

# Liquid nitrogen and salicylic/lactic acid paint in the treatment of cutaneous warts in general practice

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**SUMMARY.** *Patients with common hand warts and simple plantar warts attending a general practice wart clinic in Northern Ireland were assigned to one of three treatment groups — liquid nitrogen applied weekly, daily application of wart paint (lactic acid one part, salicylic acid one part, collodion four parts), or a combination of the two. Combination therapy cured 87% of common hand warts over a six week period, and was significantly more effective than either agent used separately ( $P < 0.05$ ). The results for simple plantar warts were disappointing and no treatment regimen proved to be significantly better than any other. These treatments were cheap, compliance and tolerance were good, and the six month recurrence rate was minimal. Given the likelihood that warts will multiply if left untreated we would recommend early active treatment for this condition.*

## Introduction

IN Northern Ireland salicylic/lactic acid paints are frequently prescribed by general practitioners for cutaneous warts. A total of 17 131 prescriptions were written for these paints in 1984 (Prescribing Information Unit, DHSS Northern Ireland, personal communication). Cryogenics, particularly liquid nitrogen, are becoming more available for use in general practice<sup>1</sup> but as yet have only been assessed in hospitals. Bunney<sup>2</sup> and colleagues assessed the treatment of common hand warts with salicylic/lactic acid paint and liquid nitrogen together and separately in a two centre hospital trial. The trial took place over 12 weeks and several operators were involved. Liquid nitrogen was applied at three weekly intervals. The centres recorded very different success rates but the results were combined for the purpose of statistical analysis. The authors claimed that liquid nitrogen and wart paint resulted in a higher cure rate than either agent used separately but the results just failed to reach statistical significance. The trial suffered several drawbacks: the number of patients dropping out was high, the treatment of simple plantar warts was not studied, patients were drawn from older age groups than those normally associated with common warts<sup>3</sup> and side effects of treatment were not assessed.

The aims of this study were, first, to establish a wart clinic in a health centre enabling patients to have relatively easy access to treatment for warts and, second, to assess the treatment of common hand warts and simple plantar warts with liquid nitrogen and wart paint together and separately. It was felt that a six week treatment period was a realistic time to maintain patient compliance and that liquid nitrogen applied weekly was

a rigorous treatment. The following hypotheses were examined: that liquid nitrogen and wart paint are more effective in the treatment of common hand warts and simple plantar warts than either agent on its own, and that the treatments are equally well tolerated.

## Method

Practitioners at the Dunluce health centre serving a population of 24 200 patients agreed to refer patients presenting with common hand warts or simple plantar warts to a weekly wart clinic held at the centre. The clinic was run by a general practitioner (K.S.) and two nurses and was equipped with liquid nitrogen facilities. Patients agreeing to cooperate in the study were allocated to one of three treatment groups using random number tables — (1) liquid nitrogen weekly, (2) liquid nitrogen weekly plus daily applications of wart paint or (3) daily applications of wart paint. Two separate trials were undertaken to compare treatments of common hand warts and simple plantar warts. Patients were not considered for either trial if they were under seven years of age, had used self medication within the previous month, had more than five distinct lesions, had mosaic, periungual, plane or filiform hand warts, or had mosaic, grouped or mother and daughter plantar warts. Patients were only included in the trials if the average diameter of lesions was 3–9 mm inclusive.

To standardize the freezing technique a single operator was involved in the study. Liquid nitrogen was applied with a cotton wool bud just smaller than the wart, using light vertical pressure until a frozen halo appeared around its base. The wart was maintained in this icy state for 10 seconds (an uninterrupted count of 15) and allowed to thaw slowly. The process was repeated. All the patient's warts were treated. Wart paint (salicylic acid one part, lactic acid one part and collodion four parts) was dispensed from the health centre pharmacy as a generic preparation. Patients were asked to apply the same amount daily, allowing it to set on the lesion like nail varnish. On alternate days patients in all three treatment groups were instructed to soak their lesions in warm water and rub them with a pumice stone or emery board.

