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Cerebrospinal Fluid Magnesium Level in Different Neurological Disorders

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ABSTRACT

Magnesium (*Mg*) *is an essential cofactor for many enzymatic reactions, especially those involved in energy metabolism. The aim of the present study was to determine the CSF concentration of Mg in various neurological disorders* (*n* = 72) *and in healthy subjects* (*n* = 75)*. The control group included* 35 *males and* 40 *females, aged* 16-89 *years* (*mean age* 53 *years*) *who were subjected to a lumbar puncture for diagnostic reasons. The CSF examination was normal mainly as concerns the macroscopically examination, the leukocyte count and the protein level. The determination of Mg was performed with xylidyl-blue photometry. Our normal CSF Mg mean value was* 0.97 ± 0.08 *mmol/l* (*range* 0.6-1.4 *mmol/l*)*. In the group of patients* (*n* = 11) *with convulsive seizures a slightly but significantly lower Mg were revealed* (0.92 ± 0.03 *mmol/l; p* = 0.001*; paired two-tailed Student's t-tests*)*. No statistically significant change of CSF Mg levels was noted in patients suffering from alcohol withdrawal syndrome, multiple sclerosis or Bell's palsy. Our results indicate that magnesium deficiency may play a role for seizure manifestation even in patients with a moderate low Mg without neurological signs. Low CSF magnesium is associated with epilepsy, further studies may determine the influence of anti-epileptic drug therapy on CSF magnesium levels.*

Keywords*: *Magnesium, Cerebrospinal Fluid, Seizures, Epilepsy

1. Introduction

The significance of trace elements concentration in the serum and various body fluids has been demonstrated in a number of publications. However, magnesium determinations in the cerebrospinal fluid (CSF) in neurological diseases has been reported only in a small number of communications [1-3]. Recently, a greater emphasis has been given to the role of trace elements in the function of the nervous system both in normal and pathological conditions. However, the results are variable and the object remains open for further investigation. It has been suggested that low serum Mg has occasionally been associated with significant effects on the central nervous system especially in epilepsy and alcoholism. Magnesium deficiency-dependent seizures may be a relevant factor for epileptogenesis. Further studies in the future may determine the influence of anti-epileptic drug therapy on CSF magnesium levels. The existing knowledge about the impact of magnesium on epilepsy and other neurological diseases is poor and controversial. Therefore, in this study, we purposed evaluation of the level of CSF concentration of Mg in a total of seventy-two neurological patients and seventy-five healthy controls.

2. Methods

2.1. Patients

We studied prospectively all patients over 16 years who were subjected to a lumbar puncture for diagnostic reasons. The control group (n = 75) had mainly attended the Neurological Department because of headache or psychoneurosis and the CSF examination was normal as concerns the macroscopically examination, the leukocyte count and the protein level. Patients who were treated with magnesium or calcium supplements or any drugs that contain these electrolytes were excluded. A contraindication for lumbar puncture or a loss of indication for performance was also exclusion criteria. Every patient had a detailed history taken and clinical examination, including general and neurological status by a neurologist. The lumbar puncture was mainly performed on admission. CSF and serum magnesium levels were checked immediately afterwards.

2.2. Chemical Analysis

The determination of Mg was performed with xylidyl-blue photometry (Hitachi 717). CSF analysis included:

cell count (normal values: total white cells < 5 cells/mm^3, protein (normal value < 0.5 g/l), glucose (normal value > 50% of blood glucose) and lactate (normal value 1.1 to 3.2 mmol/l).

2.3. Statistics

Paired two-tailed Student's t-tests were used to compare CSF magnesium in different groups. The study was approved by the ethics committee of the University of Witten/Herdecke according to the revised Declaration of Helsinki.

