Urinary Excretion of Melanocytic Metabolites in Fertile Women

R. CARSTAM,[1] C. HANSSON,[3] H. RORSMAN,[1] E. ROSENGREN,[3] N.-O. SJÖBERG[2] and L.-E. WIRESTRAND[1]

Departments of [1]Dermatology, [2]Obstetrics and Gynecology, and [3]Pharmacology, University of Lund, Lund, Sweden

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Pregnant women and women taking oral contraceptives show urinary excretion values of 5-S-cysteinyldopa and of 6-hydroxy-5-methoxyindole-2-carboxylic acid in the same range as nonpregnant women not taking oral contraceptives. The excretion of these melanoma markers can therefore be used in in the biochemical diagnosis of metastatic melanoma in pregnancy and in women taking oral contraceptives. *Key words: Pregnancy; Contraceptives; 5-S-Cysteinyldopa; 6-Hydroxy-5-methoxyindole-2-carboxylic acid.* (Received February 28, 1985.)

H. Rorsman, Department of Dermatology, University Hospital, S-22185 Lund, Sweden.

The urinary excretion of 5-S-cysteinyldopa (5-S-CD) has in recent years been used as a marker for malignant melanoma metastases. In many cases an increase can be noted before metastases become clinically apparent (1, 2).

An indolic metabolite of the eumelanin pathway, 6-hydroxy-5-methoxyindole-2-carboxylic acid (6H5MI-2-C), has been found in melanotic urine (3), and recently a method for detecting this substance in normal urine has been described (4).

Pregnancy, oral contraceptives, and supplementary postmenopausal oestrogen treatment can all induce hyperpigmentation of the face, the areolae, and the ventral midline. The mechanism is unknown, but it seems to result from oestrogen influence (5, 6, 7). Interpretation of increased excretion levels of 5-S-CD and 65MI-2-C in women operated on for malignant melanoma is often uncertain, because the effect of sexual hormones has not been studied.

The excretion of 5-S-CD and 6H5MI-2-C in pregnant women, and in nonpregnant women with and without oral contraceptives was therefore investigated.

Table I. *Urinary excretion of 5-S-cysteinyldopa (5-S-CD) and of 6-hydroxy-5-methoxyindole-2-carboxylic acid (6H5MI-2-C) in pregnant women (I), in women taking oral contraceptives (II), and in nonpregnant women not taking oral contraceptives (III)*

All values in nmol/mmol creatinine

		5-S-CD			6H5MI-2-C		
Group	*N*	Mean	SD	Range	Mean	SD	Range
I	23	48	22	18–97	33	15	7.7–63
II	20	36	25	12–96	40	16	19–68
III	21	42	36	17–190	39	28	8.2–120
Total	64	42	28	12–190	37	20	7.7–120

MATERIAL AND METHODS

64 healthy white women of different hair colour, aged 19–36 years, were studied. No subject had red hair. They were classified as follows. Group I, pregnant at about the 32nd week (N=23); Group II, women taking oral contraceptives (N=20), and Group III, women not pregnant and not taking oral contraceptives (N=21). The women in Group III were evenly spaced with regard to the menstrual cycles. For 3 months before the study none had been exposed to significant amounts of natural or artificial ultraviolet radiation. The investigation was performed during the period December to March in order to minimize the influence of natural sunlight (2).

24-hour specimens of urine were collected in plastic bottles containing 50 ml of acetic acid and 1 g of sodium metabisulphite. They were kept refrigerated during collection and up to the time of analysis, which always took place within 48 hours.

Student's t-test, 1-factor analysis of variance, and multiple comparisons according to Bonferroni were used.

Chemical analysis

The urinary 5-S-CD concentration was determined by a recently described method (8), but using 5-S-L-cysteinyl-D-dopa as an internal standard (9). The concentration of 6H5MI-2-C was determined by HPLC as described elsewhere (4, 10).

RESULTS AND COMMENTS

The results of determinations of 5-S-CD and 6H5MI-2-C are presented in Table I.

In Group III the excretion values were unrelated to the timing in the menstrual cycle. There was no difference in mean excretion values of 5-S-CD or 6H5MI-2-C between groups. The mean molar excretion of 5-S-CD and 6H5MI-2-C was of the same order of magnitude. The molar ratio 5-S-CD/6H5MI-2-C varied between 0.3 and 5.0 in the women studied. The mean ratio was 1.4 and did not differ significantly between groups. In an earlier work (10) the mean excretion levels for 6H5MI-2-C from persons with red hair and from persons with blond hair were 13 and 17 nmol/mmol creatinine, respectively, values which differe significantly from the values in this material. The excretion values for 5-S-CD, however, were similar. The differences observed in the excretion of 6H5MI-2-C may possibly be due to difference in the constitutional skin colour between the groups, as there was a selection towards lighter skin colour in the study reporting lower excretion values of 6H5MI-2-C (10).

It is evident that neither pregnancy nor oral contraceptives induced significant changes in the excretion of 5-S-CD and 6H5MI-2-C. The results show that the melanoma markers studied can be used also in pregnant women and in patients under oestrogen influence.

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