Patients were given weekly appointments and asked to attend even if their lesions had disappeared. Any remaining dead skin overlying a lesion was pared away by the operator during the clinic attendance. The operator examined the lesions with a magnifying glass and cure was assumed if the skin at the site of the lesion consisted of normal skin creases. Patients missing an appointment were contacted by telephone or letter (79% of patients admitted to the study had a telephone) and those missing more than one appointment were withdrawn from the trial. At the second and third visits to the clinic the patients were asked if they suffered any pain associated with the treatment. Patients were followed up approximately six months after completion of the trial by telephone or letter to assess the long term validity of cure.

## Analysis

Means for groups were compared using the student's *t* test supported by the non-parametric Mann–Whitney *U*-test because of

possible distribution problems. The percentages for groups were compared using the chi-square test. In all comparisons the level of significance was taken as  $P < 0.05$ .

## Results

One hundred and twenty nine patients were admitted to the hand wart trial and 13 were withdrawn, 10 because of irregular attendance, two because of pain following treatment and one because of hospital admission. Of the remaining 116 patients 37 (32%) were aged 7–15 years and 79 (68%) 16 years or more.

Seventy eight patients were entered into the plantar wart trial and five were withdrawn, four because of irregular attendance and one because of pain. Of the remaining 73 patients 43 (59%) were aged 7–15 years and 30 (41%) 16 years or more.

There was no significant difference between treatment groups for withdrawals in either trial.

### Hand wart trial

There were no significant differences between the three treatment groups distributed by age, sex or social class of patient, duration of wart prior to treatment, number of warts per patient or site of wart. Table 1 shows that 33 patients (86.8%) in the combined treatment group compared with 25 (62.5%) receiving liquid nitrogen and 23 (60.5%) receiving wart paint were

**Table 1.** Results of treatment.

	Number (%) of patients in treatment group		
	Liquid nitrogen	Liquid nitrogen plus wart paint	Wart paint
<i>Hand warts</i>			
Complete cure	25 (62.5)	33 (86.8)	23 (60.5)
Incomplete or no cure	15 (37.5)	5 (13.2)	15 (39.5)
<i>Plantar warts</i>			
Complete cure	15 (57.7)	14 (56.0)	9 (40.9)
Incomplete or no cure	11 (42.3)	11 (44.0)	13 (59.1)

cured by six weeks ( $P < 0.05$ ). Nine (22.5%) patients receiving liquid nitrogen suffered pain after the first week's treatment compared with six (15.8%) receiving combined treatment and one (2.6%) receiving paint only ( $P < 0.05$ ). After the second week's treatment nine (22.5%) patients receiving liquid nitrogen, five (13.2%) receiving combined treatment and two (5.2%) receiving paint only complained of pain (no significant difference).

### Plantar wart trial

There were no significant differences between the three treatment groups distributed by age, sex or social class of patient, duration of verrucae prior to treatment or number of verrucae per patient. After six weeks 15 (57.7%) patients receiving liquid nitrogen, nine (40.9%) receiving wart paint and 14 (56.0%) receiving combined treatment were cured (Table 1) (no significant difference). After the first week 14 (53.8%) patients treated with liquid nitrogen, 18 (69.2%) receiving combined treatment and five (19.2%) treated with wart paint complained of pain ( $P < 0.001$ ). However, after the second week of treatment this difference was no longer significant.

### Follow up

One hundred and sixteen of the 119 patients in both trials who were considered cured were contacted by telephone or letter ap-

proximately six months after the trials ended. Only two patients had had a recurrence of warts. Both had verrucae plantaris and had been receiving paint.

## Discussion

The ideal trial would have been a double blind placebo controlled trial. However, it has already been shown that after six weeks of treatment, wart paint and liquid nitrogen combined cured 77% of common hand warts compared with 5% for placebo (collodion).<sup>3</sup> In addition, liquid nitrogen does not lend itself to a double blind trial.

