

Evaluation of Magnesium Levels in Serum and Cerebrospinal Fluid of Patients with Febrile Convulsion Hospitalized in Bahrami Hospital in Tehran in 2010-2011

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Received: 31 Dec. 2013; Accepted: 22 Dec. 2014

Abstract- Evaluation of magnesium levels in serum and cerebrospinal fluid of patients with febrile convulsion (FC) hospitalized in Bahrami hospital in Tehran in 2010-2011. In the past, decreased levels of magnesium in serum and CSF of patients with FC were reported. The purpose of this study was to identify the possible role of magnesium in febrile seizures in children. Identifying this condition, we may control seizures and also prevent subsequent convulsion. In this cross-sectional study, inclusion criteria were the existence of convulsion due to fever and exclusion criteria were having a known neurological disease which could induce a seizure, and children younger than one month. In each group (cases include children with febrile convulsion and controls include febrile children without convulsion), Mg was measured in blood, and cerebrospinal fluid of 90 children and then they were compared. The data were analyzed by SPSS ($\alpha=0.05$). The mean serum and CSF levels of Mg in case and control groups were equal ($P<0.87$ and $P<0.22$ respectively). There was no difference between two groups in terms of sex, but mean age was significantly different ($P<0.003$). There was not an association between serum and CSF levels of magnesium and the presence of FC. Therefore, it's not suggested to measure the level of magnesium in serum or CSF in children with fever routinely.

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Acta Med Iran 2015;53(12):778-781.

Keywords: Febrile convulsion; Serum magnesium; Cerebrospinal fluid magnesium; Children

Introduction

Febrile convulsions (FCs) are the most common type of seizure and occur in 2-4% of all children (8). Factors like genetics, neurotransmitters level changes and a few of trace elements have been introduced as possible causes (1-3); however, the main cause is unknown yet.

Because 30- 40% of children who experience an FC will have a recurrence, it makes FC an important issue to understand and prevent (4).

In the past, blood tests (i.e. electrolytes and magnesium) for first FC in children were not suggested, but recently several studies have shown the effect of GABA, Zn, and Fe in developing FC offering possible interference of other trace elements.

Blood level disorders of Na, Ca, or Mg accompanies

the most possibility for inducing convulsion. Homeostasis of these electrolytes' blood levels is necessary for maintaining CNS function. Changes in cell membrane ions' gradient can lead to direct and indirect impacts of nervous discharges and thus facilitating convulsion like activities (5).

Magnesium (Mg) is involved in nervous system functioning and inhibits facilitating effects of calcium on synaptic transport. It has blocking and voltage dependent effect on N-methyl-D-aspartate receptor canal (6).

Mg is a chemical gatekeeper, so Ca⁺ entry to nervous cell increases due to Mg deficiency, and finally causes overstimulation, spasm, and convulsion (7).

In addition, a few studies show the relationship between FC occurrences and lower serum and CSF Mg

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levels (6,13).

With regard to these matters, this cross sectional study was designed for assessing and comparing Mg levels in serum and cerebrospinal fluid (CSF) of children with FC and children with fever without a seizure.

Materials and Methods

This study was carried out on children with FC referred to Bahrami Hospital in Tehran, Iran. Exclusion criteria were the existence of a known seizure inducer, neurologic disorder, and being neonate.

Data was collected by observation, examination and lab tests; then were entered in a checklist including demographic characteristics and other necessary information. Mg was measured and then was compared in groups, FC (A) and fever without seizure (B) groups.

Magnesium level in plasma and CSF was measured by the biochemical method (xylidyblue, Pars azmoon kit) and atomic absorption spectrophotometry (automatic analyzer 902, Hitachi, Japan). Normal range for Mg was 1.5-2.3 mg/dl in serum and 1.2-3.3 mg/dl in CSF). All costs of tests were paid by the researcher.

The method of sampling was convenience and samples in group A, and B were selected simultaneously. Then, after obtaining informed consent, blood and CSF samples were taken.

Sample size, 30 samples in each group, was calculated based on previous studies using the formula for comparing means between two groups with 95% significance level and 80% power.

Data was analyzed with SPSS (version 11) software, using Independent samples t test, Mann-Whitney U test, one sample t test, and Chi square.

All personal information was kept confidential and offered treatment didn't change even if individual rejected participating in the study.

This study was a post graduate thesis (residential level) and has been approved by scientific and ethics committee.

Results

The number of study participants was ninety (50 in A and 40 in B group). There were 49[54.5% (95%CI: 44-65)] girls and 41[45.7% (95%CI: 35-56)] boys. In FC group, the number of girls was 21 (42%) and boys 29 (58%). No difference was found in sex prevalence between A and B groups ($P < 0.45$). Mean age was different, 13.1 (± 11.2) and 36.1 (± 30) months in group A and B, respectively ($P < 0.004$). The age range was 71 months in group A and 154 months in group B.

