METABOLIC BALANCES OF SULFUR IN PATIENTS WITH HEPATOLENTICULAR DEGENERATION AND EFFECT OF THE USE OF D-PENICILLAMINE

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Though a great deal of knowledge has been achieved in regard to the metabolic disorders of Wilson's disease, many problems are still unsolved.

The metabolic balances of sulfur in two cases of hepatolenticular degeneration submitted to mixed and vegetarian diets [1] have been studied. The effect of D-penicillamine on the balance was also analyzed.

MATERIAL AND METHODS

CASE 1: V. M., a 22-year-old woman whose symptoms had started a year earlier; the neurological examination showed the characteristic facies, bilateral Kayser-Fleischer corneal rings, a severe wing-beating tremor in the upper limbs, unsteady gait, slurred speech, and mild rigidity of the upper limbs. The mean blood serum copper content was 29 μg/100 ml, ceruloplasmin level 3 mg/100 ml (Houchin method), aminoaciduria 437 mg/24 hr. The liver biopsy showed a post-necrotic cirrhosis.

CASE 2: J. C. M., a 27-year-old man whose disease started two years before with mental disorder and a severe tremor in the upper limbs. There were bilateral Kayser-Fleischer rings but muscle tone, gait, and speech were normal. The mean blood serum copper was 45 μg/100 ml, ceruloplasmin 0 mg/100 ml, aminoaciduria 410 mg/24 hr. The liver biopsy showed fatty infiltration.

The patients were submitted to a vegetarian diet containing 900 mg of sulfur and to a mixed diet containing 1,350 mg.

Case 1 was kept in metabolic balance for 42 days, including 20 days on vegetarian diet, 13 days on mixed diet, and 9 days on vegetarian diet again plus 2,000 mg of D-penicillamine (this daily dosis contains 430 mg of total sulfur, which were computed in the balance). Case 2 was kept in metabolic balance for 34 days, including 12 days on vegetarion diet, 13 days on mixed diet, and 9 days on vegetarian diet plus 2,000 mg of D-penicillamine. Each balance was divided in periods from 3 to 6 days.

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Diet	Period (1964)	Days	Ingesta (mg/day)	Excreta		Balance			Blood serum (mg/100 ml)
				Urine	Feces	mg/day	in the period (mg)	mean (mg)	
Mixed	17 Mar-20 Mar	4	1,226	921	249	+ 56	+ 224		1,385
	21 Mar-23 Mar	3	1,302	869	258	+ 175	+ 525		—
	24 Mar-26 Mar	3	1,250	1,041	289	− 80	− 240		1,360
	27 Mar-29 Mar	3	1,234	1,013	253	− 32	− 96		—
	Total	13					+ 413	31.8 ± 97.3	
Vegetarian	27 Jan-29 Jan	3	846	621	188	+ 37	+ 111		1,458
	30 Jan-02 Feb	4	872	600	215	+ 57	+ 228		1,411
	03 Feb-05 Feb	3	872	619	213	+ 40	+ 120		1,562
	06 Feb-09 Feb	4	860	649	241	− 30	− 120		1,218
	10 Feb-15 Feb	6	866	666	187	+ 13	+ 78		1,223
	Total	20					+ 417	20.8 ± 30.6	
Vegetarian	22 Apr-24 Apr	3	870 + 430	1,080	212	+ 8	+ 24		1,730
plus	25 Apr-27 Apr	3	875 + 430	1,352	279	− 326	− 978		1,995
D-penicillamine	28 Apr-30 Apr	3	844 + 430	1,719	281	− 726	− 2,178		2,269
	Total	9					− 3,132		

Table 1 — Metabolic balance of sulfur in patient V. E.

Diet	Period (1964)	Days	Ingesta (mg/day)	Excreta		Balance			Blood serum (mg/100 ml)
				Urine	Feces	mg/day	in the period (mg)	mean (mg)	
Mixed	19 Aug-21 Aug	3	1,252	901	273	+ 78	+ 234		1,306
	22 Aug-25 Aug	4	1,252	964	230	+ 58	+ 232		1,285
	26 Aug-28 Aug	3	1,186	943	170	+ 73	+ 219		1,225
	29 Aug-31 Aug	3	1,252	1,005	205	+ 42	+ 126		1,345
	Total	13					+ 811	62.4 ± 14.1	
Vegetarian	14 Oct-16 Oct	3	806	456	300	+ 50	+ 150		1,185
	17 Oct-19 Oct	3	885	669	179	+ 37	+ 111		1,225
	20 Oct-22 Oct	3	864	530	326	+ 8	+ 24		1,045
	23 Oct-25 Oct	3	827	521	318	− 12	− 36		1,020
	Total	12					+ 249	20.7 ± 25.3	
Vegetarian	07 Nov-09 Nov	3	876 + 430	1,306	215	− 215	− 645		1,515
plus	10 Nov-12 Nov	3	820 + 430	1,364	322	− 436	− 1,308		1,707
D-penicillamine	13 Nov-15 Nov	3	804 + 430	1,666	385	− 817	− 2,451		2,126
	Total	9					− 4,404		

Table 2 — Metabolic balance of sulfur in patient J. C. M.

At the end of each period feces and alimentary residues, which were collected in glass containers kept in a refrigerator, were weighed, mixed and homogenized in a Wharing Bendor. Duplicate samples of each material were then submitted to the analytical method. The ingesta were the difference between the known sulfur content of each type of diet and the concentration in the alimentary residues. Urine was collected daily under the same conditions as feces, and the 24-hour volume determined.

Total sulfur was determined by the turbidimetric method (De Jorge et al.[4]) which was detailed for metabolic balance studies elsewhere (Canelas et al.[2]).

RESULTS

The results are summarized in Tables 1 and 2.

COMMENTS

A positive sulfur balance was evidenced in both patients, particularly in J.C.M. under mixed diet, who showed then an average daily sulfur balance of $+62$ mg $\pm$ 14.1, significantly higher ($t = 5.676$, $P < 0.001$) than the normal mean (23.2 mg $\pm$ 17.3) reported by De Jorge and Cintra[3].

The administration of D-penicillamine induced a markedly negative balance, mostly through the promotion of a progressive increase of the urinary excretion.

In the blood serum the inorganic sulfur contents were always within normal limits (De Jorge et al.[5]) except when the patients were submitted to D-penicillamine therapy, in which case the levels showed a progressive rise.

SUMMARY

The metabolic balances of sulfur in two cases of hepatolenticular degeneration were studied. A positive balance was found in both cases; in one patient submitted to mixed diet, the average was significantly higher than the normal mean.

The administration of D-penicillamine promoted a marked increase in the urinary excretion of sulfur, leading to a strongly negative balance.

The blood sulfur contents, which were normal in the control periods, showed a progressive increment after D-penicillamine was started.

RESUMO

Balanços metabólicos do enxôfre em pacientes com degeneração hepatolenticular e efeito da administração de D-penicilamina.

Foram estudados os balanços metabólicos do enxôfre em dois pacientes com degeneração hepatolenticular. Em ambos foi comprovado um balanço positivo; em um paciente submetido a dieta geral, a média foi significantemente superior à normal.

A administração de D-penicilamina promoveu acentuado aumento da excreção urinária do enxôfre, levando a um balanço fortemente negativo.

As concentrações de enxôfre no sôro sangüíneo, que eram normais no período de contrôle, sofreram progressivo incremento após a instituição do tratamento com D-penicilamina.

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