ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN — POLONIA
VOL. LV, 19 SECTIO D 2000

Department of Infectious Diseases, University School of Medicine, Lublin
Katedra i Klinika Chorób Zakaźnych Akademii Medycznej w Lublinie

HANNA FOTA-MARKOWSKA,
ROMANA ROLLA-SZCZEPAŃSKA, ROMA MODRZEWSKA

Serum Mg level in measles patients during the acute phase and convalescence

Poziom magnezu w surowicy krwi chorych na odrę w ostrym okresie choroby i w rekonwalecsencji

The live measles vaccine, introduced in Poland in 1975, has proved to be highly successful in limiting the number of reported measles cases and, moreover, increased morbidity that occurred every other year disappeared. The last so called compensative epidemies were recorded in 1990 and 1998.

Measles is a severe viral infection, followed even by serious complications that occur within a few weeks after acute stage or even later, in about 1 case out of 5,000. Symptomatic CNS complications are extremely frequent and occur in 1 case out of 1,000.

Immunocompromised patients, infants and patients with chronic diseases are at the risk of suffering from a progressive fatal measles.

Therapy for measles is largely supportive and symptom-based, because no effective viral-specific treatment has been found so far [9].

Primary measles virus infection is characterized immunologically by immune activation and the induction of an effective and long-lived antiviral immune response [3].

In view of several clinical and experimental studies, magnesium is a basic trace element essential to human biologic functioning. The data found in the literature prove that *Mg* is indispensable for immunological processes, e.g. it improves phagocytosis and immunoglobuline synthesis, activates the complement and properdine system.

Therefore we found it interesting to estimate serum *Mg* level in measles patients during the acute phase and convalescence.

The aim of this study was to find answers for the following questions:

1. What was the serum *Mg* level during the acute stage of measles?
2. What was the serum *Mg* level among the same patients in the course of their convalescence?

3. Were there any differences in serum *Mg* level between the group of patients with measles and healthy volunteers?

MATERIALS AND METHODS

Clinical material

The studies included 26 measles patients, namely 8 men and 18 women at the age of 18–34 years hospitalized at the Infectious Diseases Department of Medical Academy in Lublin in the period from 1990 to 1991 (9 of these patients were vaccinated against measles according to vaccination calendar (i.e. 16–18 months after birth). The average hospitalization period was 14 (+2) days, from appearance of eruption.

The diagnosis was established on the basis of anamnesis, clinical symptoms, laboratory analysis and viral examinations.

The group we examined consisted of the patients not showing the symptoms of coexisting diseases, for which it has observed the clinical improvement after the termination of therapy.

In all examined patients the magnesium level in blood serum was determined twice during hospitalization time and additionally one time after discharging from clinic according to the following scheme:

- First examination — during first day of hospitalization,,
- Second examination — during last day of hospitalization after attainment of clinical improvement,
- Cv examination — after 3 weeks, during periodic control.

The control group included 24 persons at the aged 15–19 years selected among the schoolboys and schoolgirls of Lublin schools. The serum magnesium level of those persons was determined once. All the patients and persons from the control group have been informed about the purpose of the examination.

Methods

Blood used in investigations was sampled from elbow vein in fasting state between 7 and 8 o'clock a.m. The measurements of magnesium level were made in serum. 5 ml of sampled blood was transferred directly to demineralized test tube for centrifuge. After the formation of the clot the centrifuge conted was centrifigated at rotation speed equal to 2000 rot./min. 1 ml of serum was pipetted to scintillation containers (Plastomed) and frozen at -20°C. Thus protected samples were stored until the beginning of measurements, but no longer than 2 months.

Scintillation containers, test-tubes for centrifuge and authomatic pipette tips were soaked before use for 24 h in 10% hydrochloric acid in vessel placed under digestorium. Deminarelized laboratory vessels were flushed several times with distilled water and then dried. Before each measurement the reagents were tested in respect of *Mg* content.

The serum for investigations was defrozen and then diluted with distilled water in proportion of 1:40. Determinations of magnesium level in blood serum were made by

atomic absorption spectrometry (AAS) in Central Apparatus Laboratory of Agricultural Academy Lublin. For this purpose the AAS-3 atomic absorption spectrometer (Carl Zeiss Jena, Germany) has been used after previous calibration in the presence of standard sample at the wavelength of 285.2 nm. The level of *Mg* is expressed in μmole/l.