There was no significant difference between serum and CSF Mg levels in A and B groups (Table 1).

Table 1. Mean and standard deviation of serum and CSF Mg levels in children with FC (group A) and children with fever without seizure (group B)

Variable	group		P value	95%CI
	A	B		
Serum Mg(Mg/dl)	2.26 (± 0.27)	2.27 (± 0.22)	0.87	-0.13, 0.11
CSF Mg(Mg/dl)	2.36 (± 0.19)	2.3 (± 0.24)	0.53	-0.04, 0.15

*P value < 0.05 is significant

Mg level of serum in group A was significantly higher than 1.5 Mg/dl (minimum of serum Mg normal range) (Table 2).

Mg level of CSF in group A was significantly higher than 1.2 Mg/dl (minimum of CSF Mg normal range) (Table 2).

Table 2. Comparing mean of serum and CSF Mg with minimum of normal level (NL)

Variable	Mean		P value	Mean difference
	FC	NL		
Serum Mg	2.26	1.5	*0.001	0.76 (Mg/dl)
CSF Mg(Mg/dl)	2.36	1.2	*0.001	1.16

*P value < 0.05 is significant

Discussion

FC is the most prevalent convulsive disorder in children 6 months – 5 years old and thus, the mean age of case group was significantly lower than the control group, but sex ratio was similar. Lumbar puncture (LP) is strongly advised in children under one year old with first FC to rule out meningitis because of the probability of absence of other signs of infection. For similar reasons, LP is suggested until 18 months (8) but after that, performing LP has considerable limitations, so many studies only measure the Mg levels of serum.

However, in this study, while there was an indication, after taking informed consent, LP was done in children over 18 months old with fever but no seizure. Assessing Mg levels in CSF in addition to serum is the strength of this study.

Serum Mg level in this study didn't show any significant difference between group A and B, which is similar to studies by Burhanoglu, Donaldson, Rutter and Heipertz (2,9-11), but it was inconsistent with works by Prakash, Mroczkowska-Juchkiewicz, Papierkowski, Chhapparwel, Talebian, Derakhshan and Sadinegad which found difference between them (6,12-17).

Mg levels of CSF was similar in this study between group A and B, like Burhanoglu, Donaldson and Rutter studies (5,13,14), conversely Prakash, Mroczkowska-Juchkiewicz, Papierkowski, and Chhapparwel found a significant difference between two groups (6,9,12,13).

In Prakash study, sample sizes in subgroups were much lower than current study; in addition, children in the control group had CNS infection that may damage brain blood barrier caused electrolytes leakage to CSF; so these can be the reasons for different results.

In Mroczkowska case-control study which has been conducted on 49 children (28 cases and 21 controls), sample sizes in subgroups were fewer than ours (increased risk of chance error) (12).

Papierkowski compared Mg levels of serum and CSF between 18 children with FC and 15 healthy children. Inconsistency between results could be due to the difference between control groups in two studies which were healthy instead of febrile children or because of lower sample size in Papierkowski study (13).

In Chhapparwel study, magnesium levels of serum and CSF were compared among 100 children with FC and normal level of magnesium in the study area. It was found that this measure is significantly lower in children with FC. After 2 weeks and recheck of 36 children had increased Mg level in CSF (not serum) was seen.

Different results could be due to diversity in a number of cases (100 in Papierkowski study vs.49 in ours) or controls (healthy children in Papierkowski study vs. febrile without convulsion in ours) (14).

In Talebian's study like current study, there is a case control study with 60 febrile children without convulsion as controls. In comparison with 90 controls in this study, this number of controls could be a reason for different results. Sex ratio in the Talebian study was unlike to present study (males more than females) but there was no significant difference in FC prevalence between two sexes. Another difference in this study which could justify the results' diversity is equality of age range and mean in Talebian study. This study only measured serum magnesium (15).

Another research with different results was Derakhshan's case-control study, with lower sample size compared to this study. Mean age was similar in case and control groups which were different from present study. The control group was consisted of healthy children while it consisted of febrile children in current study. Sex ratio was inconsistent with present research (males more than females) but there was no point about any difference between them, therefore, if it existed, it could be the reason (sex factor as a confounder) (16).

Saadi nejad's cross-sectional study was conducted on 102 participants. Mean age was similar in case and control groups. This study measured serum Mg level only (17).

Overall, two major reasons for diversity in results were the difference in the target population of studies and sample sizes.

The Mg level of serum and CSF in group A was significantly higher than 1.5 and 1.2 Mg/dl (minimum of Mg normal ranges in the applied kit, respectively) which was similar to other findings of this study.

Based on this study, measuring serum and CSF Mg levels in febrile children, as a predictive factor for seizure is not recommended.

Given present discrepancies among findings, it seems that there is a need for further researches with larger sample sizes or different methodologies to show the role of Mg in inducing convulsion in febrile children.

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