxovirus and others. Methisoprinol, the p-acetamidobenzoate of dimethylaminoisopropanol inosine, is a new drug which has been reported to be effective against a wide spectrum of viral diseases such as infectious hepatitis (Type A, HAA or Australian Antigen Negative), Herpes zoster, Herpes simplex, measles, varicella, and acute bronchitis.1-8

The present study attempts to assess the efficacy of methisoprinol in pharyngitis or tonsillitis of nonbacterial origin, presumably viral. The study evaluates the drug under conditions of clinical practice without benefit of sophisticated and specific viral laboratory test. The principal criteria for inclusion of subjects in the study are: normal bacterial flora in throat cultures, absence of a rise in anti-streptolysin o titers (ASO) in the serum and normal or low leukocyte count.

MATERIALS AND METHODS

A total of 50 patients with clinical signs and symptoms of tonsillitis or pharyngitis were immediately started on methisoprinol after routine laboratory screening tests: throat culture, leukocyte count and ASO test. A second ASO determination was done 10 days later to exclude patients who showed a rise in titer, which would indicate a streptococcal etiology. Patients with positive throat cultures and elevated leukocyte counts were also excluded in the final analysis of the results of methisoprinol treatment. Methisoprinol was supplied as 500 mg. tablets and was administered at a dose of 2 tablets 3 times daily.

In the final study group of 30 subjects, the start of methisoprinol treatment was on the first day of illness in 15 patients, on the 2nd day of illness in 7 patients and on the 3rd day of illness in 8 patients. Patients were given a supply of the drug sufficient for one day's use and were examined everyday for 3 successive days. Most of the subjects were relatives of physicians and medical students to insure good cooperation in the follow-up studies. Side reactions, if any, were recorded.
RESULTS

Table 1 shows the laboratory data in 50 patients with tonsillitis or pharyngitis who were screened for possible inclusion in this study. Thirty patients who did not show evidence of a specific bacterial etiology were the subjects in the final evaluation methisoprinol.

Table 1. Laboratory Data of 50 Patients with Acute Pharyngitis

<table>
<thead>
<tr>
<th>Number</th>
<th>Bacterial Throat Cultures</th>
<th>ASO*</th>
</tr>
</thead>
<tbody>
<tr>
<td>30**</td>
<td>Normal flora</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Group A Streptococcus</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Group D Streptococcus</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Staphylococcus aureus</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Group C Streptococcus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>WBC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8,000 or less</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10,000</td>
</tr>
</tbody>
</table>

*Anti-streptolysin O titers 10 day interval between tests
**These 30 patients were the subjects of methisoprinol trials.

Table 2 shows the results of methisoprinol treatment in 30 patients with non-bacterial sore throat. In the group where treatment was started within the first day of illness, the patients all became afebrile and the upper respiratory symptoms were relieved after 2 or 3 doses of methisoprinol and the objective signs such as pharyngeal congestion, tonsillar enlargement and cervical lymph node enlargement generally subsided with 48 hours. Therapy was stopped as soon as a clear clinical response was observed so that the majority of these patients treated early in the course of their illness were considered cured after a total dose of 2. to 3 grams. In 7 patients where treatment was started on the second day of illness, 2 patients improved after 48 hours. There were 5 patients who were still acutely ill on the third day of treatment and these were considered treatment failures. There were 8 patients who, were started on methisoprinol on the third day of illness. Signs and symptoms of sore throat persisted even after 72 hours of treatment and all subjects in this group were therefore considered non-responsive.

Table 2. Results of Methisoprinol in 30 Patients with Non-bacterial Pharyngitis*

<table>
<thead>
<tr>
<th>Day of Illness</th>
<th>Treatment started</th>
<th>Results</th>
<th>Total Each Group</th>
<th>Response %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>Remission after 2-3 doses in 15 patients</td>
<td>15</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Partial response in 2 patients</td>
<td>7</td>
<td>28.5</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>No response</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

*Duration of treatment 1 to 3 days, 1 gram Methisoprinol, 3 times daily.

No side reactions were noted in the 30 patients evaluated in this study.

COMMENTS

At the moment, the precise mechanism of action of methisoprinol against viruses is not known. Viruses are essentially composed of a central nucleic acid nucleus of DNA or RNA surrounded by an envelope of proteins which determines its geometric form or appearance as seen under the electron microscope. Viruses are viable only inside living cells and they reproduce by utilizing the host cell's proteins and nucleic acid to synthesize new viral proteins and nucleic acids.

There are reasons to believe that methisoprinol acts by interfering with the virus takeover of host cell function, thereby preserving its polyribosomes, and prevents the synthesis of new viral material. If this is correct, it seems logical to expect that methisoprinol would be most
efficacious when administered in the early stages of viral infection before cellular damage and
viral reproduction has progressed to a significant degree.

In the present study of 30 patients with acute non-bacterial pharyngitis or tonsillitis, methisoprinol produced a prompt clinical remission in all cases where treatment was started
within the first day of illness. The results were considerably less satisfactory in patients who
started treatment on the second or third day of illness, in this series, the course of methisoprinol
administration was limited to 72 hours since any clinical improvement beyond this period in this
type of disease could just be the natural self-limited course seen in upper respiratory viral
infections. Under the conditions of the present study, only a prompt and dramatic response to
methisoprinol can be reasonably credited to the drug, as observed in 15 patients in the group
treated early.

For more conclusive investigation, a large series comparing methisoprinol with a placebo
or aspirin in a double blind study with laboratory confirmation of the specific viral etiology
would be ideal.

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