Statistical method

The obtained nummerical data were subjected to statistical analysis. On the basis of the results obtained for *n* persons the following statistical characteristics were determined:

- M — arithmetic mean
- SD — standard deviation
- SE — average error of arithmetic mean
- V % — coefficient of variability

Inter-measurements variations were described by variability range (from – to), and variability mean and SDd — by variability standard deviation. The significance of differences between *Mg* level in patient and in control group was verified by means of Students t-test for resolved variables. In the case of significant differences in variancies, at different numerities of compared groups such verification was performed by means of the Cochran–Cox test. In individual tables the types (t, c) and values of test functions are listed in Column T. The significance of differences between decrease and increase frequencies between comparative tests was verified by χ^2 test. The probability *p* was read from the tables containing *t*-Student distribution functions or χ^2 functions, respectively. It was assumed that the risk of conclusion error is equal to 5%. The individual *Mg* levels found during comparative studies (I with II), (I with R), (II with R) presented in the figures are obtained using correlation diagrams. The range of our norm (marked in the diagrams) is determined on the basis of *Mg* level in control group.

Mean values together with the values of standard deviations determined for control group as well the same values obtained in three tests performed in patients were illustrated in histograsms.

RESULTS

The *Mg* levels found in control groups as well as in the three tests performed in tested groups are given in Table 1, and the changes in *Mg* levels observed between three tests are given in Table 2 and illustrated in Figure 1.

In the control group the *Mg* level was 927.1 ± 110.8 mole/l (M ± SD), whereas in patients in the first test — 747.7 ± 125.2 mole/l, in the second test — 824.2 ± 202.6 and in Cv — 756.3 ± 192.9 mole/l (Figure 1, Table 1).

The results of comparing serum *Mg* levels of the tested group and the control group are as follows: in the first test it was lower by 179.4 μmole/l and this difference is highly significant ($p < 0.001$), in the second test it was lower by 102.9 μmole/l, ($p <$

Table 1. Mg level in blood serum in control group (Ct) and in measles patients in examinations I, II and Cv

Group	n	Mg level (μmole/l)				Comparison to control group								
									Number (f) and percentage (%)					
		M	SD	SE	V %	Mean difference	T	p	f	%	f	%	f	%
Ct	24	927,1	110,8	22,6	12,0	(Eigennorm: 705,5 – 1148,7)								
P I examination	26	747,7	125,2	24,6	16,7	−179,4	t	5,347	<0,001	11	42,3	15	57,7	0	0
P II examination	26	824,2	202,6	39,7	24,6	−102,9	c	2,251	<0,04	8	30,8	16	61,5	2	7,7
P Cv	18	756,3	192,9	45,5	25,5	−170,8	c	3,363	<0,01	6	33,3	11	61,1	1	5,6

Symbols used in first left column:
Ct – Control group
P – patients
Cv – convalescence

Table 2. Magnitude and direction of variation of Mg level between individual examinations

Comparable examinations		Magnitude of variations (μ			Significance of variations		Direction of variations					
		From–to	Mean	SDt	t	P	Number (f) and percentage (%)					
							Decrease		Increase			
							f	%	f	%	X^2	P
II and I	26	−248 +510	+76,5	193,61	2,016	>0,05	10	38,5	16	61,5	1,38	>0,20
Cv and I	18	−313 +444	+ 8,33	204,23	0,173	>0,80	9	50,0	7	38,9	0,25	>0,50
Cv and II	18	−510 +346	−93,11	221,25	1,786	~0,09	12	66,7	5	27,8	2,882	