In this study the number of lesions was restricted to five per patient because the concurrent treatment of large numbers of warts might be painful and the restriction to warts sized 3–9 mm was justified because the majority of common warts are within this range.<sup>3,4</sup> Although periungual and filiform warts are both 'common' and are caused by similar antigenic strains of virus to common warts, it was felt that they might respond differently to treatment and they were therefore excluded. The treatment time with liquid nitrogen was limited to 10 seconds and a standardized freezing technique was used, as described by Cage.<sup>5</sup> More vigorous application of liquid nitrogen<sup>6</sup> and employing posterior nerve blocks to prevent pain would not have been suitable as many of the study population were children. We made our own cotton wool buds in various sizes<sup>7</sup> in order to minimize the damage to tissue surrounding the wart and a well validated technique<sup>2</sup> was used to decide whether the wart was cured. The plantar wart trial was restricted to simple plantar warts because 85% of patients presenting with plantar warts in general practice possess this type.<sup>3</sup>

By directly comparing the three treatments in carefully controlled trials it has been shown that the combined treatment was significantly more effective in the treatment of common hand warts than either wart paint or liquid nitrogen used separately. However, the results of the verruca plantaris trial were disappointing with no one treatment proving to be particularly successful. The low withdrawal rate because of pain suggests that the treatments were well tolerated and the numbers of patients failing to complete the trials would probably have been much higher but for encouragement to attend by telephone and/or letter. Open access with practically no waiting time for initiation of treatment or appointments, familiarity with the health centre and nurses, and personalized treatment by the treatment room nurse kept non-compliance to a minimum. The only other published study which compared these treatments had a withdrawal rate of 35% owing to non-compliance.<sup>2</sup> Bunney and colleagues' hospital study may also be less useful because they included mosaic warts, failed to standardize the size of lesions on entry to the study and did not consider self medication or treatment given by the patient's practitioner prior to entry.<sup>2</sup> In a previous study of 826 patients<sup>3</sup> attending primary care with cutaneous warts it was found that 50% of patients treated themselves prior to consulting their doctor. Patients attending hospital clinics tend to be selected by primary care physicians and hospital trials may be less representative of the condition.

The cost of liquid nitrogen was approximately 25p per treatment while the generic wart paint, including ingredients, container and dispensing fee, cost approximately 75p per course of treatment. Similar proprietary preparations are 100% to 200% more expensive. Although after the first week patients found treatment with liquid nitrogen for both verruca vulgaris and plantaris to be more painful than the other treatments, there was no significant difference after two weeks. As patients get used to liquid nitrogen they may find it less frightening and hence less painful. More patients with plantar warts complained of pain following treatment than patients with hand warts. This

may have been because there were more younger patients in the former group or because swelling tends to occur in the tissues after plantar warts are treated, resulting in more pain.

We would support Gibson's claim<sup>8</sup> that liquid nitrogen confers no advantage as a routine therapeutic agent for verrucae plantaris and disagree with Purdey<sup>9</sup> who claimed that this agent routinely cured plantar warts within three weeks. Using salicylic acid as a treatment for simple plantar warts Bunney<sup>10</sup> achieved a cure rate of 75%, which was higher than the rate found in this study, but her treatment period was 12 weeks. Anderson<sup>11</sup> has stated that plantar warts are susceptible to any form of treatment but the results of this study do not support that view.

The nurses involved in the study found cryotherapy simple to learn and we would agree with Bunney<sup>7</sup> that liquid nitrogen is easy to apply, cost effective and takes little more time than writing a referral letter. Given the low cure rate of warts with placebo and the likelihood that warts will multiply if left untreated we would recommend early active treatment for this condition.<sup>3</sup> We would recommend weekly application of liquid nitrogen and daily application of wart paint for patients with common hand warts and that this treatment regimen should be monitored and administered by treatment room nurses.

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