Arch Psychiatr Nervenkr (1981) 230:307–314

Archiv für Psychiatrie und Nervenkrankheiten
Archives of Psychiatry and Neurological Sciences

Investigations on Enzyme Activity in the Serum and CSF of Patients with Neuromuscular Diseases

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Summary. The CPK, aldolase, GOT, GPT, and LDH concentrations in the serum and lumbar CSF of 80 patients with neuromuscular diseases and 20 controls were measured. The value obtained in serum were essentially in agreement with the data in the literature. This is the first publication reporting on regular CSF enzyme examinations in different neuromuscular disorders, particularly the results obtained in neurogenic muscular atrophies, which have certain characteristic features. The LDH activity in CSF was decreased in peroneal muscular atrophy, the GPT concentration in CSF was elevated in spinal muscular atrophy, and the mean activity of CSF aldolase was increased in amyotrophic lateral sclerosis. The simultaneous determination of enzymes in serum and CSF can provide valuable information in the research of certain details of pathomechanisms and thus lead to further improvement of diagnosis.

Key words: Enzymes – Blood – Cerebrospinal fluid – Neuromuscular diseases

Zusammenfassung. Bei 80 Patienten mit neuromuskulären Erkrankungen und bei 20 Kontrollpatienten wurden die Enzymaktivitäten der CPK, Aldolase, GOT, GPT und LDH im Serum und im lumbalen Liquor vergleichend gemessen. Die Ergebnisse der Serumbestimmungen stimmen mit den Werten der Literatur überein. Die neuartigen Liquorbefunde zeigen signifikante Veränderungen bei motorischen *neurogenen Systemerkrankungen,* während myogene Atrophien keine Abweichungen zeigten. Bei peronealer Muskelatrophie war die LDH-Aktivität im Liquor herabgesetzt. Patienten mit spinalen Muskelatrophien zeigten eine Erhöhung der GPT-Aktivität. Bei Amyotrophischer Lateralsklerose war die mittlere Aldolase-Aktivität signifikant vermindert. Die simultane Bestimmung mehrerer Enzymaktivitäten im Serum und im Liquor kann zur Diagnosestellung und Prognosebeurteilung bei neuromuskulären Erkrankungen beitragen.

Schlüsselwörter: Enzyme – Liquor – Blut – Neuromuskuläre Krankheiten

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0003-9373/81/0230/0307/$01.60

Table 1. Distribution of diagnoses

Myogenic lesions		No. of patients	Neurogenic lesions	No. of patients
Muscular dystrophy			Peroneal muscular atrophy (N I)	8
Duchenne type	(M Ia)	22		
Limb-girdle type	(M Ib)	8	Spinal muscular atrophy (N II)	7
Polymyositis	(M II)	6		
Myasthenia	(M III)	13	Amyotrophic lateral sclerosis (N III)	9
Myotonia congenita	(M IV)	7		
Total		56	Total	24

Introduction

The most sensitive enzyme assayed in muscular diseases is generally considered to be *serum* creatine phosphokinase *(CPK),* which was first used in clinical practice by Ebashi et al. (1959). The highest values of serum CPK have been measured in Duchenne muscular dystrophy (Pearce et al. 1964; Pennington 1977). In polymyositis, especially in the acute forms, serum CPK is usually increased. Contrary to previous findings, more than 50% of patients with neurogenic muscular atrophy were observed to have a rise in serum CPK by Williams and Bruford (1970) and Welch and Goldberg (1972).

A rise in activity of *serum aldolase* is also most expressed in Duchenne muscular dystrophy. However, it decreases with the progression of the disease. Normal values were found in myasthenia and neurogenic muscular atrophies.

The determinations of serum glutamic-oxaloacetic transaminase *(GOT),* glutamic-pyruvic transaminase *(GPT),* and lactic dehydrogenase *(LDH)* have less clinical importance, because their tissue specificity is lower than that of CPK or aldolase.

In the *CSF* of patients with neuromuscular diseases, enzyme determinations have been carried out only by Banerji et al. (1969), who found above normal CPK activity in the CSF of 15 of 26 patients with Duchenne muscular dystrophy.

