

# Treatment of anogenital warts

## Comparison of trichloroacetic acid and podophyllin versus podophyllin alone

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**SUMMARY** Seventy-three patients with anogenital warts were randomly allocated to a double-blind comparison of treatment with trichloroacetic acid (50%) and podophyllin (25%) versus podophyllin (25%) alone. There was no significant difference in the resolution of warts in the two treatment groups among patients followed for three months. Of patients free of warts at six weeks, treatment with trichloroacetic acid/podophyllin required significantly fewer applications (mean 2.9) compared with podophyllin alone (mean 4.0). Five (17%) patients in the former group reported side effects but none in the latter group.

### Introduction

Probably the most commonly used preparation for the treatment of genital warts is podophyllin, yet there are few data on its efficacy. In a recent study Simmons<sup>1</sup> showed that results with podophyllin were disappointing; only 22% of patients were clear of genital warts three months after initiation of treatment. Locally applied aqueous trichloroacetic acid in various strengths is also frequently used in the treatment of genital warts.<sup>2</sup> A double-blind comparative study was carried out to test the hypothesis that trichloroacetic acid and podophyllin together might be more effective than podophyllin alone.

### Patients and methods

All men with anogenital warts attending the department of genital medicine at St Bartholomew's Hospital, London, were considered for entry into the trial providing they had not had treatment for genital warts in the three months before their initial visit. Those who were willing to enter into the study, after giving informed consent, were offered an appointment at a special weekly warts clinic to encourage regular attendance. All patients were screened for other sexually transmitted diseases as described<sup>1</sup> and treated for any concurrent infection

as appropriate. During and after treatment patients were advised to have sexual intercourse only when protected with a condom. Where possible sexual partners were also examined and when necessary treated.

### ALLOCATION AND TREATMENT

Patients were allocated by means of a random numbers table to one of two treatment regimens: (a) podophyllin 25% in industrial methylated spirits and (b) trichloroacetic acid 50% and podophyllin 25% in industrial methylated spirits saturated with a dark brown inert dye (Hexacol chocolate brown dye supplied as a powder by Pointing Ltd). Both solutions were prepared by one pharmacy and dispensed in stock 10 ml bottles labelled A and B. The pharmacy alone held the code key and this was not revealed to us until the end of the trial. The trichloroacetic/podophyllin/dye solution was considered by the pharmacy to be stable with no cross reactions between the three components. Chocolate brown dye is a stock food dye which is permitted for human use.

Treatment was carried out by one doctor at weekly intervals. The solution was applied with an orange stick, and care was taken to ensure that the application was strictly limited to the wart and the surrounding skin was avoided. Each application was allowed to dry in air for five minutes out of sight of the doctor. For treatment of intrameatal warts patients were advised to micturate just before application of treatment and then not to pass urine for at least four hours. Patients with external warts

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were asked to wash off the solution four hours after the first visit, 12 hours after the second, and 24 hours after their third and subsequent visits. No treatment was prescribed for self-medication at home. If patients developed soreness at the site of treatment they were asked to wash with saline twice daily. Assessment of clearance of warts was clinical and made by the same doctor.

If warts persisted after six weeks, the treatment was changed to 100% trichloroacetic acid or cryocautery on a non-trial basis. Patients were followed for a minimum period of three months from initiation of treatment.

#### STATISTICAL ANALYSIS

The  $\chi^2$  test with Yates's correction and Student's *t* test were used.

#### Results

Of the 73 men admitted to the trial, 13 defaulted. Of the remaining 60 followed for the full three months' surveillance period, 29 were treated with podophyllin 25% and 31 with trichloroacetic acid 50% and podophyllin 25%. The two groups of patients were statistically comparable in age range, country of origin, sexual preference, and sites of warts present.

There was no significant difference between the two treatments in terms of numbers of patients clear of warts at both six weeks and three months (table). At six weeks 20 patients were clear of warts after treatment with podophyllin alone and 21 after treatment with podophyllin and trichloroacetic acid. By three months only nine men remained clear of warts in the first group and 10 in the second group. Of the patients without warts at six weeks, those treated with podophyllin alone required a mean of 4.0 applications but those treated with podophyllin and trichloroacetic acid required a mean of 2.9 applications. The difference between the two groups in this respect is statistically significant ( $0.02 > p > 0.01$ ).

No side effects were reported in the group treated with podophyllin alone. In the trichloroacetic acid/podophyllin group five patients reported side effects; three had superficial ulceration at the site of treatment and two complained of excessive soreness a day or two after treatment.

#### Discussion

A recent comparative study<sup>3</sup> illustrated the value of electrocautery and cryocautery in the treatment of anogenital warts, both methods being particularly useful in reducing the number of visits required to rid a patient of warts. Useful though both methods are when sufficient time is available, in a busy genito-urinary clinic they have disadvantages compared with local applications. In both cases apparatus has to be set up, treatment itself is relatively time consuming and, in the case of electrocautery treatment produces anxiety because of the local anaesthetic and the electrode itself. Local applications are easier and quicker.

Locally applied trichloroacetic acid can be considered as a form of chemical cautery and is frequently used for treatment of anogenital warts. There are, however, no data on its efficacy compared with the most commonly used local application, podophyllin. The difficulty of devising a direct double-blind comparison between trichloroacetic acid and podophyllin proved insurmountable; though dye could be added to trichloroacetic acid to resemble podophyllin, the white discolouration of the wart produced by the acid could not be disguised. After experimentation with various strengths, however, a combination of trichloroacetic acid, podophyllin, and an inert brown dye was found which looked identical to a solution of podophyllin in the same solvent and which masked the white appearance produced by trichloroacetic acid.

The number of patients free of warts at three months was disappointing with both solutions. There was no significant difference between either

TABLE Outcome of trial

Treatment	No of patients	No defaulted	No clear at 6/52*	Mean No (SD) of treatments to clear warts at 6/52‡	No clear at 3/12†
Podophyllin 25%	38	9	20	4.0 (1.6)	9
Podophyllin 25% and trichloroacetic acid 50%	35	4	21	2.9 (1.1)	10

\* $\chi^2 = 0.03$

† $\chi^2 = 0.03$ ;  $p > 0.5$

‡ $t = 2.58$ ;  $df 39$ ;  $0.027 > p > 0.01$

treatment at three months with a mean clearance rate of 32%. Using podophyllin alone and with observation over a similar period Simmons<sup>1</sup> had a clearance rate of 22%; his study, however, was larger, but both studies confirm poor results compared with earlier experience using podophyllin.<sup>4,5</sup>

In the patients free of warts at six weeks, those treated with trichloroacetic acid and podophyllin had required significantly fewer applications, but the clinician has to balance this advantage against the higher rate of side effects using this combination. Though we would not advocate the combined solution for routine use, as it was formulated for the comparative trial, we would recommend further evaluation of podophyllin and other methods of treating warts.

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