3. Results

Seventy-two patients (40 male and 32 female) and seventy-five healthy subjects (35 males and 40 females) fulfilled the criteria of the study. Their ages ranged from 16 to 93 years (mean 53.6 y). The patient-group included neurological diagnosis like bell's palsy (n = 12), multiple sclerosis (n = 10), alcohol withdrawal syndrome (n = 16), Lyme disease (n = 4), stroke (n = 6), HSV-encephalitis (n = 3), meningitis (n = 3), dementia (n = 3), polyneuropathy (n = 5), Guillain Barrè syndrome (n = 2) and other (n = 8). The magnesium CSF level averaged 0.97 mmol/l, SD 0.08 mmol/l (range 0.6-1.4 mmol/l; normal values 0.77-1.17 mmol/l). Serum Mg and CSF Mg do not correlated. CSF magnesium varied not as a function of age (**Figure 1**). The correlation between CSF Mg and CSF protein failed to reach significance (**Figure 2**). In the group of patients with convulsive seizures (n = 11) a slightly but significantly lower Mg were revealed (0.92 ± 0.03 mmol/l; p = 0.001; paired two-tailed Student's t-tests; **Figure 3**). No statistically significant change of CSF Mg levels was noted in patients suffering from alcohol withdrawal syndrome, multiple sclerosis or Bell's palsy.

4. Discussion

There are many previous studies of serum Mg concentration of normals and patients, but only few of CSF concentration of the same metal. Our normal values are in accordance with these [4-6].

Hypomagnesemia is common in alcoholic patients admitted to the hospital; in one study for example, the

