Pseudouridine Excretion in Patients with Psoriasis

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The excretion of pseudouridine in the urine of 17 patients with psoriasis was significantly increased. The largest increase was found in patients with psoriatic arthritis. No correlation between the extent of psoriasis and pseudouridine excretion was found. The excretion of pseudouridine was followed in 10 of the 17 patients during treatment with anthralin or PUVA. Pseudouridine excretion decreased significantly during therapy. The possible application of pseudouridine excretion in monitoring the disease activity in psoriasis is discussed. (Received September 12, 1986.)

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Pseudouridine (5-ribosyl-uracil) is a normal, but quantitatively small component of RNA, in particular transfer-RNA. In humans it is neither recycled nor further metabolized and is excreted quantitatively in the urine. It reflects the catabolism of t-RNA and has been shown to originate from specific turnover of t-RNA rather than from cell death (1). Pseudouridine and various other t-RNA specific, modified purines and pyrimidines have been demonstrated in increased amounts in the urine from patients with certain malignant neoplasms (2–5). The excretion of pseudouridine has been examined in several non-neoplastic diseases and has been either normal or slightly and inconsistently increased (3). The present study was undertaken to see if pseudouridine excretion were increased in a proliferative non-neoplastic disease. Psoriasis is such a disease with a considerably increased cell turn over of the epidermis. When an increased pseudouridine excretion was found we proceeded to follow the patients with measurements of pseudouridine excretion to see if it was correlated with the disease activity and finally whether pseudouridine excretion was changing during therapy.

MATERIAL AND METHODS

Patients

Seventeen patients with psoriasis entered the study, 9 females and 8 males. Their mean age was 52.5 years, range 26 to 72 years. The psoriasis was of the nummular and plaque type. The extent of psoriasis was estimated as either slight, moderate or severe. Three patients had psoriatic arthritis.

Treatment

Ten patients (severe psoriasis in 6, moderate psoriasis in 4) were followed with determinations of pseudouridine before and during treatment of their psoriasis. Seven patients were treated with anthralin in a short-time application schedule (6) and 3 patients received PUVA. Preceding the antipsoriatic therapy a stabilization period of at least 1 week on indifferent topical management (emollifying creams) was included. No specific diet was prescribed.

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Determinations of pseudouridine

Pretreatment determinations of pseudouridine and subsequent weekly determinations were performed currently and were discontinued when remission of the psoriasis was achieved or when the patients were discharged from the department. Eight hour urine collections were obtained, mostly overnight. The urine samples were stored at 4°C during collection, and aliquots of 30 ml were then stored at −180°C in plastic bottles, till they were analysed.

Assays

The assay of pseudouridine was performed as previously described (7). In brief, ammonium acetate buffer, pH 9.5, 0.20 ml was added to 0.50 ml aliquots of urine. After centrifugation (12 000 × G, 5 min.) the supernatant was transferred to an ion-exchange boronate affinity gel column (150×5 mm) equilibrated with ammonium acetate buffer, pH 8.8. The nucleosides were eluated with 0.1 M formic acid, and millipore filtered (0.5 μm). The eluate was analyzed in a high pressure liquid chromatograph (Isocratic liquid Chromatograph Model 330, Altex Sci. Inc., California). Determinations of creatinine in the urine were performed spectrophotometrically by Jaffe's reaction as earlier described (7). The excretion of pseudouridine is calculated as μmol of pseudouridine excreted per mmol of urinary creatinine to compensate for interindividual differences due to variations in body weight.

For statistical evaluation Wilcoxon's method of paired comparison was applied.

RESULTS

The mean pseudouridine excretion was increased in the 17 patients with psoriasis (Table I). There was no significant difference between females and males. No correlation to the intensity or the extent of psoriasis was found. The highest values, however, were found in the 3 patients with psoriatic arthritis (Table I). Fifteen patients had pseudouridine excretion values above normal mean +2 SD.

The pseudouridine exretion decreased in 9 of the 10 patients during therapy (Fig. 1). The decrease is statistically significant ($p<0.02$). The pseudouridine excretion was normalized in 3 patients, but remained elevated (above normal mean +2 SD) in 7 patients (Fig. 1). All 10 patients showed varying degrees of clinical remission during the study period; complete remission in 3 patients, almost complete remission in 3 and partial remission in 4 patients. The decrease of pseudouridine excretion was not correlated to the extent of the psoriasis, but a trend of positive correlation between the decrease of pseudouridine excretion and the degree of remission was found (Fig. 2). The correlation is not statistically significant.

No influence of the treatment modalities, anthralin or PUVA, on pseudouridine excretion was found. None of the 3 patients with psoriatic arthritis were included in the sequential study of pseudouridine excretion during therapy.

The patient whose pseudouridine excretion rose during therapy achieved almost complete remission. However, only 1 week after therapy (and the last pseudouridine determination) she experienced a severe relapse. Unfortunately she was lost for further measurements of pseudouridine excretion.

