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Urinary 3-methylhistidine and urinary 3-methylhistidine/creatinine ratio in Duchenne-muscular dystrophy in hemizygotes and in gene-carriers

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The informative value of urinary 3-methylhistidine excretion and urinary 3-methylhistidine/creatinine ratio was investigated in DMD hemizygote male children (n = 13) and in gene-carrier mothers. A significant increase of the urinary 3-methylhistidine/creatinine ratio was found in DMD hemizygotes.

There was no significant correlation between serum CK and the clinical stages of DMD and the above mentioned laboratory parameters. These parameters were not found suitable in genetic counselling concerning the DMD gene-carrier status.

The primary metabolic defect in Duchenne muscular dystrophy (DMD) is still a riddle. The rate of degradation and synthesis of muscle protein has frequently been discussed in the literature of recent years as an increased protein synthesis followed by increased protein degradation was found both in animal experiments [1, 3] and in patients with DMD [7]. Rennie et al [7] reported on direct measurements of protein synthesis in striated muscle obtained from DMD patients by biopsy and found a significant reduction, using the 1—13 C-leucine incorporation method. In addition, the urinary 3-methylhistidine/creatinine ratio was also increased. In view of the questionable reliability of creatinine kinase (CK) in the detection of DMD carriers, we have studied the rate of urinary 3-methylhistidine excretion and the urinary 3-methylhistidine/creatinine ratio in DMD hemizygotes and their mothers.

MATERIAL AND METHODS

Urinary creatinine [2] and 3-methylhistidine [6] excretion was determined in 24 hour urine in 13 DMD hemizygote patients of 6—19 years of age, 12 mothers and 9 healthy control children free from DMD.

RESULTS

The rate of creatininuria, 3-methylhistidinuria and the urinary 3-methylhistidine/creatinine ratio in the three groups is shown in Table I. The average urinary 3-methylhistidine/creatinine ratio exceeded the average of the control group, but a significant increase was perceived only in the

DMD hemizygous group. In the group of DMD gene-carrier mothers the deviation was not significant.

The correlation of CK and urinary creatinine in mothers with normal and increased CK was calculated by comparing CK and urinary 3-methylhistidine excretion as well as the CK and 3-methylhistidine/creatinine ratio; here no significant correlations were found.

The relation between the clinical stage of DMD and the above mentioned parameters was examined in 5

TABLE I

Laboratory values of DMD hemizygotes and heterozygotes

	CK U/l	Creatinine μmol/24 h urine	3-methylhistidine μmol/24 h urine	3-methylhistidine/creatinine x 10^3	
DMD hemizygotes (n = 13)					
$\bar{X}$	996.5	2.23	203.7	80.28*	
SD ±	880.2	±0.82	±100,8	±28.2	$p^* < 0.01$
DMD heterozygotes (n = 12)					
$\bar{X}$	117.7	6.55	373.2	61.85*	
SD ±	188.2	±3.05	±209.1	±33.9	$p^* > 0.1$
Control group (n = 9)					
$\bar{X}$	32.67	5.51	194.3	35.24	
SD ±	14.5	±3.44	±255.6	±41.7	

Correlation coefficient =	R	p
DMD CK-3-methylhistidine	0.08	> 0.1
DMD CK-3-methylhistidine/creatinine	—0.03	> 0.5
DMD-heterozygotes:		
CK-3-methylhistidine	—0,09	> 0.5
CK-3-methylhistidine/creatinine	—0.04	> 0.5

TABLE II

Correlation between creatininuria, 3-methylhistidinuria and urinary 3-methylhistidine/creatinine ratio and the clinical stage of DMD

Clinical stage	Creatinine μmol/24 h urine		3-methylhistidine μmol/24 h urine		3-methylhistidine/creatinine x 10^3	
I + II	$\bar{X}$	2.51	194.3		74.4	
n = 5	SD ±	0.83	±124.3		±36.2	
		p > 0.05		p > 0.05		p > 0.05
III + IV.	$\bar{X}$	2.29	209.6		93.7	
n = 8	SD ±	0.47	±92.1		±42.2	

	R	p
DMD stage I + II.		
CK-creatinine excretion	0.24	>0.5
CK-3-methylhistidine excretion	—0.07	>0.5
CK-urinary 3-methylhistidine/creatinine	—0.08	>0.5
DMD stage III + IV.		
CK-creatinine excretion	0.55	>0.05
CK-3-methylhistidine excretion	—0.11	>0.05
CK-urinary 3-methylhistidine/creatinine	—0.31	>0.05

children in stage I and II and 8 DMD patients in stage III and IV. The correlation between the clinical stage of DMD and urinary CK as well as the parameters referring to muscle destruction i.e. urinary 3-methylhistidine excretion and urinary 3 methylhistidine/creatinine ratio, did not prove significant statistically (Table II).

Discussion

3-methylhistidine occurs in actin and certain myosin heavy chains and is not metabolized in man, so its excretion should be a quantitative index of the rate of actin and myosin heavy chain degradation [9]. Creatinine excretion may be considered an index of skeletal muscle mass even in cases of muscle disease [5]. The urinary 3-methylhistidine/creatinine ratio is increased in DMD patients showing considerable myofibrillar degradation [4, 8].

In DMD gene-carriers, studies of urinary 3-methylhistidine excretion the urinary 3-methylhistidine/creatinine ratio have not been carried out. In the present study, the urinary 3-methylhistidine/creatinine ratio of both gene-types exceeded that of the control group, but a significant increase was found only in the DMD hemizygote group.

The clinical progression of DMD was not found to be mirrored in a prognostically useful manner in the laboratory parameters characteristic of muscle destruction.

References

1. Ballard FJ, Thomas FM, Stern LM: Increased turnover of muscle contractile proteins in Duchenne muscular dystrophy as assessed by 3-methylhistidine and creatinine excretion. Clin Sci 56: 347, 1979
2. Jaffe M: Über den Nierenschlag, welchen Pikrinsäure im normalen Harn erzeugt und über eine neue Reaktion des Kreatinins. Z physiol Chem 10:391, 1886
3. Li JB: Protein synthesis and degradation in skeletal muscle of normal and dystrophic hamsters. Am J Physiol 239: 401, 1981
4. McKeran RO, Halliday D, Purkiss PJ: Increased myofibrillar protein catabolism in Duchenne muscular dystrophy measured by 3-methylhistidine excretion in the urine. J Neurol Neurosurg Psychiat 40:979, 1977
5. Murray CE, Warnes DM, Ballard FJ, Tomas FM: Creatinine excretion as an index of myofibrillar protein mass in dystrophic mice. Clin Sci 61:737, 1981
6. Radha E, Bessman SP: A rapid colorimetric method for 3-methyl-histidine in urine. Anal Biochem 121:170, 1982
7. Rennie MJ, Edwards RHT, Millward DJ, Wolman SL, Halliday D, Matthews DE: Effects of Duchenne muscular dystrophy on muscle protein synthesis. Nature 296:165, 1982
8. Wernes DM, Tomas FM, Ballard FJ: Increased rates of myofribrillar protein breakdown in muscle-wasting diseases. Muscle Nerve 2:2, 1981
9. Young VR, Munro HN: N-methylhistidine (3-methylhistidine) and muscle protein turnover: an overview. Fed Proc 37:2291, 1979

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