ABSTRACT:
BACKGROUND:
Warts are commonly acquired viral tumors, caused by Human Papilloma Virus (HPV). This virus can infect and cause disease at any site in the stratified squamous epithelium either keratinizing or non-keratinizing. A plantar wart (also called verruca plantaris) is a lesion that appears on the plantar surface of foot as a small, shining, sago-grain papule which soon assumes the typical appearance of a sharply-defined rounded lesion with a rough keratotic surface, surrounded by a smooth collar of thickened horn.

OBJECTIVE:
To compare the efficacy and safety of oral zinc sulphate versus topical application of salicylic (16.7%) & lactic acid (16.7%) combination, in the treatment of plantar warts.

STUDY DESIGN:
Comparative interventional study.

SETTING AND DURATION OF STUDY:
Department of Dermatology Unit-I, King Edward Medical University, Mayo Hospital Lahore, from 15 February, 2009 till 14 February, 2010.

METHODOLOGY:
After informed consent, one hundred patients of plantar warts were selected from the outpatient Department of Dermatology, Mayo Hospital, Lahore. The patients were divided into two equal groups; in group A, 50 patients were given oral zinc sulphate (10 mg/kg/day) in two or three divided doses and in group B, 50 patients were advised to apply a combination of salicylic (16.7%) & lactic acid (16.7%) once at night daily. In group A, using oral zinc sulphate, the treatment was given for two months and follow up continued for next 4 months. In group B, the topical preparation was also continued for 2 months or till the complete removal of wart (if before two months) and follow up was extended up to 4 months after treatment.

RESULTS:
The mean age of patients in group A was 26.2 ± 8.1 years and in group B 26.3 ± 7.3 years. The mean number of warts in group A was 7.9 ± 3.5 and in group B 5.7 ± 2.6. The mean duration of disease in group A was 6.9 ± 4.1 months and in group B 6.0 ± 3.9 months. On follow up at 2nd month, in group A, 41 (82%) patients showed an excellent efficacy while 9 (18%) patients observed poor efficacy. In group B, 31 (62%) cases experienced an excellent response, 2 (4%) had a good efficacy and 17 (34%) patients showed a poor efficacy. At 4th month of follow-up, no recurrence of warts was seen in both groups in complete responders. On follow up of the non
responders no further clearance of warts was observed.

CONCLUSIONS:
It was concluded from this study that oral zinc sulphate is significantly more effective (p-value <0.05) than topical application of salicylic (16.7%) and lactic acid (16.7%) combination in the treatment of plantar warts.

KEY WORDS:
Plantar warts, oral zinc sulphate, salicylic acid, lactic acid

INTRODUCTION:
Warts are commonly acquired viral tumors, caused by Human Papilloma Virus (HPV).
This virus can infect and cause disease at any site in the stratified squamous epithelium either keratinizing or non-keratinizing.
A plantar wart (also called verruca plantaris) is a lesion that appears on the plantar surface of foot as a small, shining, sago-grain papule which soon assumes the typical appearance of a sharply-defined rounded lesion with a rough keratotic surface surrounded by a smooth collar of thickened horn.
Warts occur at any age, but are common among children.
It is estimated that 7-10% of the United States (US) population have plantar warts.
Though the exact statistical data regarding the incidence of warts in Pakistan is not available, it comprises a significant patient turnover in the outpatient Department of Dermatology, Mayo Hospital, Lahore. The virus can survive many months without a host, making it highly contagious.
Plantar warts are caused by infection with human papilloma virus types 1, 2, 4 and 63.
The virus attacks the skin through direct contact, entering via tiny cuts and abrasions in the stratum corneum.
The common sites of plantar warts are beneath pressure points (the heel or the metatarsal heads).
The duration of plantar warts is very variable. Spontaneous regression occurs sooner in children.
In adults, warts may persist for years.
Treatment modalities, that have been found to be effective, include keratolysis, which involves the peeling away of dead surface skin cells with trichloracetic acid or salicylic acid.
Cryosurgery with liquid nitrogen, electro-surgical desiccation and excision has also been employed.
Topical application of diluted glutaraldehyde (a virucidal chemical) is an older effective wart treatment.
Intralesional injection of antigens (mumps, candida or trichophytin) is a new treatment of warts.
With the help of this treatment, distant, non-injected warts may also disappear. More modern chemotherapeutic agents (e.g. 5-fluorouracil) are also effective topically or intralesionally.
Systemic (isotretinoin) or topical retinoids may be effective.
Lasers may be effective, especially the 585nm pulsed dye laser.
The topical application of salicyclic and lactic acid combination in a collodion is a common form of treatment with once daily application. It is an effective treatment option with few side effects.
It is used as an initial therapy for treatment of plantar warts with minimum cost and minimal pain.
Salicylic acid causes keratolysis thus helps in removing the thickened epidermis.
Oral zinc sulphate is also an effective therapy in the treatment of warts.
Zinc has an important effect on the immune system and it has been used as an immunomodulator to treat a variety of skin disorders.
The present study was planned in the Department of Dermatology Unit-I, KEMU/ Mayo Hospital, Lahore, to assess the efficacy and safety of oral zinc sulphate and combination of topical application of salicyclic and lactic acid in the treatment of plantar warts, because no study of this kind has been done before in our community.

