

Podophyllin 10% and 25% in the treatment of ano-genital warts

A comparative double-blind study

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SUMMARY One hundred and forty male patients with ano-genital warts were randomly allocated to a double-blind study of 10% and 25% podophyllin in tincture of benzoin compound. One hundred and nine patients attended for a three-month period of surveillance. Only 24 (22%) patients were free of warts after having podophyllin treatment alone, 12 each after treatment with 10% and 25% podophyllin. There was no significant difference in the number of applications needed with each treatment. Neither hypersensitivity nor chemical ulceration occurred.

Introduction

The treatment of genital warts is generally acknowledged to be difficult, time-consuming, and to give poor results. Many forms of treatment have been advocated, including the local applications of podophyllin,¹ 5-fluorouracil,² and colchicine.³ Few comparative studies have been reported, and these are often poorly controlled with inadequate follow-up. Probably the most widely used preparation is podophyllin, but there is little information on the best concentration or solvent. A double-blind study to compare the results of treatment with 10% and 25% podophyllin in tincture of benzoin compound (TBC) was therefore undertaken.

Patients and methods

Male patients with ano-genital warts attending the departments of genital medicine at St Bartholomew's Hospital and the Prince of Wales's Hospital, London, who had received no treatment for genital warts in the previous three months, were admitted to the trial. The diagnosis of warts was a clinical one and other infections were treated concurrently.

LABORATORY INVESTIGATIONS

To exclude other sexually transmitted diseases (STD), all patients had blood taken for the Venereal

Disease Research Laboratory (VDRL) and *Treponema pallidum* haemagglutination (TPHA) tests. Those with urethral exudate had specimens taken for Gram-stained smears and culture for *Neisseria gonorrhoeae*^{4 5}; specimens of voided urine were collected for the two-glass urine test. Patients with unexpected urinary abnormalities were asked to attend for microscopical examination and culture of an early morning sample.⁶ All homosexual men had a proctoscopic examination for rectal lesions; rectal specimens for smear and culture and throat specimens for culture for *N gonorrhoeae* were also taken. Blood was collected for tests for hepatitis B antigen from these patients. Investigations for *Candida* species and *Trichomonas vaginalis* were performed when indicated.

ATTENDANCE AND TREATMENT

During the study period patients were advised to have sexual intercourse only when protected by a condom. Sexual partners were examined whenever possible. To encourage regular attendance a special weekly clinic with appointments was initiated so that patients were guaranteed a quick visit.

Patients were randomly allocated by a random number table to one of two treatments, 10% and 25% *Podophyllum emodi* in TBC prepared in one pharmacy and dispensed in stock bottles labelled A and B. The pharmacy alone had the code key, which was broken only when the trial was complete. Treatment was applied by one doctor once weekly for six weeks with cotton-wool swabs. Patients with intrameatal warts were advised to micturate immediately before undergoing treatment and then

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not to pass urine for at least four hours. External warts were washed free of podophyllin after 4, 6, 8, 12, and 24 hours at their first to fifth attendances respectively. No treatment was dispensed for self-application at home. If warts remained after six weeks, treatment was changed to trichloroacetic acid or electrocautery. Patients were followed up for a minimum of three months after the start of treatment.

Results

Of 140 patients admitted to the trial, 109 attended for the full three months' surveillance. Of those followed, 54 received 10% podophyllin and 55, 25% podophyllin. The two treatment groups were statistically comparable in their age range, marital state, country of origin, sexual orientation, previous STD including warts, and numbers and sites of warts present.

Twenty-four patients were clear of warts at three months after application of podophyllin alone (12 in each group). The 12 patients treated with 10% podophyllin required a mean of 4.3 weekly applications and those treated with 25% podophyllin a mean of 3.7 applications. These differences were not significant by Student's *t* test. Overall, the 109 patients followed for three months required a mean of 10.7 weekly applications irrespective of whether they first received 10% or 25% podophyllin. Thirty-three patients had 10% or less of their original warts left at six weeks; 17 had received 25% podophyllin and 16, 10% podophyllin.

Discussion

In 1977-78, the latest year for which figures are available in England, 23 332 cases of warts were reported by STD clinics. This compares with 57 501 cases of gonorrhoea.⁷ The problem of management of warts is therefore important. Early reports of the use of podophyllin in the treatment of ano-genital warts were very encouraging,^{1 8} but the above results show only 22% patients with no warts after three months. Furthermore, the concentration of the podophyllin preparation did not influence the results.

Lignans in podophyllin inhibit mitosis causing cellular necrosis in the basal cell layer and adjacent parts of the stratum spinosum,⁹ and it was expected that a higher dose of podophyllin would shorten the treatment period needed. Von Krogh¹⁰ also had poor

results using podophyllin and examined the lignan content of the various podophyllins. He found the highest lignan content was contained in *Podophyllum emodi*, and this preparation was used by us.

Neither hypersensitivity nor chemical ulceration occurred with either concentration of podophyllin. However, the time the preparations were left on the warts was carefully graded. This seemed easier than the older methods of protecting local skin by paraffin applications. Podophyllin applications were made for a maximum of six weeks, since King and Sullivan¹¹ have shown that some warts treated with podophyllin develop increased cornification, which diminishes its efficacy, thus causing genital warts to behave rather like common skin warts in response to podophyllin.

The present results are disappointing in comparison with earlier reports. Further comparative studies are required to help formulate a rationale for the treatment of ano-genital warts.

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