In the serum and lumbar CSF of our patients with neuromuscular disease, the activities of CPK, aldolase, GOT, GPT, and LDH were regularly determined to obtain data on the varying enzyme levels in various pathological processes, as well as on the relationship of enzyme activities in serum and CSF.

Patients and Method

A total of 80 patients were investigated, and the data of 20 subjects free from neuromuscular, organic neurological and internal diseases were used as controls. The diagnostical distribution of the patients is shown in Table 1: 56 of 80 patients suffered from myogenic and 24 from neurogenic muscular diseases. Venous blood and lumbar CSF samples were taken after the patients had had 12 h of bed rest and fasting.

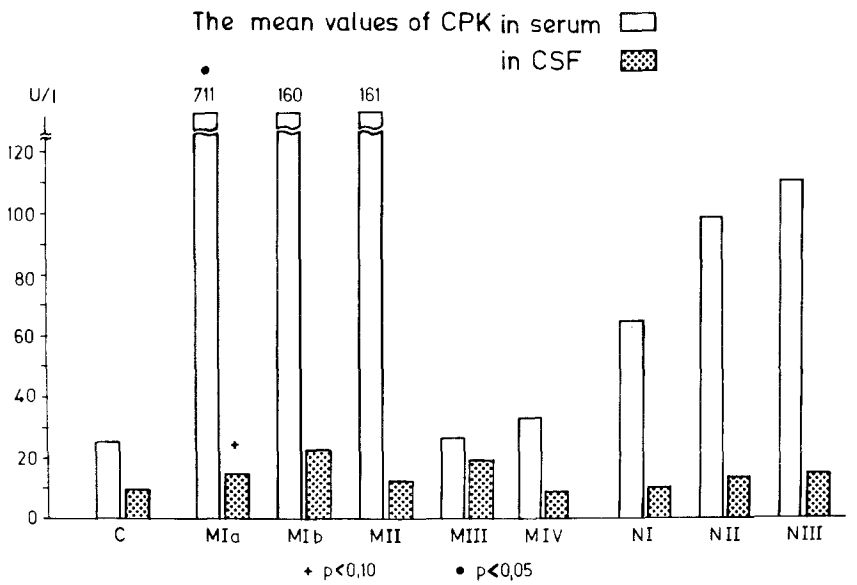

Fig. 1. Comparison of CPK enzyme values of serum and CSF in eight groups of neuromuscular patients (MIa–MIV myogenic, NI–III neurogenic, see Table 1) and controls *(C)*

The activity of CPK, aldolase, GOT, GPT, and LDH was determined both in serum and CSF by the Boehringer UV spectrophotometric method. The total protein concentration of patients and controls was determined by the Exton turbidimetric test in CSF (see Gernand and Hajek 1966). The results were statistically evaluated in the Computer Center of Kossuth University in Debrecen by S. Rochlitz. Student's *t*-test or, where the variances differed significantly, Welch's variant (Welch 1937) were applied. A probability level of $P < 0.05$ was considered statistically significant.

Results

The mean activity of *serum CPK* in Duchenne muscular dystrophy was highly and significantly elevated in comparison to both the controls and the other diseases under study; however, this increase was not significant in the limb-girdle type of muscular dystrophy, probably owing to the high scatter. Of the neurogenic muscular atrophies the value was highest in amyotrophic lateral sclerosis (ALS), but this was also not significant. The mean concentration of *CPK in CSF* in the patients did not differ significantly from that of the controls, but it might be important to note that in Duchenne muscular dystrophy the increase was nearly significant (Fig. 1).

The mean activity of *serum aldolase* in all patients with *myogenic muscular diseases* was higher than in controls. This increase was significant in Duchenne dystrophy, limb-girdle type of muscular dystrophy, myasthenia, and myotonia congenita. In peroneal muscular atrophy (PMA) the serum aldolase value was also significantly elevated. In *CSF* the mean *aldolase* value was, except in ALS, similar to that of the controls; in ALS it was significantly elevated (Fig. 2).