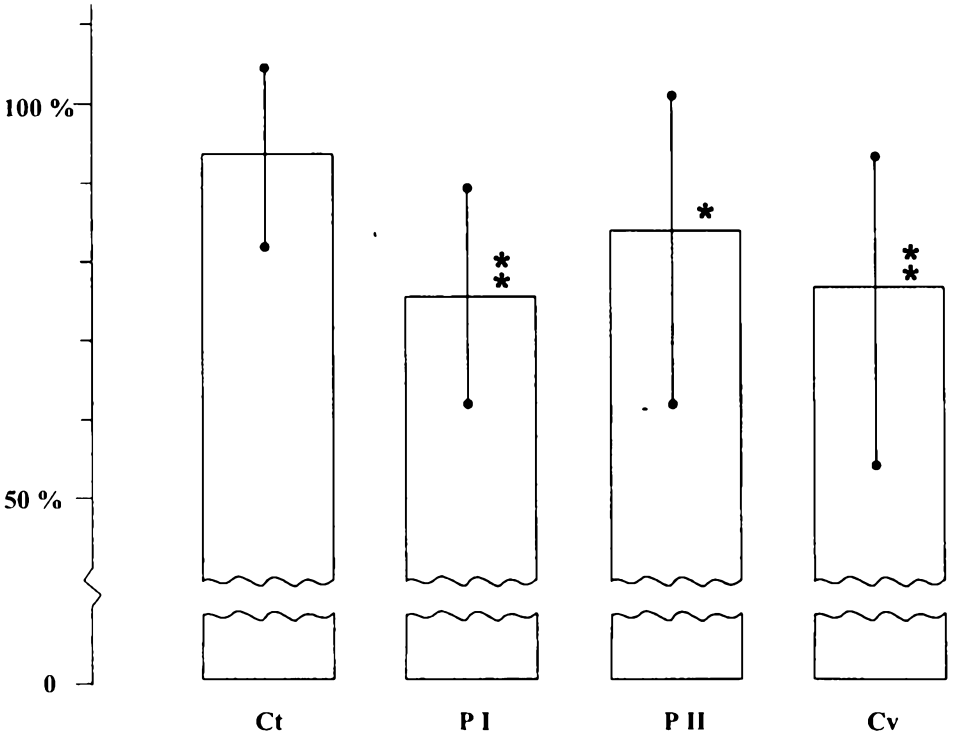

Figure1. Magnesium level (M + SD) in control group (Ct) and in patients in examinations I, II and Cv

0.04) and in Cv lower by 170.8 μmole/l and this last difference is also higly significant ($p < 0.01$).

Assumming that our norm is equivalent to magnesium level ranging from 705.5 to 1148.7 μmole/l, the reduced values were found in 11 among 26 patients (i.e. 42.3%) in the first test, in 8 among 26 (i.e. 30.8%) in the second test and in 6 among 18 (i.e. 33.3%) in the convalescents. In the period between the first and second test we observed a decrease of *Mg* level in 10 patients (38.5%) and an increase in 16 patients (61.5%). It has not been found that the increase occurred significantly more frequently that the decrease ($p > 0.20$).

In the period between the first and second test *Mg* level changed from -248 μmole/l (decrease) to +510 μmole/l (increase), in other words it has increased by 76.54 μmole/l and, assumming the risk of conclusion error to be 5%, this difference is not significant ($p > 0.05$).

Comparing *Mg* level in Cv and in the first test, the increase of this level was found in 9 patients (i.e 50%) and the decrease in 7 patients (38.9%). The decrease was observed with similar frequency as the increase of $p > 0.50$. The variations ranged from -313 to +444 μmole/l, and the average increase was only 8.33 μmole/l and therefore it is significantly better ($p > 0.80$) (Table 2).

Comparing the *Mg* level in Cv to that in the second test, the increase of this level was found in 5 patients (27.8%), the decrease in 12 patients (66.7%), and the lack of any changes in 1 patient. The decrease of *Mg* level was observed more frequently that the increase, however this difference is typically accidental ($p > 0.09$).

In the convalescence period the mean variations between II and Cv changed from –510 μmole/l to +346 μmole/l, and in comparison test II the *Mg* level was lower by 93.11 μmole/l, but this decrease is not significant assumming that the risk of conclusion error is 5% ($p > 0.09$) (Table 2).

Thus, the results of the performed analysis show that a significant decrease of *serum Mg* level occurs in measles patients. The variations observed during hospitalisation and convalescence are purely accidental:

1. No significant statistical differences in serum *Mg* level in acute measles stage have been found.
2. The serum *Mg* level was statistically significantly lower both in acute measles stage and convalescence in comparison to control group.