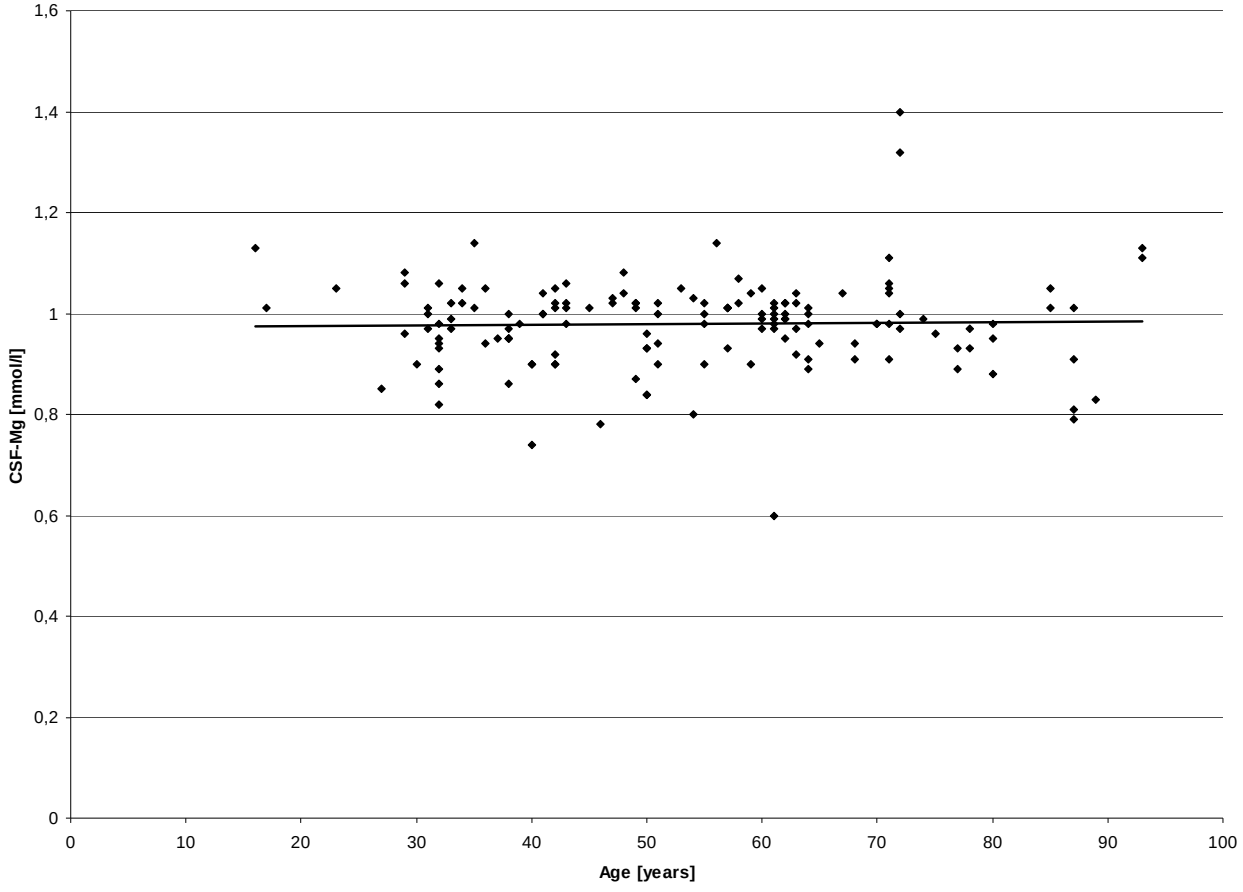

Figure 1. Age distribution of CSF-magnesium.

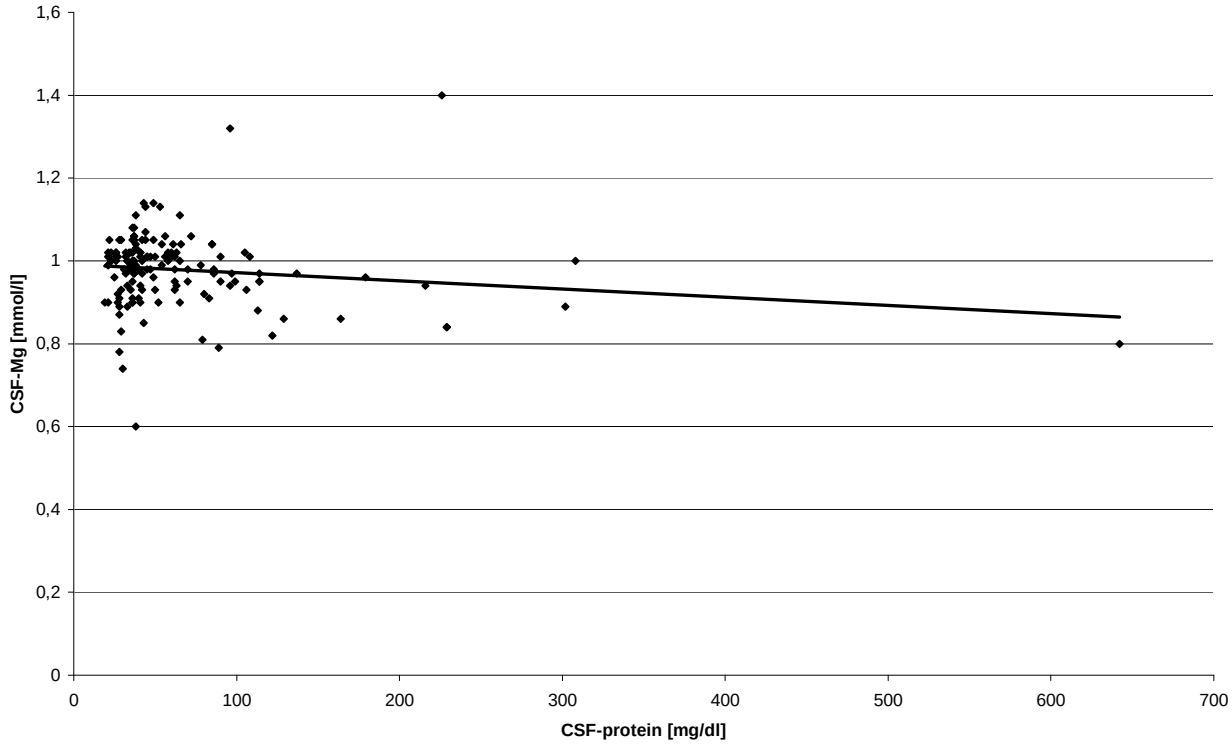

Figure 2. Correlation between CSF-Mg and CSF-protein.

