

Comparing Treatment Response and Complications Between Podophyllin 0.5%/0.25% in Ethanol vs Podophyllin 25% in Tincture Benzoin for Penile Warts

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ABSTRACT

Aim: The aims of this study were to: 1) ascertain if podophyllin resin in 0.5% [PE(0.5%)] and 0.25% [PE(0.25%)] in ethanol (PE) self-applied sequentially for 3 days with 4 days break cycle is as effective as supervised podophyllin 25% in tincture benzoin (PB) applied in the clinic bi-weekly in treating penile warts and 2) ascertain if PE causes less skin irritation than PB.

Methods and Results: The clearance rate of penile warts was 36.4% (4/11) in PE (0.5%) treated group, 66.7% (4/6) in the PE (0.25%) treated group and 33.3% (6/18) for PB treated group after 1 week (ns). The wart clearance rate at 6 weeks for PE (0.5%) treated group, PE (0.25%) treated group and PB treated group were 81.8% (9/11), 100% (6/6) and 83.3% (15/17) respectively (ns). There were 47 individual warts on the penis of the 17 patients in the PE treated group and 58 individual warts on the penis of the 18 patients in the PB treated group. Based on the response of individual warts to the 2 treatment regimens, the clearance rate was 42.6% (20/47) for the PE treated group and 25% (15/56) for the PB treated group after 1 week treatment (ns). At 6 weeks follow-up, the clearance rate for the PE treated group and the PB treated group were 85.1% (40/47) and 73.2% (41/56) respectively (ns).

Skin irritation including superficial erosions, pain and itch were observed in 47% (8/17) in patients treated with PE compared to 38.9% (7/18) in patients treated with PB (ns) during the 6 weeks follow-up period.

The clearance rate of patients treated with PE (0.25%) was compared to those treated with PE (0.5%). Four out of six of PE (0.25%) treated patients had clearance of warts after 1 week and 100% clearance at the end of 6 weeks. None experienced any skin irritation.

Conclusion: This study demonstrates that 0.5% podophyllin (and possibly 0.25% podophyllin) in ethanol is effective in eradicating penile warts. It can be used by patients for self-treatment at home with greater convenience and is more cost effective than the conventional podophyllin 25% in tincture benzoin paint.

Keywords: genital warts, sexually transmitted disease (STD), condyloma accuminata

INTRODUCTION

Genital wart infection is a common viral sexually transmitted disease (STD) seen at the public STD clinic in Singapore. The multiplicity of treatment modalities available to treat genital warts bears testimony to the current lack of a satisfactory mode of treatment.

Podophyllin resin, which is derived from the dried rhizomes of *Podophyllum emodi* and *Podophyllum peltatum*, is an established method of treatment for genital warts. It is available as podophyllotoxin (the purified compound) in 0.5% ethanolic solution or as a crude resinous extract mixture in tincture benzoin (25% podophyllin paint)(PB). The main disadvantages with the use of PB are its inconvenience (patients need to travel to the clinic twice a week for the doctor/nurse to apply the paint) and its lesser efficacy compared with podophyllotoxin⁽¹⁻⁶⁾.

Podophyllotoxin (0.5% ethanolic solution) is available as a home treatment to the patient. It is applied twice a day for 3 consecutive days in a week with a break of 4 days before the next cycle of application. Its main disadvantage however, is its high cost compared to PB.

The aims of this study were to: 1) ascertain if podophyllin resin in 0.5%(PE 0.5%) and 0.25%(PE 0.25%) in ethanol (PE) self-applied sequentially for 3 days with 4 days break cycle is as effective as supervised PB applied in the clinic biweekly in treating penile warts and 2) ascertain if PE causes less skin irritation compared to PB.

If PE (which contains a lower concentration of podophyllin resin) proves to be as efficacious as PB, and caused less skin irritation, we may then have a preparation that patients can use at home which is also more cost effective than PT.

MATERIALS AND METHODS

The study population consists of all consecutive male patients presenting to our Department of STD Control (DSC) Clinic with penile warts. Patients above 16 years of age were recruited into the study after obtaining informed consent.

The following patients were excluded from the study:

1. Those with more than 5 warts present on the penis

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2. Those who had received treatment within the last 2 weeks
3. Those with keratinised penile warts
4. Those with HIV infection or immunocompromised

Patients who satisfied our inclusion criteria were randomly assigned to the 2 treatment regimens viz:

Group PB were patients whose penile warts were treated with podophyllin 25% solution in tincture benzoin (PB). PB was applied by the doctor/nurse at our STD Clinic twice weekly. The PB was washed off 4 hours later.

