

## PUSTULOSIS PALMARIS ET PLANTARIS TREATED WITH HYDROXYUREA

T. Hattel and J. Søndergaard

*From the Department of Dermatology, University of Copenhagen, Rigshospital, Copenhagen, Denmark*

**Abstract.** Hydroxyurea (Hydrea®) has been used for treatment of patients suffering from pustulosis palmaris et plantaris (PPP). Thirteen volunteer patients were given hydroxyurea (1.5 g daily) and a placebo, each for 3 weeks, double-blind randomized. The patients were clinically examined weekly and the numbers of pustules in palms and on soles were counted. Redness, thickening and scaling was also recorded. Scores were given for severity of disease. No significant difference in scores for severity of disease were noted between treatment and placebo periods, thus indicating that treatment of PPP with hydroxyurea for 3 weeks is ineffective. The failure of hydroxyurea to improve PPP may be due to a too-short period of treatment. Hydroxyurea caused a significant fall in white blood cell count. No other side effects were noted.

Pustulosis palmaris et plantaris (PPP) is a clinical entity of unknown etiology characterized by a chronic eruption of yellowish sterile pustules occurring on the palms and soles. The affected skin is red, infiltrated, and scaling. The pustular eruptions in PPP are usually extremely resistant to treatment and furthermore highly incapacitating to the patients (2, 3). Treatment including systemic administration of antibiotics or sulfonamides, Bucky radiation therapy, potent corticosteroids topically or intradermally administered and various tar preparations may afford temporary benefit (2, 3).

Hydroxyurea (Hydrea® Squibb & Sons, New York, N.Y., USA), a new antimetabolite, was recently found efficacious in the management of refractory psoriasis (1, 6). Encouraging results have also been obtained in a small group of patients suffering from pustular psoriasis of von Zumbusch's type (7). Like PPP, this disease is extremely resistant to treatment. We therefore attempted to treat PPP patients with hydroxyurea and the results are presented in the present report.

### MATERIAL AND METHODS

Thirteen volunteer patients attending the out-patient clinic of the University Department of Dermatology, Rigshospital, Copenhagen, during 1972 were studied. These were all patients suffering from PPP selected for this study on the following clinical and histological criteria: Yellowish, sterile pustules were present on the palms especially on the thenar and hypothenar eminences and on the sole or sides of the heel. The affected skin appeared red, thickened and inflamed. The pustules often appeared dry, forming brownish exfoliating scales. Typical psoriatic lesions were absent. Histologically, the typical spongiosiform pustules of pustular psoriasis were absent. The age of the patients ranged from 17 to 72 years.

Each patient was given hydroxyurea (0.5 g three times daily) and a placebo, each for 3 weeks, double-blind randomized. Skin biopsies, hemoglobin and creatinine were obtained prior to treatment, and white blood cell count (WBC), serum glutamic transaminase (SGPT), platelet count and urinary analysis for sugar and protein were performed weekly. Photographs were obtained before and after each 3-week period. The patients were clinically examined weekly and the number of pustules in palms and on soles were counted. Redness, thickening and scaling were also recorded. For each of the palms and soles, scores were awarded according to severity of the disease, and a total score (sum of four pustule-scores and of four redness-thickness-scores) for each patient determined weekly, the following system being adopted:

- 0: No pustules, normal-appearing skin.
- 1: Less than 15 pustules, redness.
- 2: Between 15 and 100 pustules, redness and thickening.
- 3: More than 100 pustules, redness, thickening and scaling.

Throughout the trial indifferent ointment was used topically.

### RESULTS

Treatment with hydroxyurea in comparison with the placebo treatment caused no significant reduction in the number of pustules, thickening, redness or scaling.

Seven patients were given hydroxyurea during the

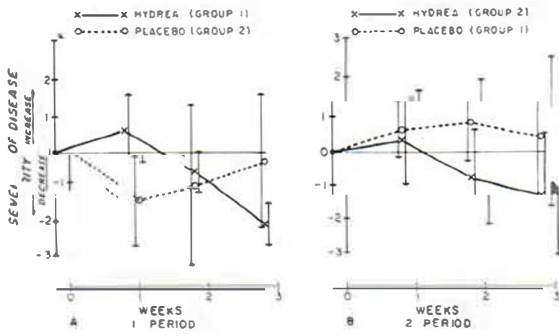


Fig. 1. (A) Severity of disease after treatment of 7 patients with hydroxyurea (group 1) and 6 patients with placebo (group 2) for 3 weeks. Mean changes  $\pm$  S.E.M. are calculated as increase or decrease in total score for pustules, redness, thickening and scaling before as well as after 1, 2 and 3 weeks.