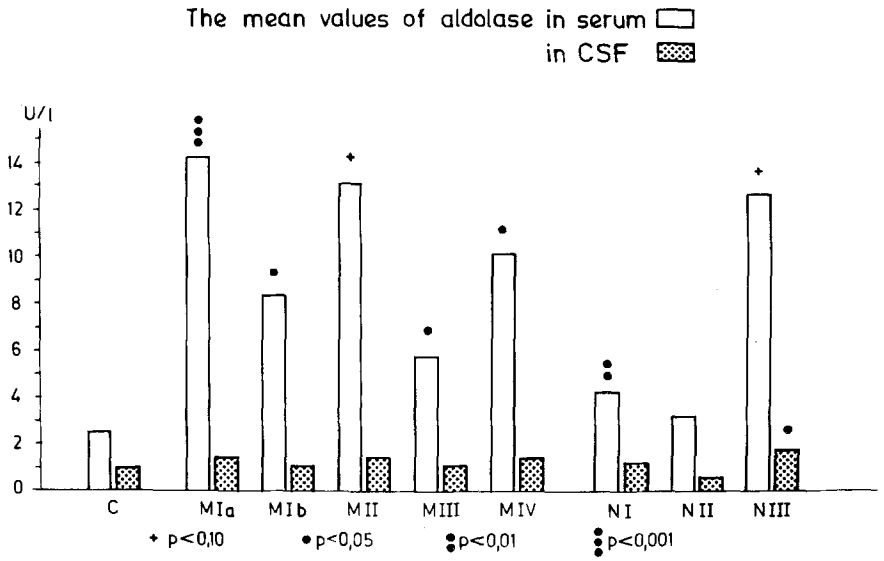

Fig. 2. Comparison of mean aldolase values of serum and CSF in different neuromuscular disorders. Symbols as in Fig. 1 and Table 1

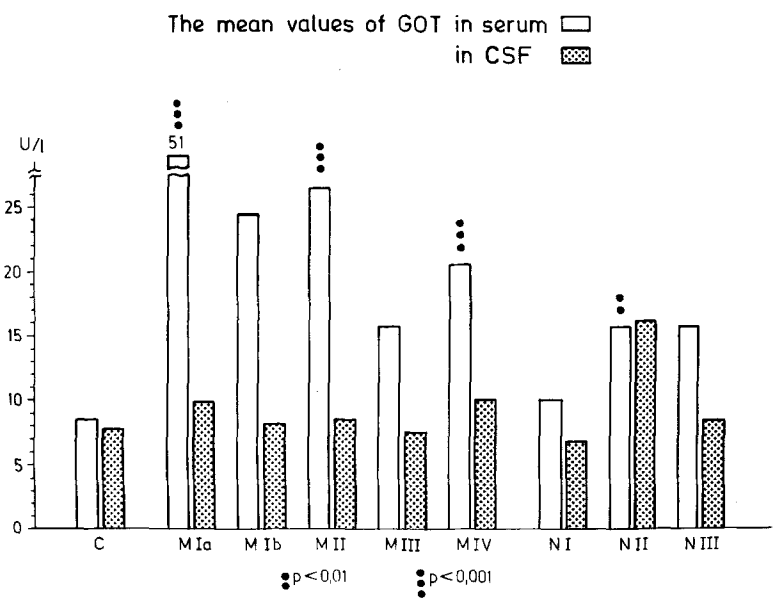

Fig. 3. Mean GOT concentrations of serum and CSF in eight groups of neuromuscular patients. Symbols as in Fig. 1 and Table 1