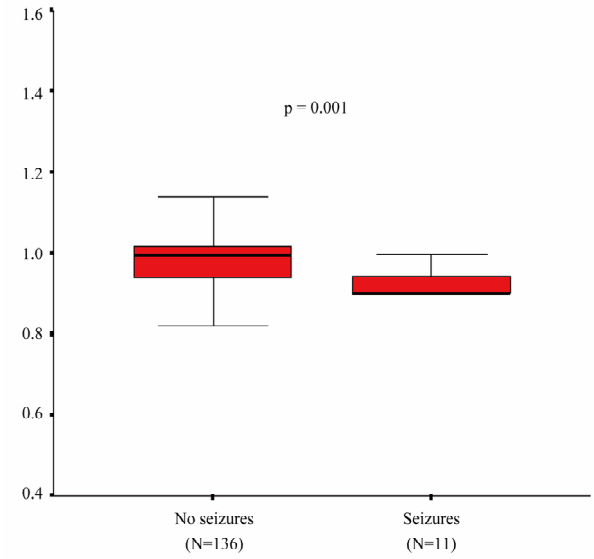

Figure 3. Significantly lower CSF-Mg in the group of patients with convulsive seizures.

prevalence was 30 percent [7]. In a prospective study of 82 patients with alcohol-related admission diagnoses 14 were hypomagnesemic while 16 had a normal plasma magnesium concentration [8]. However, consistent with other studies we found normal CSF magnesium in alcohol withdrawal syndrome and a lack of correlation between plasma and CSF magnesium levels [9]. Although the role of magnesium in neuronal function is not completely understood, a lowering of CSF or brain magnesium can induce epileptiform activity and there is an association between decreased CSF magnesium and the development of seizures [10-15]. Over 300 intracellular enzyme processes depend on magnesium for activation. Many of these enzymes, including pyruvate kinase, adenylate cyclase, and pyrophosphatase, undergo a conformational change when magnesium binds, thus activating the enzyme. Altering the magnesium concentrations within the physiological range results in concentration-dependent changes in the Na+/K+ -ATPase activity, which may result in increased seizure susceptibility [11]. Within the cell, an optimal concentration of magnesium is required for DNA synthesis, making protein synthesis in part dependent on adequate magnesium levels [16]. In addition, magnesium is required for cell membrane fluidity and stability and regulates the permeability of membrane to other cations such as potassium and calcium. Finally, magnesium regulates the binding or function of opiate and N-methyl-D-aspartate (NMDA) receptors. Magnesium, at physiological concentrations, blocks NMDA receptors in neurones [17]. Many NMDA receptor antagonists have a potent antiepileptic properties and activation of NMDA

receptors may also contribute to epileptogenesis. The mechanisms of epileptogenesis are not well established. Several studies in the last few years suggested that the body electrolytes, level of some trace elements, and membrane lipid peroxidation due to increase in free radicals or decrease in activities of antioxidant defense mechanisms may be causally involved in some forms of epilepsies and also to increase the recurrence of seizures. The therapeutic consequence of these findings may have some importance.

5. Conclusions

Our results indicate that magnesium deficiency may play a role for seizure manifestation even in patients with a moderate low CSF Mg without neurological signs. In accordance with our results Miyamoto *et al*. showed recently in a study in convulsive children significantly lower CSF Mg than in non-convulsive children [18]. The role of low CSF magnesium concentration in the induction of seizures is not fully understood but may involve alteration of NMDA receptor regulation in the central nervous system.

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