

5-S-CYSTEINYLDOPA IN THE PLASMA OF MELANOMA PATIENTS AND THE RENAL CLEARANCE OF THIS AMINO ACID

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Abstract. 5-S-cysteinyl-dopa has been demonstrated in the plasma of two patients with metastases of malignant melanoma and a high excretion rate of 5-S-cysteinyl-dopa in the urine. In one patient the plasma clearance of 5-S-cysteinyl-dopa was 30 ml/min and in the other 69 ml/min. These clearance values were 43 and 45%, respectively, of the creatinine clearance in the two patients.

Key words: Melanoma; Cysteinyl-dopa; Amino acids, sulfur; Amino acids, diamino; Amino acids, dicarboxylic

There is strong evidence that 5-S-cysteinyl-dopa, a recently synthesized amino acid, plays a role in the production of pheomelanins (6). This amino acid was first detected in a human melanoma (2) and it is present in substantial amounts in the urine of patients with melanoma metastases (4). 5-S-cysteinyl-dopa has also been demonstrated in the urine of healthy subjects (1). So far, 5-S-cysteinyl-dopa has not been demonstrated in the plasma either of healthy subjects or of melanoma patients. In this paper we report the 5-S-cysteinyl-dopa plasma levels and the renal clearance of this amino acid in two patients with widespread melanoma.

MATERIAL AND METHODS

A short history and clinical data of the patients investigated are given below.

Patient I. A 33-year-old man of light complexion. No freckles. Height 173 cm. Body weight 90 kg. The patient had noted for several years a growing, pigmented lesion below the right mamilla. One year prior to this study the lesion was diagnosed as a melanoma and excised, together with lymph nodes containing metastases from the right axilla. The patient also received 60-Co radiation treatment. Three months before the study, skin and lung metastases were diagnosed and the patient received melphalan (Alkeran®; Burroughs Wellcome Co., London, England). A pleural effusion was diagnosed repeatedly during the last month and several thoracenteses produced an exudate with tumour cells. The patient died 2 weeks after this study, with

widespread pigmented melanoma metastases which, however, did not involve the kidneys or the urinary tract.

Patient II. A 44-year-old man of dark complexion. No freckles. Height 171 cm. Body weight 74 kg. Four years before this study he was operated on with a wide dissection for cervical lymph nodes and which had showed pigmented melanoma metastases. No primary tumour could be found. Ten days before this study, pigmented liver metastases had been diagnosed.

Urine was collected for 24 hours in 2-litre plastic bottles containing 1 g sodium metabisulphite and 50 ml acetic acid. To a 20 ml sample of this urine 2 ml 4 N perchloric acid was added. After centrifugation the clear supernatant was used for determination of 5-S-cysteinyl-dopa.

Venous blood samples were taken on the day of urine collection in plastic tubes and the plasma was separated by immediate centrifugation. From patient I, 5 ml plasma was used and from patient II, 10 ml plasma. 4 N perchloric acid was added to the plasma to obtain a final concentration of 0.4 N, whereafter the specimens were centrifuged and filtered. 5-S-cysteinyl-dopa was determined as described previously (5).

Creatinine in urine was determined as described by Clark & Thompson (3) and creatinine in plasma with an auto-analyser (Technicon AutoAnalyzer II).

RESULTS AND COMMENTS

The results of the examinations performed are summarized in Table I. The 24 hour urine volume was 2 100 ml in patient I and 1 500 ml in patient II. Plasma creatinine was 0.010 mg/ml in patient I and 0.008 mg/ml in patient II. Urine creatinine was 0.48 mg/ml in patient I and 1.19 mg/ml in patient II.

Both patients had large amounts of 5-S-cysteinyl-dopa in the urine. This amino acid was also demonstrated in the plasma of both patients. The renal plasma clearance of 5-S-cysteinyl-dopa was calculated to be 30 ml/min in patient I and 69 ml/min in patient II.

Table 1. 5-S-cysteinyl-dopa in plasma and urine, and renal clearance of 5-S-cysteinyl-dopa and creatinine

	5-S-cysteinyl-dopa				Creatinine clearance (ml/min)
	Urine (mg/24 h)	Urine (μ g/ml)	Plasma (μ g/ml)	Clearance (ml/min)	
Patient I	42.2	20.1	0.976	30	70
Patient II	32.0	21.6	0.328	69	155

The creatinine clearance was calculated to be 70 ml/min in patient I and 155 ml/min in patient II. Thus, renal function was not severely impaired in either of the patients. Furthermore, autopsy of patient I showed no metastases affecting the urinary tract.

The clearance values for 5-S-cysteinyl-dopa found are therefore probably representative of the renal handling of this amino acid, at least when the plasma concentration is high. If the creatinine clearance is accepted as a measure of glomerular filtration, the values obtained for 5-S-cysteinyl-dopa indicate that nearly 50% of the cysteinyl-dopa filtered in the glomeruli is excreted in the urine. 5-S-cysteinyl-dopa, thus, does not behave in the same manner as the majority of the amino acids which are effectively reabsorbed by the kidney tubules. 5-S-cysteinyl-dopa belongs to the same group as β -amino-isobutyric acid, 1- and 3-methylhistidine, and β -alanine with regard to renal plasma clearance (7).

It cannot be assumed *a priori* that 5-S-cysteinyl-dopa will be handled in the same way by the kidney in normal subjects and in melanoma patients who have high plasma concentrations of 5-S-cysteinyl-dopa. When urinary 5-S-cysteinyl-dopa levels are within normal limits, however, it has not been possible to demonstrate the amino acid in plasma even though the analytical method used is sensitive and capable of detecting as little as 25 ng of 5-S-cysteinyl-dopa. This suggests that the renal clearance

of 5-S-cysteinyl-dopa will be similar in normal subjects to that reported here for patients with metastatic melanoma. Thus, the investigation of 5-S-cysteinyl-dopa metabolism in normal subjects may require more sensitive methods than those currently available.

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