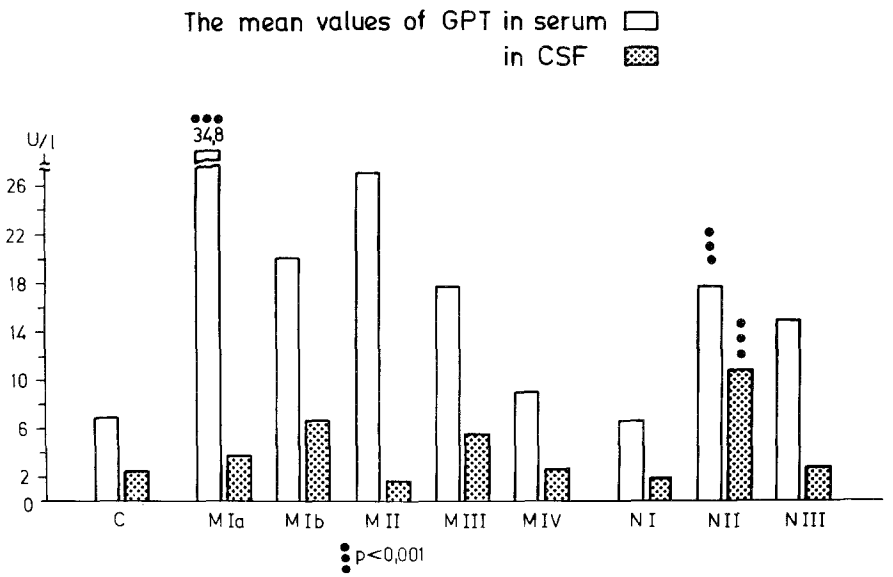

Fig. 4. Mean GPT activities of serum and CSF in eight groups of neuromuscular patients. Symbols as in Fig. 1 and Table 1

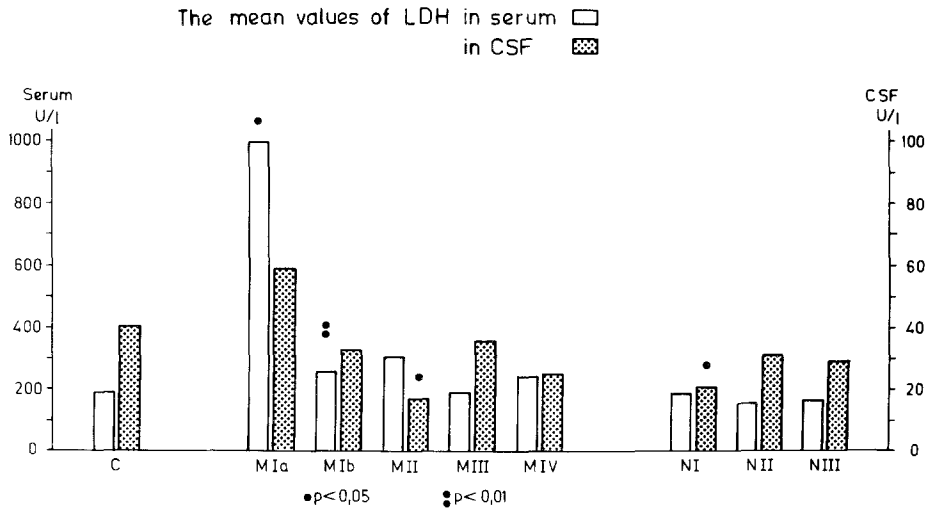

Fig. 5. Comparison of mean LDH enzyme value of serum and CSF in different neuromuscular diseases. Symbols as in Fig. 1 and Table 1

The mean concentration of *serum GOT* was significantly higher in Duchenne dystrophy, in polymyositis, and in myotonia congenita than in controls. A significant increase in activity was observed in spinal muscular atrophy (SMA). In *CSF* the mean *GOT* values for patients did not differ significantly from that of the controls (Fig. 3).

Only in Duchenne muscular dystrophy and in SMA was the mean *serum GPT* level significantly higher than in the controls. In *CSF* the mean concentration of *GPT* significantly increased in SMA (Fig. 4).

The mean *LDH* value of the *serum* was significantly elevated as compared to the controls in Duchenne and limb-girdle types of muscular dystrophy. In *CSF* the mean LDH concentration was significantly lower in polymyositis and PMA than in the controls (Fig. 5).

The CSF total protein content was reduced only in Duchenne muscular dystrophy, while the values in other groups were similar to those of controls. No correlation was found between the changes in enzyme values and total protein concentration in different groups. Similar findings were reported in cerebrovascular diseases by Wroblewski et al. (1957).