METHODOLOGY:
The study protocol was approved by the hospital ethical committee. This was an open clinical trial (interventional quasi experimental study) carried out at the Department of Dermatology Unit-I, King Edward Medical University/ Mayo Hospital, Lahore, from 15 February, 2009 till 14 February, 2010. One hundred patients of either sex, aged 10 to 60 years with plantar warts were enrolled after a written informed consent. Patients were excluded who had already been treated for warts or with diabetes mellitus & Human immunodeficiency virus (HIV) and women who were pregnant or lactating. History was taken and clinical examination performed on the first visit. A proforma was used to record the history, physical examination and the results of screening tests which were HIV, Hepatitis B virus and Hepatitis C virus.
The patients were divided into two groups; in group A, 50 patients were given oral zinc sulphate (10 mg/kg/day) and in group B, 50 patients were given topical application of salicylic acid 16.7% and lactic acid 16.7% in combination
once at night time. In group A, using oral zinc sulphate, the treatment was given for two months. In group B, the topical preparation was also continued for 2 months or till the complete removal of warts (if before two months). Patients were followed every month for next 4 months after the completion of treatment. At each visit, clinical examination was performed for decrease in size and number of warts. Patients were inquired about the side effects of treatment. The response to treatment was recorded as poor (less than 30% clearance), satisfactory (>30-60% clearance), good (>60-90% clearance) and excellent (>90% clearance or complete removal of warts).

Collected information was transferred to SPSS (statistical package for social sciences) version 11 computer software programme and was analyzed accordingly. Mean and standard deviation was calculated for quantitative variables like age, number of warts and duration of disease. Frequency and percentage was calculated for qualitative variables like sex, and efficacy of treatment. Chi Square test was applied to compare the efficacy of treatment in both groups. A p value of <0.05 was considered as significant.

RESULTS:

In group A that was treated with oral zinc sulphate, there were 14 (28%) male and 36 (72%) female patients while in group B, treated with salicylic acid 16.7% and lactic acid 16.7% (combination), there were 16 (32%) male & 34 (68%) female patients [Figure-1].

![Figure-1: Sex distribution of patients](image)

Mean age of the patients in group A was 26.2 ± 8.1 years and in group B, it was 26.3 ± 7.3 years. In group A, there were 16 (32%) patients in the age range of 10-20 years, 20 (40%) of 21-30 years and 14 (28%) patients between 31-40 years. In group B, there were 11 (22%) patients in the age range of 10-20 years, 24 (48%) of 21-30 years & 15 (30%) patients between 31-40 years.