(B) Severity of disease after treatment of 6 patients with placebo (group 1) and 7 patients with hydroxyurea (group 2) for 3 weeks. Mean changes  $\pm$  S.E.M. are calculated as increase or decrease in total score for pustules, redness, thickening and scaling before as well as after 1, 2 and 3 weeks.

first 3-week period and placebo during the following 3 weeks. The mean total score  $\pm$  S.E.M. for severity of disease before treatment with hydroxyurea was  $11.4 \pm 0.8$ . The remaining 6 patients received placebo initially and hydroxyurea during the subsequent 3-week period. The mean total score  $\pm$  S.E.M. for severity of disease was  $11.8 \pm 1.0$  before the placebo period. The results obtained during the first and the second 3-week period are shown in Fig. 1. No difference between hydroxyurea and placebo was found at the 5% level of significance.

Hydroxyurea caused a significant fall in WBC. This effect was noticeable after 1 week of treatment, and then remained constant, mean  $\pm$  S.E.M. before treatment being  $7.7 \pm 0.6$ , decreasing by  $2.0 \pm 0.5$  to  $5.7$  after 1 week ( $p < 0.01$ ) and by  $2.6 \pm 0.7$  to  $5.1$  after 3 weeks ( $p < 0.01$ ). This effect, however, was easily reversed, since during the subsequent treatment with placebo, WBC returned to normal values within 1 week. No changes in hemoglobin, creatinine, SGPT, platelet count, and urinary sugar and protein were noted between treatment and placebo periods.

## DISCUSSION

The present results show that treatment of patients having pustulosis palmaris et plantaris with hydroxyurea for 3 weeks is ineffective. This failure is prob-

ably not related to the dosage used. Striking results were obtained in patients with pustular psoriasis receiving a similar dosage (7) and Leavell & Yarbro (5) recommend one-third (0.5 g daily) of the dosage used by us for treatment of refractory psoriasis. Dosages exceeding 1.5 g daily may cause leucopenia, thrombocytopenia and anemia (4). In a study on the long-term effects of hydroxyurea in psoriasis, anemia and leucopenia proved frequent and troublesome side-effects (1), when doses of 0.5–1.5 g daily were used.

The failure of hydroxyurea to improve PPP may be due to a too-short period of treatment. In 16 patients with psoriasis treated with hydroxyurea the first evidence of improvement was noted within 2 to 3 weeks of starting treatment, but maximum benefit at any oral dose level was not achieved until 4 to 8 weeks' treatment (1). On the other hand, Stein et al. (7) found that treatment for about 1 week caused a significant improvement in patients with pustular psoriasis.

The fall in WBC observed by us after treatment with hydroxyurea is in agreement with the findings of several other authors (1, 4). Although this effect may be troublesome, requiring temporary discontinuance of treatment, this may well be due to a main pharmacological action of hydroxyurea as hypothesized by Stein et al. (7). These authors suggest that in pustular psoriasis, hydroxyurea could be primarily directed against and suppress the efferent cell of the early inflammatory cycle, viz. the neutrophil. This, however, would not seem to be the case in PPP, since, although WBC was significantly reduced, no reduction in the number of pustules or severity of the disease was observed.

## ACKNOWLEDGEMENT

Hydroxyurea (Hydrea®) was kindly supplied by Squibb & Sons.

## REFERENCES

- Dahl, M. G. C. & Comaish, J. S.: Long-term effects of hydroxyurea in psoriasis. *Br Med J* 4: 585, 1972.
- Everall, J.: Intractable pustular eruptions of the hands and feet. *Br J Dermatol* 69: 269, 1957.
- Hellgren, L. & Mobergen, H.: Pustulosis palmaris et plantaris. *Acta Dermatovener (Stockholm)* 51: 284, 1971.
- Kennedy, B. J. & Yarbro, J. W.: Metabolic and therapeutic effects of hydroxyurea in chronic myeloid leukemia. *JAMA* 195: 1038, 1966.
- Leavell, U. W. & Yarbro, J. W.: Treatment of psoriasis by hydroxyurea. *South Med J* 64: 1253, 1971.

6. Rosten, M.: Hydroxyurea: A new antimetabolite in the treatment of psoriasis. *Br J Dermatol* 85: 177, 1971.
7. Stein, K. M., Shelley, W. B. & Weinberg, R. A.: Hydroxyurea in the treatment of pustular psoriasis. *Br J Dermatol* 85: 81, 1971.

*Received September 11, 1973*

J. Søndergaard, M.D.  
Department of Dermatology  
Rigshospital  
Blegdamsvej 9  
DK-2100 Copenhagen  
Denmark