Group PE consisted of patients whose penile warts were treated with podophyllin 0.5% in ethanol and Group PE (0.25%). Patients were given the PE to be applied at home twice a day for 3 consecutive days and repeated one week later if the warts persisted. PE is prepared by mixing crude podophyllin resin (Hitchia, Hertfordshire, England) with ethanol (w/v) without filtration. The 0.5% and 0.02% solution is then used for treatment.

Both treatment groups were reviewed at weekly intervals up to 6 weeks.

On the first visit, demographic data were collected and the number of sites of warts were carefully described and recorded in a protocol. At each subsequent visit, the lesions were again described and symptoms and signs of local toxicity or other adverse effects were recorded.

The clearance rates of the penile warts between the two treatment groups and occurrence of local side effects were compared using chi-squared and Fisher's exact tests.

RESULTS

Forty-five patients were recruited into the study but only 35 could be utilised for statistical analysis because the remainder either did not return after the first clinic visit or missed the pre-arranged assessment dates.

The racial distribution of our patients included 37(82.2%) Chinese, 7(15.1%) Indians, and 1(2.7%) Others. There were no Malays among the study cohort. There were no significant differences between the treatment groups in terms of age and racial composition.

The age range of the study cohort was between 20 and 71 years but the majority were within the ages of 20 and 39,(93.3% in the PB group and 100% in the PE group).

Sixty-eight percent of the patients presented with warts that were less than 1 month in duration and this was similar for both treatment groups. Fifteen percent of the patients (for both treatment groups) had a past history of penile warts.

The common location of the genital warts were, corona(43.5%), glans(26.1%), followed by frenulum, prepuce, meatus and shaft in descending order of frequency for patients in the PE group. Patients treated in the PB group showed a similar

distribution except that the warts were more commonly found on the prepuce than the frenulum.

The clearance rate of penile warts was 36.4% (4/11) for PE (0.5%) treated group, 66.7% (4/6) in the PE (0.25%) treated group and 33.3% (6/18) for PB treated group after 1 week (ns). The wart clearance rate at 6 weeks for PE (0.5%) treated group, PE (0.25%) treated group and PB treated group were 81.8% (9/11), 100% (6/6) and 83.3% (15/17) respectively (ns).

There were 47 individual warts on the penis of the 17 patients in the PE treated group and 58 individual warts on the penis of the 18 patients in the PB treated group. Based on the response of individual warts to the 2 treatment regimens, the clearance rate was 42.6% (20/47) for the PE treated group and 25% (15/56) for the PB treated group after 1 week treatment (ns). At 6 weeks follow-up, the clearance rate for the PE treated group and the PB treated group were 85.1% (40/47) and 73.2% (41/56) respectively (ns).

Adverse effects

Skin irritation including superficial erosions, pain and itch were the main side effects reported by the patients in both treatment regimens. However, these were well tolerated by the patients. Skin irritation was observed in 47% (8/17) in patients treated with PE compared to 38.9% (7/18) in patients treated with PB (ns) during the 6 weeks follow-up period.

Six out of a total of 17 patients in the PE treated group received the 0.25% preparation while 11 received the preparation containing the 0.5% podophyllin in ethanol. The clearance rate of patients treated with PE (0.25%) was compared to those treated with PE (0.5%). Four out of 6 PE (0.25%) treated patients had clearance of warts after 1 week and 100% clearance at the end of 6 weeks. None experienced any skin irritation.

DISCUSSION

This study was done to compare the relative efficacy and safety of PE (0.5%) applied at home with PB showed that both are nearly equal in efficacy in eradicating penile warts observed in 47.1% and 33.3% of the recipients respectively after one week. After 6 weeks, the relative wart clearance rate for PE treated and PB treated groups were 88.2% and 83.3% respectively. This compares favourably with clearance rates reported by other workers in previous studies, which varies from 38%⁽²⁾, 55%⁽³⁾, 63%⁽¹⁾ to 71%⁽⁴⁾ using podophyllin paint for genital warts. Lim et al proposed that podophyllin 25% lotion (PB) can be given to patients for self-application without an increase in the incidence of side-effects⁽⁷⁾. However, our clinical experience indicated that PB can cause severe irritation. A lower concentration could reduce contact dermatitis.

In fact, the 6 patients who used a lower concentration of PE (0.25%) demonstrated similar clearance rate as PE (0.5%) but with no side effects, suggesting that the lower concentration of podophyllin in ethanol might be adequate.

Skin irritation including erosions, pain and itch appeared to be more prevalent in patients treated with PE (47%) compared to 39% in the PB treated group. The difference was not statistically significant. However these side effects were fairly well tolerated by the patients.

This study demonstrates that 0.5% podophyllin (and possibly 0.25% podophyllin) in ethanol is effective in eradicating penile warts. It can be used by patients for self-treatment at home with greater convenience and is more cost-effective than the conventional podophyllin 25% in tincture benzoin paint.

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