Table I. *Urinary excretion of pseudouridine μmol/creatinine mmol*

	Psoriasis (mean)	All patients (range)	Psoriatic arthritis (mean)	Normal Controls (mean (±2 SD)
Females	49.2	(31.4–79.8)	67.4	25.3 (±5.3)
		(n=9)	(n=2)	
Males	32.9	(25.3–51.0)	51.0	20.0 (±6.8)
		(n=8)	(n=1)	

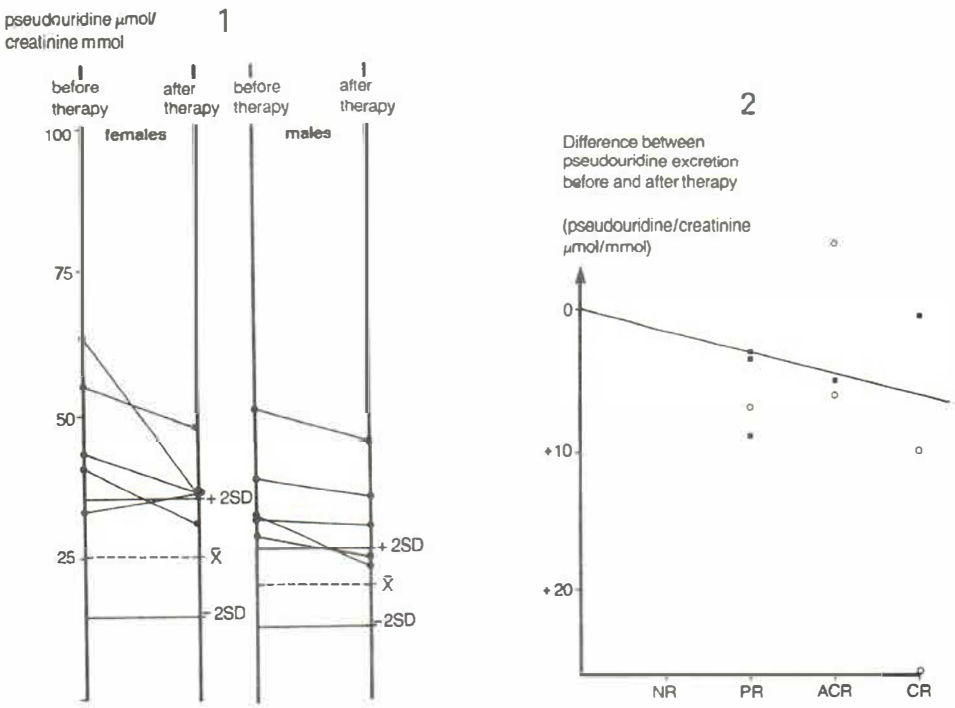

Fig. 1. Decrease in pseudouridine excretion in 10 patients with psoriasis during treatment. Pseudouridine excretion is measured relative to creatinine excretion. The broken line denotes the normal mean excretion. SD are indicated by horizontal lines.

Fig. 2. Correlation between change in pseudouridine excretion and response to antipsoriatic therapy. The correlation is not significant. NR (no remission) PR (partial remission) ACR (almost complete remission) CR (complete remission). Females (open circles). Males (closed squares).

DISCUSSION

The study demonstrates an increased urinary excretion of pseudouridine in patients with psoriasis. Similar results were obtained by Weissmann et al. (8), who studied 13 patients with psoriasis, not further specified. They found increased pseudouridine excretions in most of the patients, but the increase was not statistically evaluated and the subjects in the control group showed a wide interindividual variation in the excretion. They did not relate the excretion of pseudouridine to that of creatinine. When pseudouridine excretion is calculated as a function of urinary creatinine excretion, as we did, the interindividual variations among normal controls are reduced (9).

Our results are in contrast to those of Nagayo & Way (10), who found no differences in pseudouridine excretion between patients with psoriasis and healthy controls. The authors graded the severity of psoriasis into mild, moderate, and severe attacks, but included only 1 patient with "severe" psoriasis. Since our patients were moderately to severely affected, this might explain the discrepancy. On the other hand, however, we were unable to demonstrate any correlation between extent of psoriasis and the amount of pseudouridine excreted

Some patients with malignant neoplasms excrete increased amounts of modified nucleosides (3), and in some reports patients with leukemia, malignant lymphoma, and mesothelioma have responded to therapy with a decrease in the excretion along with clinical

improvement (11–13). The present study demonstrates a similar decrease in pseudouridine excretion following successful antipsoriatic therapy. Since two essentially different principles of therapy were applied (PUVA and anthralin) it seems fair to ascribe the effect on pseudouridine excretion to the remission of psoriasis rather than to the treatment *per se*. The trend of a positive correlation between degree of remission and decrease in pseudouridine excretion corroborates this interpretation.

It is interesting that the patients with PA showed the highest levels of pseudouridine excretion. The patients with arthritis, however, were not followed sequentially during treatment.

The only patient who showed persistingly increased pseudouridine excretion in spite of almost complete remission in her psoriasis had a relapse shortly after discontinuation of therapy. This course is interesting since the monitoring of pseudouridine excretion in patients with cancer have shown increasing levels during relapse and unaltered high excretions during unsuccessful therapy (14). Whether a steadily high pseudouridine excretion during treatment of patients with psoriasis really indicates an impending relapse, even if the skin lesions seem to heal, remains to be demonstrated. If so, persistingly increased pseudouridine excretions, irrespective of clearing of the skin, may indicate that prolonged and/or intensified therapy should be attempted in order to minimize or prevent the expected exacerbation.

We conclude that pseudouridine excretion is elevated in patients with psoriasis and that it decreases during therapy. It may prove useful in monitoring the disease, but this remains to be proved.

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