Mean number of warts in group A was 7.9 ± 3.5 and in group B, there were 5.7 ± 2.6. In group A, 13 (26%) patients had 1-5 warts, 30 (60%) patients had 6-10 warts, 5 (10%) patients had 11-15 and 2 (4%) patients presented with 16-20 warts. In group B, there were 28 (56%) patients with 1-5 warts, 20 (40%) patients with 6-10 and 2 (4%) patients with 11-15 warts.

Mean duration of disease in group A was 6.9 ± 4.1 months and in group B, it was 6.0 ± 3.9 months. In group A, there were 35 (70%) patients with a disease duration of 1-6 months, 9 (18%) patients with 7-12 months duration, 2 (4%) patients with 13-18 months duration and 4 (8%) patients with a duration of 19-24 months. In group B, there were 36 (72%) patients with a duration of 1-6 months, 12 (24%) patients with 7-12 months duration and 2 (4%) patients with duration of 19-24 months.

Regarding the efficacy at 1st month, in group A, 10 (20%) patients showed a good efficacy while 40 (80%) patients had a poor efficacy. In group B, 15 (30%) patients had a good efficacy and 35 (70%) patients showed a poor efficacy [Table 1].

![Table 1: Distribution of patients by efficacy at 1st month of treatment](image)

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Group A (n=50)</th>
<th>Group B (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>Excellent</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Good</td>
<td>10</td>
<td>20.0</td>
</tr>
<tr>
<td>Poor</td>
<td>40</td>
<td>80.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

χ² = 0.4

df = 1

p = 0.6

KEY: N = Number of patients
At the end of 2nd month of treatment in group A, 41 (82%) patients had an excellent efficacy (>90% clearance or complete removal of warts) and 9 (18%) patients had a poor (<30% clearance) efficacy. In group B, 31 (62%) patients had an excellent efficacy (>90% clearance), 2 (4%) patients had a good efficacy (>60-90% clearance) and 17 (34%) patients had a poor efficacy (<30% clearance) with a p value of 0.003 [Table 2].

Table 2: Distribution of patients at 2nd month of treatment

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Group A (n=50)</th>
<th>Group B (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>Excellent</td>
<td>41</td>
<td>82.0</td>
</tr>
<tr>
<td>Good</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Poor</td>
<td>9</td>
<td>18.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

\[\chi^2 \approx 4.2\]
\[df = 1\]
\[p = 0.003\]

KEY: n=Number of patients

There was no recurrence of warts observed at 4th month of follow-up in both groups in complete responders. Further clearance of warts was not observed in patients with poor efficacy at 4th month of follow up in both groups. Side effects observed in group A: only 6 (12%) patients had nausea and 1 (1%) patient had vomiting. In group B, 3 (6%) patients had itching and 3 (6%) experienced bleeding from warts [Table 3].

Table 3: Distribution of patients by side effects

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group A (n=50)</th>
<th>Group B (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>Itching</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>6</td>
<td>12.0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Key: n=Number of patients

DISCUSSION:
Warts are a common dermatological problem caused by HPV.1,6 A plantar wart (also called verruca plantaris) is a lesion that appears on the plantar surface of foot as a discrete benign epithelial hyperplasia with varying degrees of surface hyperkeratosis, manifested as minute papules to large plaques.1,5 Lesions may become confluent, forming a mosaic.1,5 Common therapeutic modalities for viral warts include keratolytics, cryotherapy, topical immunotherapy with contact sensitizers, oral cimetidine, antimitotic agents, carbon dioxide laser, electrosurgery, photodynamic therapy, intralesional injection of antigens and topical immune response modifiers.7,8 The topical application of salicylic (16.7%) and lactic acid (16.7%) combination is a common form of treatment with once daily application.5

In HPV infection, antigen presentation occurs very slowly and infection does not induce inflammatory cytokines; therefore, therapeutic options aimed at modulating the immune system and facilitating the production of cytokines have also been proposed.9,10 Various international studies have shown the efficacy of oral zinc sulphate in the treatment of warts.11-16 Zinc, a micronutrient, is necessary for the normal functioning of cells. More importantly, this element modulates DNA- and RNA-related enzymes and is also involved in many immunologic processes.13,17

