medium contained high concentrations of L-lysine and low concentrations of L-arginine, and suggested that a high lysine/arginine ratio was associated with poor conditions for virus growth.

In our previous double-blind, placebo-controlled therapeutic trial on recurrent herpes simplex labialis (3), lysine 1 000 mg daily for 5 days had no effect on the rate of healing of the episodes.

Griffith et al. (1), in an uncontrolled study, observed the beneficial effect of long-term treatment with lysine 300–1 000 mg daily on patients with recurrent cutaneous and labial herpes simplex.

The present study demonstrates clearly that lysine prophylaxis with 1 000 mg daily has no effect on the rate of healing or on the course of herpes labialis. Furthermore there is no unequivocal effect on the frequency of recurrences, although the interpretation of these results is somewhat more complicated. In patients initially treated with placebo there was a tendency towards fewer recurrences during subsequent lysine treatment (Table I). Also, patients initially treated with lysine had a lower number of recurrences on placebo treatment than had patients initially treated with placebo. Theoretically this could be attributed to a prophylactic long-term effect of lysine. However, analysis of the data does not support such an interpretation; of the 38 recurrences recorded during placebo treatment after crossover (Table I), 15 occurred within the first 4 weeks, 9 within the second 4 weeks and 14 within the third 4 weeks after lysine withdrawal, the differences being insignificant.

Significantly more patients were recurrence-free during lysine than during placebo treatment (Table II). This finding is probably accidental, but might also suggest an effect of lysine in some of the patients.

As demonstrated in earlier studies (2, 3, 4) there is a large placebo response in recurrent herpes simplex, presenting a considerable pitfall to clinical trials. Also, due to the great inter- and intra-individual variations in the frequency and course of recurrent herpes, evaluation of a prophylactic treatment presents great investigational problems; it requires large patient materials, long observation periods and makes the employment of double-blind, controlled trials absolutely necessary.

To sum up, lysine had no significant prophylactic effect, either on the duration or on the recurrence rate of herpes simplex labialis. However, the results suggest that certain patients may benefit from such treatment, and further investigations are indicated to clarify this hypothesis.

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Topical Treatment of Penile Condylomata Acuminata with Colchicine at 48–72 Hours Intervals

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Abstract. We previously demonstrated that 8% solutions of colchicine in ethanol eradicated penile warts in 36% of patients after a single application and in an additional 12% after a second application performed at least a week after the first. In the present study only 30% of 115 men were cured when penile warts were painted twice at intervals of 48 hours with 2% solutions and 72 hours with 4% and 8% solutions of colchicine. The lack of additive therapeutic effect accruing from the second application and the high frequency of intolerable side effects when using the latter treatment program indicate that this regimen is unsuitable for condylomata therapy.

Key words: Condylomata acuminata; Topical drug therapy; Colchicine

Table I. *Eradication of penile warts when painted twice with colchicine in ethanol (≥3 months of follow-up)*
Figures within parentheses denote percentages

Schedules				
Conc. of colchicine	2%	4%	8%	
Interval between appl.	48 h	72 h	72 h	
Materials				Total
No. of patients	37	38	40	115
No. of location sites	47	56	56	159
Cure rates				
All warts	10 (27)	11 (29)	13 (33)	34 (30)
Type I (urinary meatus)	1/6	2/5	0/3	3/14 (21)
Type II (preputial cavity)	13/28 (46)	12/37 (32)	17/37 (46)	42/102 (41)
Type III (transitional area inner/outer aspect of prepuce)	2/10	2/12	4/12	8/34 (24)
Type IV (penile skin)	1/3	1/2	0/4	2/9 (22)

Successful treatment of condylomata acuminata with topical colchicine has been reported sporadically (1, 2, 4, 5), but the materials studied have been small and practical details concerning the appropriate regimens have been sparse. We have previously reported that 8% colchicine in ethanol eradicated penile warts in 36% of patients after a single application and in a further 12% of cases after a second application at least a week after the first (3). When effective, the drug achieves necrosis of warts within 4–5 days (4).

Therapy with antimitotic substances is rational in so much as the lesions regularly demonstrate a high degree of mitosis (Steigleder 1978). A suggested way of achieving arrest of cellular proliferation in venereal warts more effectively is to administer the drugs more frequently than once a week. The present study was initiated in order to investigate what additional biological potential of colchicine on penile warts might accrue when applied twice with an interval of 48–72 hours.

