Treatment of Herpes Simplex by Zinc Sulphate

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ABSTRACT
Background: Herpes simplex virus type 1 causes recurrent herpes labialis, a common disease afflicting up to 40% of adults worldwide. A randomized, double-blind trial was conducted to compare the effectiveness & the patient tolerance of topically applied 0.5% zinc sulphate suspension with those of a placebo in the treatment of herpes simplex lesion.

Patients & Methods: Sixty patients were enrolled in this study. The effectiveness & symptomatic relief of pain were recorded and Fisher exact test were used.

Results: The zinc sulphate group showed significantly complete healing (p=0.001) than the placebo group & pain free during the follow-up period. The zinc sulphate group showed significantly better than the placebo group during the follow-up period. The safety that has been recorded of the drug were satisfactory, there is no pain with zinc sulphate group, no side effects.

Conclusion: Topically applied 0.5% zinc sulphate suspension is an effective drug for the treatment of herpes simplex lesion in a short period with pain less.

Keywords: Zinc sulphate, herpes simplex. (J Coll Dentistry 2005; 17(1): 54-6)

INTRODUCTION
Herpes simplex is a secondary or latent infection caused by the Herpes simplex virus type I or type II. Most type I infections involve the orofacial regions & most type II infections involve the genitals. Recurrent episodes of oral herpes simplex activation can affect any age group. Episodes may be triggered in different individuals by a variety of exogenous or endogenous factors such as physical injury, systemic disease, or emotional stress. Each episode usually begins with prodromal tingling or discomfort of several hours duration that is localized to the site of eventual lesion formation.(1)

Multiple clear, fluid-filled vesicles less than 3mm in diameter form in a cluster located most often on the lip vermilion, perioral skin, gingiva, or palatal mucous. The vesicles are transient, usually lasting no more than a few hours before rupturing to form multiple ulcers that frequently coalesce. Healing is usually complete within 2 weeks Implication for clinical management of herpes simplex virus recurrence during radiotherapy.(2) A study characterized a mutagenic peptide of HSV-1, coded from the minimum transforming region & have shown it to be expressed early in infection.

They reported the amino-acid sequence of the mutagenic peptide to be very basic, containing glycine-arginine repeats, & demonstrated that it had the ability to bind to DNA. (3)

Das et al suggested that interaction with cofactors would be necessary for the peptide to contribute to the development of oral cancer.(4)

The usefulness of Acyclovir for treating & suppressing HSV infection, but emphasizes the unanswered questions of long-term safety & emergence of drug resistance.(5) Other studies with lysine monohydrochloride(6), sodium hypochloride(7) were used in the treatment of herpes simplex virus infections. Also ethylether was used as topical application for treatment of recurrent herpes simplex.(8)

Zinc sulphate (ZnSO₄.7H₂O) is white crystalline powder each g of zinc sulphate represents 3.5 mmol of zinc. Zinc sulphate 220 mg is approximately equivalent to 50 mg of zinc. Its solubility: 1 in 0.6 of water & 1 in 2.5 of glycerol.

Zinc sulphate which is the form of zinc often used for oral administration causes adverse gastro-intestinal effects. It has been given by mouth in doses of up to 220mg three times daily in the treatment of conditions associated with zinc deficiency such as acrodermatitis enteropathica. Externally, Zinc sulphate is used as an astringent in lotions & eye drops.(9)

The objective of the present trial was to compare the effectiveness of & patient tolerance & measure the pain and time of healing of herpes simplex of topically applied 0.5% zinc sulphate suspension with those of a placebo in the treatment of herpes simplex lesions.
PATIENTS & METHOD

This trial was conducted in a double-blind technique randomized, placebo-controlled. 60 patients were participating in this study, 45 of them were female & the other 15 were males. The age varied between 10 to 59 yrs., 35 patients treated with zinc sulphate & 25 patients used placebo.

Patients were randomly assigned to either zinc sulphate or placebo. Pregnant & nursing mothers were excluded. Each patient was followed up regularly & daily during the period of application of medication to the lesion (4days). Zinc sulphate 0.5 % suspension (suspension) applied topically three times daily, was used in this study compared with placebo.

RESULTS

In this trial there were 60 patients enrolled (35 patients treated with zinc sulphate 0.5% suspension, 25 given the placebo). A high percentage was shown with age 20-29 in female & male, table (1, 2).

The duration of daily treatment of herpes simplex in the present study was decided to be 4 days, complete healing had been occur from 2-4 days of the treatment, and symptomatic relief of pain after the first dose of applied 0.5% zinc sulphate suspension while placebo did not show such effect, fig. (1). The P value for zinc sulphate versus placebo = 0.001, P value calculated by Fisher’s test of exact probability.

DISCUSSION

Management for most episodes of recurrent herpes simplex is supportive. Some patients have found topical application of acyclovir (antiviral agent) to be of value in reducing the symptoms & over all healing time. It is the drug of choice for herpes simplex virus infection.\(^{10, 11}\) Freeman et al. in 1990 postulate that in its current formulations acyclovir can not be delivered in sufficient tissue concentration to produce a clinically significant result.\(^{12}\)

The highest incidence was seen with cases treated by zinc sulphate 0.5% suspension, by comparing the effect of zinc sulphate on healing process with the placebo by fishers test of exact probability p=0.001. zinc sulphate is more effective in the treatment of herpes simplex. The significant enhancement of healing was seen with zinc sulphate 0.5%. The time required for treatment of patients with zinc sulphate0.5% suspension varies between 2-4 days while placebo 7 to 14 days.

Zinc is an essential element of nutrition & traces are present in a wide range of food. It is a constituent of many enzyme systems & is present in all tissues. Features of zinc deficiency include growth retardation & defects of rapidly dividing tissue such as the skin, the immune system & the intestinal mucous.

Delay in healing of wounds & ulcers could be caused delay in migration of the granulating epithelium, this could be due to zinc deficiency, reduce the time for complete epithelialization. So zinc sulphate participate in healing process by re-epithelialization of tissue & repair leading to complete healing of herpes simplex lesion with in short period of time .

Enveloped viruses herpes simplex attach to the host cell membrane by means of membrane surface glycoproteins present on the viral envelop .After they attach to the host cell, enveloped viruses penetrate the cell by fusion of the viral envelop with the cell membrane. From this point replication methods are rather similar for both enveloped & non enveloped viruses.\(^{13}\) Zinc sulphate may prevent attachment of the virus by interfering with membrane surface glycoproteins involved with recognition & attachment to specific host cells. Zinc sulphate may prevent penetration of the viron in to the cell because of viral envelope disruption, which prevents fusion with the host cell membrane.

No allergic skin reaction or toxic effects have been reported with Zinc sulphate suspension usage & this probably encouraged people to use it as a safe topical agent. So the author recommended zinc sulphate (0.5%) suspension in the treatment of herpes simplex because of its efficacy & safety.

Table (1) Distribution of patients according to the age groups.

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Female No.</th>
<th>Female %</th>
<th>Male No.</th>
<th>Male %</th>
<th>Total No.</th>
<th>Total %</th>
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</thead>
<tbody>
<tr>
<td>10-19</td>
<td>7</td>
<td>15.5</td>
<td>1</td>
<td>6.6</td>
<td>8</td>
<td>13.3</td>
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<td>20-29</td>
<td>21</td>
<td>46.6</td>
<td>10</td>
<td>66.6</td>
<td>31</td>
<td>51.6</td>
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<td>30-39</td>
<td>10</td>
<td>22.2</td>
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<td>13.3</td>
<td>12</td>
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<td>40-49</td>
<td>5</td>
<td>11.1</td>
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<td>13.3</td>
<td>7</td>
<td>11.6</td>
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<td>45</td>
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<td>60</td>
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Table (2) Characteristics of treated groups.

<table>
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<tr>
<th>Patients characteristics</th>
<th>Zinc Sulphate N=15</th>
<th>Placebo N=25</th>
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<tr>
<td>Age (years) X±SD</td>
<td>7±3.83</td>
<td>5±2.10</td>
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<tr>
<td>Gender</td>
<td>28/7</td>
<td>17/8</td>
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</table>

REFERENCES

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7- Hunter DT. Sodium hydrochloride was used in the treatment of herpes simplex virus infections. Cutis 1983; 31: 328-332.