In our study, mean age of the patients in group A was 26.2 ± 8.1 years and in group B 26.3 ± 7.3 years while in a similar study done by Stefani et al,7 mean age of the patients in group A was 27.0 ± 21.8 years and in group B 22.1 ± 14.4 years, which is comparable with our study. Similarly in another study, the mean age of patients was 26 which is comparable with our results.11

The present study revealed a greater preponderance of female patients (In group A; 36 females and 14 males, in group B; 34 females & 16 males). In the study of Reza et al,12 the zinc sulphate treated group included 32 patients, 18 were females and 14 males. In the study of Sadighha et al,18 zinc sulphate-treated group had 13 patients, 8 were females and 5 males. These two studies revealed a female preponderance as it was seen in our study. The greater incidence of viral warts in females can be attributed to the fact
that females have low immunity because of poor nutritional status.19

In our study, the mean number of warts in group A was 7.9 ± 3.5 and in group B 5.7 ± 2.6. In the study of Stefani et al,7 the mean number of warts was 43.6, which is much greater than our study, because in our study the number of warts ranged from 1 to 20, while in the study of Stefani et al,7 the number of warts varied from 11 to 120, which makes the difference in mean number of warts. The low number of warts in our study may be due to the fact, that in our society, people do not use public swimming pools commonly, which is a source of spread of plantar warts.20

In the present study, the mean duration of disease in group A was 6.9 ± 4.1 months and in group B 6.0 ± 3.9 months. In the study of Stefani et al,7 the mean duration of disease in group A was 22.5 ± 17.5 months and in group B 21.8 ± 17.4 months, which is much greater from our study due to the fact that the duration range in our study was 1 to 24 months, while in the study of Stefani et al7 the duration range was from 4 to 60 months. In the study of Al-Gurairi et al,6 the mean duration of warts in zinc treated group was 24 months. The duration of warts in our study is much shorter in contrast to various international studies,11,12,18 which may be attributed to the fact that, in their studies, mostly the patients with recalcitrant viral warts, not responding to common treatment modalities, were enrolled while in the present study, previously treated cases were excluded.

In our study, follow up at 2nd month, in group A (zinc sulphate treated) 82% patients had an excellent efficacy that is comparable with the study of Stefani et al7 in which the efficacy of zinc sulphate was found to be 85.72%. The efficacy of zinc sulphate in the study conducted by Reza et al15 was 78% which is again comparable to our study. Similarly Al-Gurairi et al6 used 10 mg/kg/day of zinc sulphate (maximum 600 mg/day) to treat recalcitrant warts. Out of 40 patients, only 23 completed the study and 87% patients were cured from lesions within 2 months which is again comparable to our study. In the present study, in group B (salicylic 16.7% & lactic acid 16.7% combination), 62% patients had an excellent efficacy while 34% patients had poor efficacy. In the study of Dhar et al,21 the efficacy of salicylic and lactic acid combination in plantar warts was 70% which is not comparable with our study. This discrepancy may be due to different duration of treatment used in both studies.

Comparing the efficacy profile of two treatments, both were seen effective with complete resolution of warts, after two months of therapy but effects with zinc sulphate were better as compared to topical combination with a significant difference in p-value (<0.05). These results correlate well with other international studies.6,12,21

Safety profile of oral zinc sulphate revealed that nausea and vomiting were the side effects seen in few patients in accordance with other studies.6,7,11,12 The side effects noted with topical combination treatment were pain, bleeding and itching similar to those mentioned in other studies.21 However, all these adverse effects were of mild intensity and reversible in nature. Overall, both the oral zinc sulphate and topical application of salicylic & lactic acid combination were well-tolerated.

CONCLUSIONS:
The present study showed both treatment modalities to be effective, well-tolerated and safe for plantar warts. However, oral zinc sulphate, a new cost-effective therapeutic option, is significantly more effective than the combination of salicylic (16.7%) & lactic acid (16.7%) in the treatment of plantar warts which are very common in our society.

REFERENCES:


