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Ion Concentrations in Serum and Cerebrospinal Fluid of Patients with Neuromuscular Diseases

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Summary. The Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, and P_i concentrations in serum and lumbar CSF of 17 controls and 62 patients with neuromuscular diseases were determined and the values statistically evaluated. Although alterations in ion concentrations specifical to different groups were not observed in either of these biological fluids, the significant increase in serum P_i concentration in Duchenne muscular dystrophy seems to be remarkable. It is suggested that the possible alterations in the ion content of the serum and CSF may contribute additional data to the diagnosis of various neuromuscular diseases.

Key words: Ions – Cerebrospinal fluid – Neuromuscular diseases

Zusammenfassung. Bei 62 Patienten mit neuromuskulären Erkrankungen und bei 17 Kontrollpatienten wurde die Konzentration von Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^- und anorganischem Phosphor (P_i) im Serum und im lumbalen Liquor vergleichend gemessen, und die Werte wurden statistisch bearbeitet. Obwohl keine für die verschiedenen Erkrankungstypen charakteristischen Veränderungen beobachtet werden konnten, ist die signifikante Erhöhung der P_i-Konzentration im Serum bei Duchenne-Dystrophie doch erwähnenswert. Die eventuellen Veränderungen der Ionenkonzentration im Serum und im Liquor können zur Diagnosestellung bei verschiedenen neuromuskulären Erkrankungen beitragen.

Introduction

The role of ions in neuromuscular disorders was first noted in studies on the hyperkalemic and hypokalemic forms of periodic familial paralyses as well as in reports on the so-called "nutritive" or "ion-deficient" myopathies (Cohen et al. 1952; Heggtveit 1969; Nielsen and Thaysen 1971; Oh et al. 1971; Smith et al. 1950; Ravid and Robson 1976; Wolf et al. 1972).

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Apart from these pathological conditions there is little literature on determinations of ion content in the serum of patients with neuromuscular diseases. Danowski et al. (1956) measured ion concentrations in the sera of patients with childhood muscular dystrophy and found that the P_i and Ca^{2+} content was elevated, Cl^- content was decreased whilst Na^+ and K^+ values remained essentially normal. Smith et al. (1962) observed significantly lower serum Mg^{2+} values in patients with muscular dystrophy than in the control group. Ludmány et al. (1972), however, found lower than normal Mg^{2+} concentrations in the CSF of children with muscular dystrophy. The measurement of ion contents has been carried out in the majority of the cases in serum. There is no data available on regular ion determinations in the CSF of patients with various neuromuscular diseases.

The present paper refers to systemic and simultaneous determinations of ion concentrations in serum and lumbar CSF of patients with neuromuscular disorders in order to detect any possible relationships between the various forms of diseases and the differences in ion contents.

Patients and Methods

The examinations were performed on 62 patients. For control values the data on 17 subjects free from symptoms of neuromuscular, organic neurological, or internal diseases were used. The diagnostic distribution of the patients (Table 1) shows that 44 of the patients suffered from myogenic and 18 from neurogenic muscular diseases. There were 24 males (mean age: 17.6 years) and 20 females (mean age: 31.5 years) in myogenic group and 8 males (mean age: 30.2 years) and 10 females (mean age: 36.0 years) in neurogenic group. The control group consisted of 9 males and 8 females with mean ages of 26.0 and 32.8 years, respectively. Cases of periodic paralysis due to abnormalities in ion metabolism, as well as patients with nutritive myopathy were not included in this study. Neither the patients nor the control subjects received drugs or a diet which could specifically influence the ion determinations.

K^+, Na^+, Ca^{2+}, Mg^{2+}, Cl^- and P_i (inorganic phosphorus) concentrations were determined in the serum and lumbar CSF of both patients and controls. Determinations of Na^+, K^+ and Ca^{2+} were performed by flame photometry following deproteinisation with 20% trichloroacetic acid. The measurement of Mg^{2+} and P_i was carried out photometrically with titanium yellow and ammonium molybdate, respectively. Cl^- concentration was determined mercurometrically. The scatter of errors of the laboratory techniques used was within generally accepted limits (± 1–3%)

Table 1. Distribution of diagnoses

Myogenic lesions		No. of patients	Neurogenic lesions	No. of patients
Muscular dystrophy			Peroneal muscular atrophy	
Duchenne type	(M Ia)	17	(N I)	6
Limb-girdle type	(M Ib)	8	Spinal muscular atrophy	
Polymyositis	(M II)	5	(N II)	5
Myasthenia	(M III)	10	Amyotrophic lateral sclerosis	
Myotonia congenita	(M IV)	4	(N III)	7
Total		44	Total	18

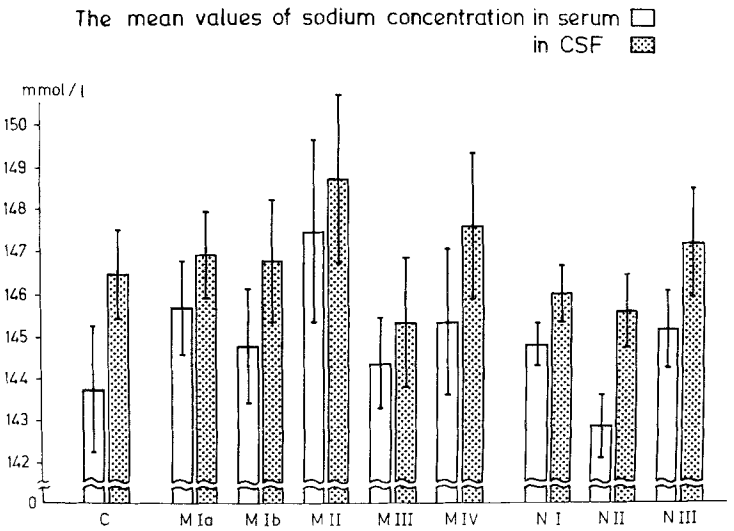

Fig. 1. Mean sodium values of serum and CSF in 8 groups of neuromuscular patients (M Ia–M IV: myogenic, N I–N III: neurogenic, see as in Table 1) and controls (*C*)

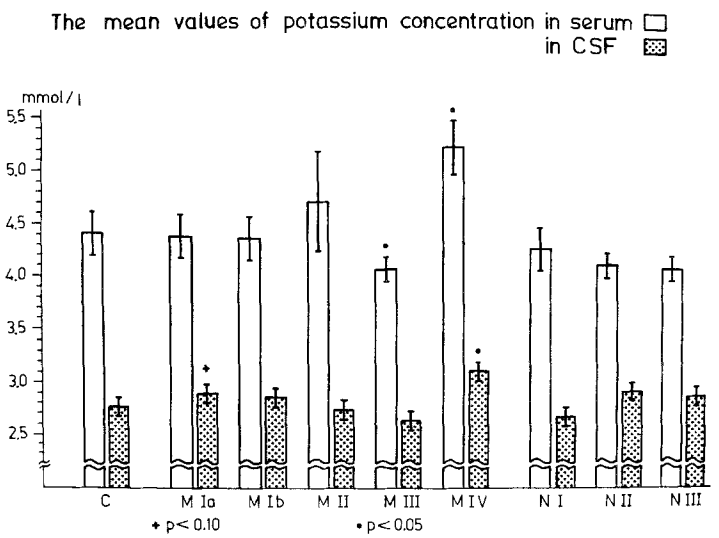

Fig. 2. Mean potassium concentrations of serum and CSF in 8 groups of neuromuscular patients. Symbols as in Fig. 1 and Table 1

and repeat measurements were rarely performed. The data were statistically evaluated, using the Student's t-test and the Welch's test (Welch 1937). A probability level of $P < 0.05$ was considered statistically significant.

Results

The mean *sodium* values in patients did not differ significantly from those in controls either in serum or in CSF (though in Duchenne muscular dystrophy and in polymyositis a moderate but not significant increase in serum Na^+ concentration was observed) (Fig. 1).

In muscular dystrophies, polymyositis and neurogenic lesions the serum *potassium* concentration was similar to that of the control group, whilst it was mildly but significantly decreased in myasthenia ($P < 0.05$), but in the cases of myotonia congenita it was elevated ($P < 0.05$). The K^+ concentration of *CSF,* similarly to that of the serum, was elevated in myotonia congenita ($P < 0.05$). Moreover, a tendency to an increase in CSF K^+ concentration was observed in Duchenne muscular dystrophy. Values of K^+ content in CSF found in the other types of myogenic lesions and the neurogenic muscular atrophies did not differ

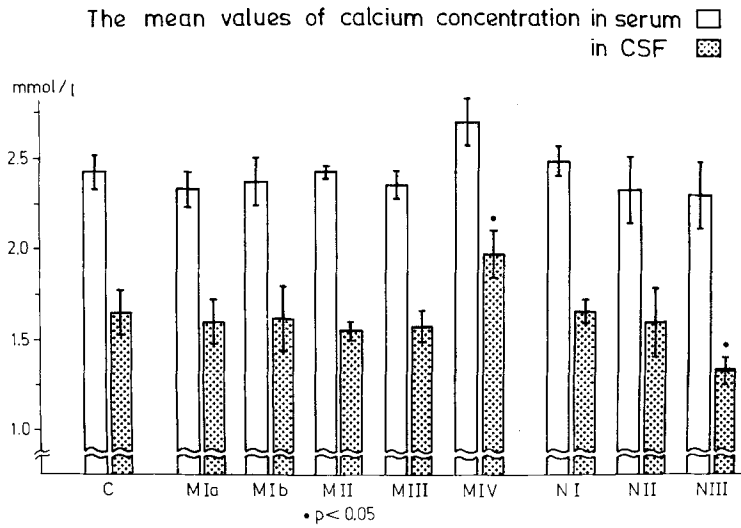

Fig. 3. Mean calcium concentrations of serum and CSF in different neuromuscular disorders. Symbols as in Fig. 1 and Table 1

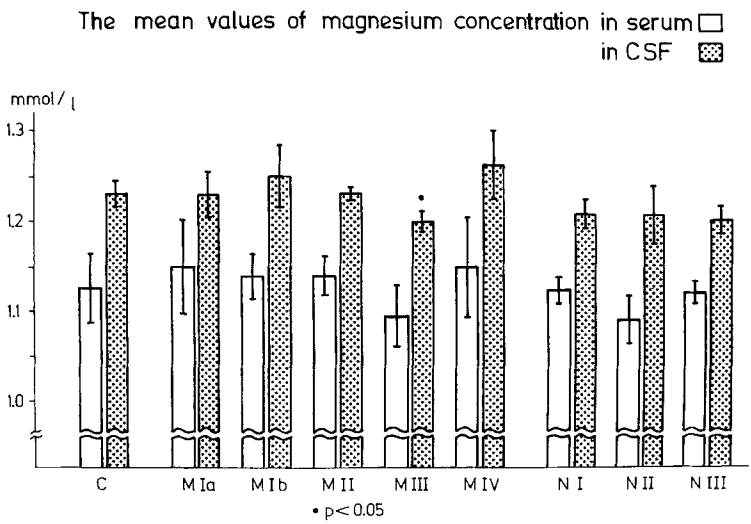

Fig. 4. Mean magnesium values of serum and CSF in various neuromuscular diseases. Symbols as in Fig. 1 and Table 1

from those in controls. Comparing the data obtained in different groups we found that the K^+ content of CSF was higher in Duchenne dystrophy than in peroneal muscular atrophy (Fig. 2).

The concentration of *calcium* in the *sera* of patients did not show significant deviation from that of the controls. A significant increase ($P<0.05$) of Ca^{2+} concentration in *CSF* was observed in myotonia congenita, whereas there was a significant decrease in amyotrophic lateral sclerosis ($P<0.05$, Fig. 3).

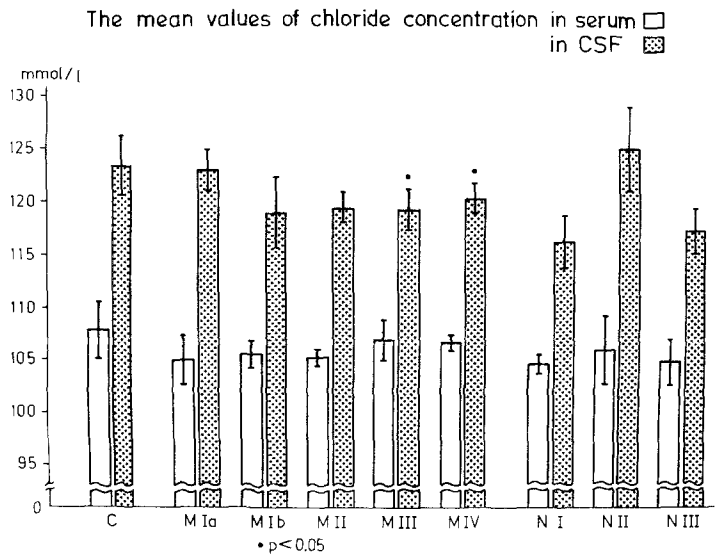

Fig. 5. Mean chloride concentrations of serum and CSF in 8 groups of neuromuscular patients. Symbols as in Fig. 1 and Table 1

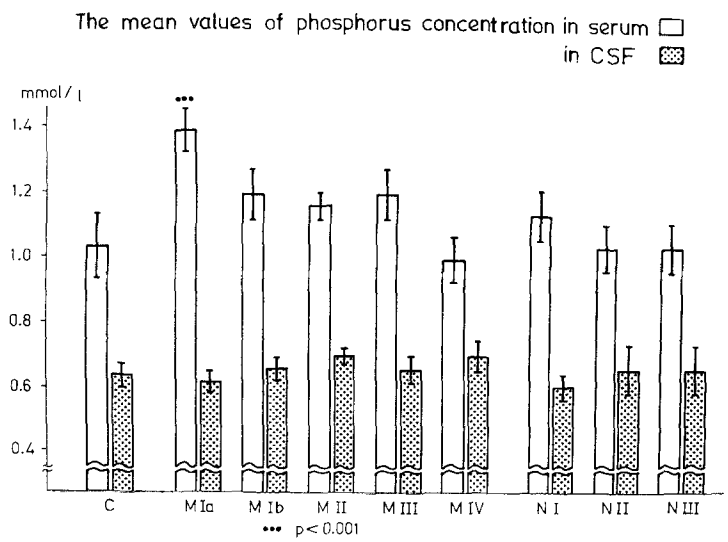

Fig. 6. Mean phosphorus concentrations of serum and CSF in 8 groups of neuromuscular patients. Symbols as in Fig. 1 and Table 1

The concentration of *magnesium* in *serum* and *CSF* was essentially identical in the neuromuscular diseases and in the control group except in myasthenia where the Mg^{2+} concentration in CSF was mildly but significantly lower ($P < 0.05$) than in the controls (Fig. 4). The value of the CSF Mg^{++}/serum Mg^{++} quotient was 1.06 in muscular dystrophy, and 1.07 in the control group.

The decrease in mean values of serum *chloride* in the patients was not significant. Similarly, the Cl^- content of *CSF* was a little lower than in the controls; however, the difference was significant only in myasthenia gravis and myotonia congenita ($P < 0.05$, Fig. 5).

The raised concentration of *inorganic phosphorus* (P_i) in *serum* was highly significant ($P < 0.001$) in Duchenne muscular dystrophy. On the other hand, in the other types of myogenic lesions and in neurogenic muscular atrophies the serum P_i values were normal. The P_i concentration of *CSF* showed no significant change either in the myogenic or in the neurogenic muscular disorders (Fig. 6).

Discussion

The ion concentration of CSF truly reflects the ion concentration of the extracellular space of the central nervous system (Davson 1967; Plum and Siesjö 1975). The ion content of the serum, on the other hand, refers to the ion content of the interstitial fluid space of the body. This may be reflected by changes in the chemical composition of muscle leading to alterations in the ion composition of body fluids (Pennington 1969).

However, the number of publications in this field is very small, and the results are often contradictory. Our results, too, only partially confirm the otherwise scanty data in the literature. Similarly to Danowski et al. (1956), we observed the very significant elevation of serum P_i content in patients with Duchenne muscular dystrophy, on the other hand, we found no such change in serum Ca^{2+} and Cl^- concentrations. To explain the causes of the high serum P_i content in Duchenne dystrophy, only speculative assumptions can be suggested. It may reflect the delay of "biochemical maturation" only, but it is also possible that the hyperphosphatemia is related to a disturbance of creatine metabolism.

Smith et al. (1962) found low serum Mg^{2+} levels in human muscular dystrophy, while Ludmány et al. (1972) observed significantly lower Mg^{2+} concentrations only in the CSF in children with muscular dystrophy. They calculated the value of the CSF Mg^{2+}/serum Mg^{2+} quotient to be lower in muscular dystrophy (1.15) than in the control group (1.35). We could not confirm these data since in our patients with muscular dystrophy the Mg^{2+} concentration did not differ from the controls either in serum or in CSF. The CSF Mg^{2+}/serum Mg^{2+} quotient was also identical in controls and patients with muscular dystrophy. (In contrast, the CSF Mg^{2+} content decreased in myasthenia.)

It is of interest that the concentration of potassium was slightly increased while the ratio of Na^+/K^+ was lower in CSF of the patients with Duchenne muscular dystrophy compared to the controls. The changes in the electrolyte concentrations may reflect a disturbance in membrane transport mechanisms. In an analysis of the carbohydrate metabolism we found remarkable lactacidosis and a NADH/NAD^+

ratio in CSF indicating a shift to the reduced form in Duchenne muscular dystrophy (Mechler et al. 1981). These findings are consistent with the concept of a disturbance in energy metabolism of the central nervous system in that disease.

A similar NADH/NAD^+ ratio was found in peroneal muscular atrophy, however, the K^+ concentration was almost normal indicating that the disturbance of the energy metabolism was not severe enough to interfere with the membrane transport mechanisms. The causes of ion alterations observed in serum and CSF of patients with neuromuscular disorders are unknown. Nevertheless, the data on ion content determinations can be used to make the diagnosis more precise. In myotonia congenita the increase in K^+ concentration of serum and CSF, the elevation of Ca^{2+} concentration in CSF, and the decrease in Cl^- content in CSF appear to be obvious. However, owing to the small number of cases no definite conclusions can be drawn from these findings. In myasthenia the serum K^+ and CSF Mg^{2+} concentrations decreased. The incrase of serum P_i content in Duchenne muscular dystrophy is remarkable. In amyotrophic lateral sclerosis the concentration of Ca^{2+} in CSF was moderately decreased, otherwise the ion concentrations were normal in the neurogenic muscular atrophies.

Thus, in the different neuromuscular diseases the slight deviations of ion contents from the normal values may contribute to an improvement in accuracy of the diagnosis. It is well known that the interpretation of ion concentration, primarily as a consequence of the variety in regulatory mechanisms, involves serious difficulties. However, we consider that a more detailed investigation of ion concentrations both in muscles and body fluids has promising prospects in the various neuromuscular diseases.

Appendix

There were 24 males (mean age: 17.6 years) and 20 females (mean age: 31.5 years) in myogenic group (male/female: 17/0, 4/4, 1/4, 0/10 and 2/2 in M Ia, M Ib, M II, M III, and M IV subgroups, respectively) as well as 8 males (mean age: 30.2 years) and 10 females (mean age: 36.0 years) in neurogenic group (male/female: 2/4, 2/3 and 4/3 in N I, N II and N III subgroups, respectively). The control group consisted of 9 males and 8 females with mean age of 26.0 and 32.8 years, respectively.

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