When single groups were compared one with the other in pairs, the statistical evaluation indicated that the serum CPK values in ALS, the serum aldolase activity in PMA and SMA, the serum GPT concentration in PMA and ALS, and the serum GOT and LDH values in all three forms of neurogenic muscular atrophy were significantly lower than in Duchenne muscular dystrophy.

Discussion

The determination of serum enzyme activities has been indispensable in clinical practice for nearly three decades. Indirect evidence supports the hypothesis on the muscular origin of serum enzymes in neuromuscular diseases; thus, the level of serum enzymes in neuromuscular disorders is decisively determined by the concentration of the enzymes present in the muscle. However, there is no exact parallelism (Pennington 1969). Enzyme leakage from the muscle tissues is only one essential factor in the formation of serum enzyme concentrations. The increased enzyme leakage from the muscle fibers has drawn attention to the changes of the muscle membrane.

Thus, the regular determination of certain enzymes in serum and CSF may give information of great value for differential diagnosis as well as the courses of pathomechanisms of neuromuscular disorders.

Considerable changes in enzyme values have been found in the different myogenic and neurogenic muscular diseases in the present study. The mean *serum* concentrations of all enzymes studied were markedly higher in *Duchenne muscular dystrophy* than in the controls. Similarly, high serum enzyme values were not obtained in any other neuromuscular diseases. In Duchenne dystrophy, CPK had the highest concentration. After CPK, the order of sensitivity was: aldolase, GOT, GPT, and LDH.

In limb-girdle type of muscular dystrophy, the increase of mean enzyme values in serum was significant only with aldolase and LDH. The mean values of serum

aldolase were slightly, but significantly higher in each myogenic disease than in controls; this supports the idea that aldolase is sensitive to all types of muscle damage, although its increase might be less than that of CPK.

The mean *CSF* enzyme values are practically normal in all myogenic diseases, but the CPK level increases slightly in Duchenne muscular dystrophy. This confirms the findings of Banerji et al. (1969), who state that the increase of CPK concentration in CSF may be due to damage of the brain tissue, increased serum concentration, or to both.

Theoretically, the raised serum enzyme levels may cause the increase of enzyme values in CSF. However, reports on comparison of serum and CSF enzyme values in different neurological disorders found no correlation between CSF and blood serum values (Dubo et al. 1967; Schiavone and Kaldor 1965; Wolintz et al. 1969).

Recent papers have also reported on increased *serum* enzyme activity in *neurogenic muscular atrophies.* Williams and Bruford (1970) observed elevated CPK values in the sera of over 50% of their patients with SMA; however, they found no correlation between enzyme activity and the progression of the disease. Munsat et al. (1973) found serum CPK values rising parallel with the progression of the disease in infantile spinal muscular atrophy.

Valuable data on enzyme values in *CSF* of patients with neuromuscular disorders are not available in the literature. *In PMA* we observed a slight increase in the activity of serum aldolase and a decrease of LDH concentration in CSF. *In SMA* we found significantly elevated GPT values both in serum and CSF, which seem to be characteristic of that disease, and GOT concentration was significantly increased in serum. In *ALS* the elevation of serum CPK was not significant; however, the wide range of values indicates that there were two groups of patients, one with normal, the other with abnormal values. This may represent two different types of the disease. The mean concentration of aldolase in CSF of the patients with ALS showed a significant increase.

Thus, in motor neuron diseases the concentration of some enzymes (aldolase, GPT) can be elevated in CSF. The normal CSF values of aldolase and GPT in patients with muscular diseases are evidence against the peripheral origin (blood serum) of the enzyme activities. Also, the relatively higher CSF enzyme values support the participation of the central nervous system in these pathological processes.

Our results are in agreement with the literature and also emphasize the role of enzyme determinations in the diagnosis of neuromuscular disorders. The simultaneous determination of several enzymes, possibly the above-mentioned five, in serum and in CSF as well as their relationship may contribute to the accuracy of diagnosis and an estimation of the progression of disease.

Acknowledgements. The authors are grateful to M. Kovács for her help in laboratory investigations. This study was supported by the Ministry of Health, Hungary, grant No. 2-20-0303-01-0/M.

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Received January 26, 1981