MATERIAL AND METHODS

Patients

Of 142 men attending the clinic because of penile condylomata between March 1977 and January 1978, 6 were excluded because of simultaneously occurring anal warts, and another 21 cases for practical problems preventing participation in the regimen. 37 of the remaining 115 men were treated on two occasions with 2% colchicine solution with a 48 hour interval, and 39 and 45 twice with 4% and 8% colchicine solutions respectively with a 72 hour interval (Table I). Their ages ranged between 16 and 72 (mean 24.5) years. There were no differences in mean ages of the men comprising the different groups. Follow-up examination was provided 3–6 weeks after treatment. Cure rates were checked at least 3 months after therapy by using an inquiry form.

The warts were classified into four types (Table I) according to location site: the urinary meatus including fossa navicularis (Type I), the preputial cavity (Type II: glans penis, coronal sulcus, fraenum and the inner aspect of the prepuce), the transitional area between the inner and outer aspect of the prepuce (Type III) and penile skin (Type IV). On each examination the distribution and the number of tumours were recorded, as well as the range of their diameters at each site. These data enabled us to carefully assess the effect of treatment at each site.

Preparation of solutions

Colchicine (obtained from Sandoz Ltd, Basle) was diluted in 70% ethanol to produce 2, 4 and 8% solutions to which 0.05% methylrosaniline was added to facilitate visual control of painted areas.

Treatment procedures

After retraction of the prepuce, the solutions were applied with a cotton wool swab, so that the warts were thoroughly painted, though avoiding excess spread to adjacent tissues. The solutions were allowed to dry before the prepuce was freed. Application within the urinary meatus was done immediately after voiding. The patients were then instructed not to urinate for the next 6 (–8) hours. In the case of condylomata on other locations, the patients were instructed to wash the treated area after 6 (–8) hours with soap and water. In order to prevent reinfection and to evaluate the true relapse frequency, the men were instructed to use condoms during intercourse throughout the period of treatment, and for a further month after clinical healing.

Statistical analysis

Statistical evaluation was conducted using the χ-square analysis.

RESULTS

The 115 men exhibited warts distributed among 159 sites (Table I). Initially, 46% of the men seemed to be cured, but relapse occurred in 16% within 4–12 (mean 7) weeks. 34 men (30%) showed eradiction of all warts 3 months after treatment, the effect being best seen with preputial cavity warts. These disappeared in 42 of 102 men (41%) as opposed to other wart types which healed in 13 of 57 cases (23%) ($p<0.05$). No statistical differences were found between the treatment series.

Absence of side effects was noted in only 27 patients (20%). 67 men (58%) complained of itching, burning or a slight tenderness for a few days; 21 (18%) experienced an intermittent, severe pain up to 7 days, frequently radiating along the shaft of the penis to perineal and inguinal areas. 4 men developed balanoposthitis, which also occurred in 3 of the 136 men in the original series, and consequently preventing a second application. Thus, the latter type of complication developed in 5% of cases painted 1–2 times; caused by 8% solutions in 3, 4% solutions in 4 and 2% solutions of colchicine in one case. In all but one of these cases relatively large numbers of warts were present, frequently confluent in larger plaques.

DISCUSSION

The results from previous studies on penile warts with a single application of colchicine are identical with those achieved when a second treatment was given within 72 hours. This is most clearly evident when comparing the effect on warts affecting the preputial cavity (3). A reassessment of previous series using 8% solutions of colchicine reveals that eradication of preputial cavity warts is obtained in 50% of cases after a single treatment. Applications of identical concentration of the substance twice with a 72-hour interval cured preputial cavity warts in 46% of patients. The latter regimen evokes an intolerable frequency of troublesome side effects.

The cytobiological effect of colchicine is mainly due to binding of the substance to microtubule proteins which constitute ultrastructurally rather complicated building blocks of the spindle structures being involved in chromosome movements during cell division. Colchicine-binding activity may decay due to changes in physical environment, a phenomenon conceivably related to structural changes of microtubules (6). The first colchicine application on condylomata may alter physical conditions in the cells sufficiently to achieve a temporary block of binding ability when the substance is administered a second time. Lack of therapeutic benefit and intolerable side effects seen with the reported regimen may be concentration dependent.

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Porphyria Variegata: Failure of Chloroquin Treatment

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Abstract. A 27-year-old woman affected by porphyria variegata was treated with chloroquin for 1½ years without any clinical improvement. Urinary excretion of porphyrins was not convincingly altered during treatment.

Key words: Porphyria variegata; Phlebotomy; Chloroquin

Porphyria variegata (PV) was described for the first time in 1924, by Thiele. It is an autosomal dominant trait and the clinical findings are a combination of those occurring in acute intermittent porphyria