Reduced Excretion of the Main Urinary Metabolite of Prostaglandin $F_{1\alpha}$ and $F_{2\alpha}$ in Psoriatic Patients

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Abstract. Twenty-four hour excretion of the main urinary metabolite of prostaglandin $F_{1\alpha}$ and $F_{2\alpha}$ (PGF-MUM) in 18 patients with stable psoriasis (9 males and 9 females) and 18 almost age-matched healthy subjects (9 males and 9 females) was examined. The mean excretion level of PGF-MUM in male psoriatic patients (15.2±4.0 μg/day) was significantly lower than that in male healthy subjects (22.8±3.3 μg/day) ($p<0.01$). A similar tendency was observed between female psoriatic patients (10.6±3.0 μg/day) and female healthy subjects (13.3±2.4 μg/day) although the difference in the excretion level was not so remarkable ($p=0.05$) compared with male subjects. These results suggest an altered endogenous prostaglandin synthesis in psoriatic patients.

Key words: Psoriasis; Prostaglandin; The main urinary metabolite of prostaglandin $F_{1\alpha}$ and $F_{2\alpha}$ (PGF-MUM)

Accumulated evidence has suggested that the arachidonic acid-prostaglandin (PG) system is involved in the pathophysiology of psoriasis (1, 2, 3). Recently we noted that psoriatic lesions were definitely exacerbated by both systemic and topical administration of indomethacin, a potent inhibitor of PG biosynthesis (4). The present study was undertaken in order to explore whether psoriatic patients are affected by altered endogenous PG synthesis. Concerning the synthesis and metabolism, it has been shown that the levels of PG metabolites in urine reflect more exactly the endogenous synthesis of PGs than the levels of PGs in blood or serum (5, 6). Thus, in this study, the excretion of the main urinary metabolite of $PGF_{1\alpha}$ and PGF (PGF-MUM) which was identified as 5,7-dihydroxy-11-keto-tetranorprosta-1,16-dioic acid by Granström & Samuelsson (7) was assayed as one of indices of endogenous PG synthesis in psoriatic and healthy subjects.

MATERIALS AND METHODS

Patients

Eighteen patients (9 males and 9 females) with stable psoriasis covering 5–30% of the body surface and 18 healthy subjects (9 males and 9 females) were selected. The patients were of plaque type except for 2 women of chronic guttate type. Male psoriatic patients were aged 20–37 years (mean 31.0 years) and male healthy subjects 21–33 years (mean 24.6 years). Female psoriatic patients were aged 11–43 years (mean 26.9 years) and female healthy subjects 19–59 years (mean 33.9 years).

During at least 3 months before this study, none of the subjects studied had been irradiated with ultraviolet rays and none had been treated with aspirin or similar drugs that are known to inhibit PG biosynthesis.

Urine samples were collected for 24 hrs and aliquots were stored at −20°C until analysis.

Assay of PGF-MUM

Urinary levels of PGF-MUM were determined by the double antibody technique of radioimmunoassay described by Ohki et al. (8). PGF-MUM, PGF-MUM-^{125}I-tyramine amide, PGF-MUM antiserum and sheep anti-rabbit IgG were kindly supplied by Ono Pharmaceutical Co., Osaka, Japan. Antiserum did not show any significant cross-reaction with either natural PGs or metabolites in blood, e.g. 15-keto $PGF_{2\alpha}$, 15-keto PGE_2, 15-keto PGE_1 and 13,14-dihydro-15-keto PGE_1. A slight cross-reaction was found with 7-hydroxy-5,11-diketo-tetranorprosta-1,16-dioic acid, the main urinary metabolite of PGE_1 and PGE_2 (9). Thus, the 24-hr excretion levels of PGF-MUM examined in this study may reflect precisely the extent of endogenous synthesis of $PGF_{1\alpha}$ and $PGF_{2\alpha}$.

RESULTS

Data are summarized in Fig. 1 and Table I. The mean excretion level of PGF-MUM in male psoriatic patients was significantly lower than that in male healthy subjects ($p<0.01$, Student's t-test). A similar tendency was observed between female psoriatic and healthy subjects, although the difference in the excretion level was not so remarkable ($p=0.05$) compared with male subjects. Reduced levels of PGF-MUM in psoriatic patients, however, were not necessarily proportional to the extent of involvement in either sex. Additionally, a significant difference in the excretion level was noted between male (19.0±5.0 μg/24 h, $n=18$) and female subjects (11.9±3.0 μg/24 h, $n=18$) ($p<0.01$).

DISCUSSION

In the present study, 24-h urinary excretion of PGF-MUM was assayed as one of indices of endogenous PG synthesis in psoriatic and healthy subjects.

Table 1. *Urinary excretion of PGF-MUM (μg/24 h)*

	Healthy subjects	Psoriatic patients	*p*-valuc
Male			
Mean	22.8±3.3[a] (*n*=9)	15.2±4.0 (*n*=9)	<0.01
Range	18.7–26.5	7.5–19.9	
Female			
Mean	13.3±2.4 (*n*=9)	10.6±3.0 (*n*=9)	=0.05
Range	9.8–16.8	5.8–16.4	

[a] Mean value ± SD.

The significant difference in the excretion of PGF-MUM observed between male and female subjects is in agreement with previous reports (6, 8, 10).

The excretion level of PGF-MUM in psoriatic patients was significantly lower than that in healthy subjects in either sex. Aso et al. reported that production of $PGF_{2\alpha}$ as well as of PGE_2 in involved psoriatic epidermis was decreased, compared with that in uninvolved epidermis (3). On the other hand, Hammarström et al. detected a 40% and a 80% increase in lesional levels of PGE_2 and $PGF_{2\alpha}$, respectively (2). As suggested by Voorhees (1), however, this increase is minimal compared with a 26-fold and a 82-fold increase in levels of free arachidonic acid and 12L-hydroxy-5,8,10,14-eicosatetraenoic acid (12-HETE), which can be interpreted as a relative deficiency in endogenous synthesis of PGE_2 and $PGF_{2\alpha}$ in psoriatic lesions.

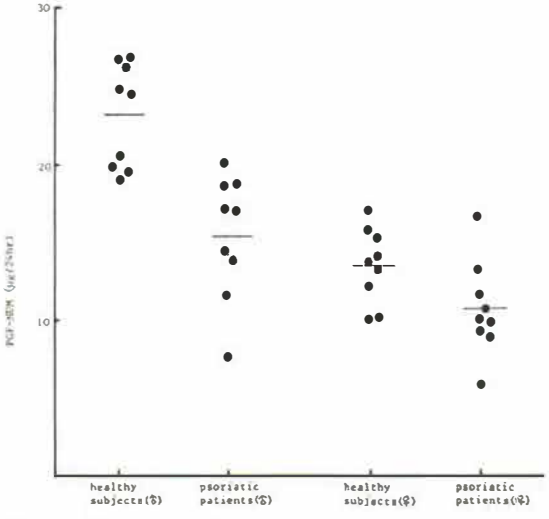

Fig. 1. Twenty-four-hour urinary excretion values of PGF-MUM in psoriatic and healthy subjects.

Thus our data may be consistent with that of Aso et al. and of Hammarström et al. However, it may be premature to believe that this reduced excretion of PGF-MUM is due directly to a decreased endogenous synthesis of $PGF_{1\alpha}$ and $PGF_{2\alpha}$ in psoriatic lesions, since these PGs are synthesized in various tissues and organs other than skin (11, 12).

Further studies are needed to clarify the pathophysiological role(s) of PGs in psoriasis.

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Bone Mineral Content in Systemic Sclerosis Measured by Photonabsorptiometry

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Abstract. The bone mineral content of the radius in 37 patients with systemic sclerosis was measured with Americium^{241} photon absorptiometry. The content was found reduced ($p<0.05$) in patients with systemic sclerosis compared with a group of healthy controls matched for age and sex. Analyses of calcium 'total', calcium ion, phosphate and the parathyroid hormone level in the serum, and the excretion of calcium and phosphate in the urine all proved normal. It is discussed whether the reduced bone mineral content in systemic sclerosis may be an effect of the immobilization of the hands affected by the disease.

Collagen is quantitatively the most important product of the osteoblast, and an important component of the organic bone matrix. The subsequent mineralization occurs on the surface of the collagen fibrils (2).

Collagen of the skin and collagen of the bone belong to the same immunological type.

Systemic sclerosis is characterized by an abnormal production of collagen, and calcifications of the skin in the form of hydroxyapatite are seen in about 20% of the patients (3). Cultured skin fibroblasts from patients with systemic sclerosis show increased accumulation of calcium (1).

Previous studies on the bone mineral content in patients with systemic sclerosis have been performed using only radiological techniques (6). In the present study, the mineral content of the forearm bones in a group of patients with systemic sclerosis was measured quantitatively by photon absorptiometry. The results were correlated to the clinical status and to laboratory parameters of mineral metabolism.

MATERIAL AND METHODS

Patients with a diagnosis of systemic sclerosis treated at the Department of Dermatology, Rigshospital, were selected according to the following criteria:

1. diagnostic criteria fulfilling the demands of the American Rheumatism Association,
2. duration of the disease ⩾3 years,
3. age below 70 years,
4. no hormonal therapy (including corticosteroids),
5. no known endocrine diseases,
6. no previous fractures of the distal radius.

Of 45 patients, 37 met these criteria, 30 women and 7 men. Their mean age was 55.7 years (range 20–69) and the mean duration of systemic sclerosis was 8.9 years (range 3–13). Twenty-eight patients received treatment with penicillamine combined with glutamine. Nine patients received treatment for systemic sclerosis with other drugs (glutamine, hydralazine, phenytoin).

The bone mineral content (BMC) of the radius was measured by Americium^{241} photon absorptiometry. A standardized part of the distal radius of the right arm, 5–10 cm from the end, was selected for the determination according to the method described by Søren Madsen et al. (4).

Serum concentrations of total calcium, ionized calcium, and of phosphate were determined by routine laboratory techniques. Parathyroid hormone levels were determined at Medicinsk Laboratorium A/S, Copenhagen, by radioimmunoassay.

Radiological examination of both hands was performed to diagnose calcifications of the soft tissues.

Frequencies were compared assuming a Poisson distribution, mean values by Student's *t*-test, and correlations were performed by the method of least squares. Probability values below 0.05 were considered statistically significant.