DISCUSSION

The determination of serum magnesium (*Mg*) level represents less than 1% of *Mg*. However, it is significant due to the fact that its blood content is very stable and contributes to detecting even slight changes. Magnesic blood homeostasis depends directly on enteric absorption, normal kidney function as well as on hormonal suprarenal mechanisms. There is no correlation between serum *Mg* level and a person's physical activity [11]. However, it has been proved that a very important role is played by genetic and environmental factors.

Statical study of serum *Mg* level helps to show disturbances of magnesic balance, especially in population clinically defined. For clinical purpose, the assessment of serum *Mg* level is regarded as one of significant criteria showing disturbances of magnesic balance [1].

Since AAS is very specific and highly sensitive it is a valuable analytical method used to estimate concentration of trace elements [5].

Available writings do not provide data concerning serum *Mg* level in patients suffering from measles. Furthermore, it is not surprising that there is not much information about the disease and trace elements because of widespread prophylaxis.

In our research hypomagnesaemia was observed in measles patients during the acute stage of the disease and convalescence in comparison with a control group. The resultes of our research have proved that serum *Mg* level in our control group (0.7–1.14 mmol/l, i.e. 705.5–1148.7 μmol/l) correlates with standards provided by the 'SI Unite Conversion Guide' [8]. There are no significant differences noted between females and males in the tested group.

It is difficult to assess whether hypomagnesaemia in the group of our patients correlates with the actual shortage of *Mg* in human organism. Only original hypomagnesaemia enables us to observe the pathology directly related to low serum *Mg* level:

However, derivative hypomagnesaemia should be analysed in correlation with other symptoms of the basic disease.

Changes of serum *Mg* level were described during the course of many acute infectious diseases of viral etiology. Hypermagnesaemia was observed in the course of influenza and rubella. The increase of serum *Mg* level was described in patients suffering from varicella (chicken-pox) and HSV infection [13]. It has been claimed that the phenomenon is generated by stress caused by infectious diseases, which leads to relieving *Mg* form a cell into extracellural space. However, the thesis seems to be incoherent. Hypomagnaemia has been described in acute stage of hepatitis B, however immunopathological mechanisms leading to the hepatocyte damage are more complecated in this case [6, 7].

On the other hand, it has been proved that stress may cause *Mg* deficiency, bacause it leads to disregulation of homeostasis of magnesium and hipermagnesuria. Stress resulting from *Morbillirvirus* infection can be one of the reasons for hypomagnesaemia observed in our patients. It would be helpful to determine *Mg* excretion in urine, due to the fact that stress intensifies activity of suprarenal thyreoid and antidiuretic hormones.

REFERENCES

1. *Durlach J.*: Magnez w praktyce klinicznej, Państwowy Zakład Wydawnictw Lekarskich, Warszawa 1991.
2. *Griffin D.E. et al.*: Immune Activation during Measles: Interferon-g and Neopterin in Plasma and Cerebrospinal Fluid in Complicated and Uncomplicadet Disease. JID, 161, 449, 1990.
3. *Griffin D.E. et al.*: Immune Activation during Measles: $\beta 2$ — microglobulin in Plasma and Cerebrospinal Fluid in Complicated and Uncomplicated Disease. JID, 166, 1170, 1992.
4. Griffin D.E., Ward B.J.: Differential CD4 T Cell Activation in Measles. JID 168, 275, 1993.
5. *Holcombe J.A., Hassell D.C.*: Atomic absorption, atomic emission and flame emission spectrometry, Anal. Chem., 62, 169R, 1990.
6. *Kryska A. et al.*: Pierwiastki śladowe: cynk, miedź i magnez u chorych na przewlekłe, przetrwałe zapalenie wątroby — ocena zmian w przebiegu leczenia. Pol. Tyg. Lek., 55, 987, 1990.
7. *Kryska A., Kiczka W.*: Ocena stężeń wybranych mikroelementów w przebiegu wirusowego zapalenia wątroby. Diag. Lab., 20, 331, 1984.
8. *Laposata M.*: SI unit conversion guide. NEJM Books, Boston, Massachusetts, 1992.
9. *Marniemi J. et al.*: Blood vitamins, mineral elements and inflammation markers as risk factors of vascular and non-vascular disease morality in an elderly population. Int. J. Epidemiol., 27, 799, 1998.
10. Measles: Report of the Committee on Infections Diseases, American Academy of Pediatrics, 308, 1994.
11. *Nuviala R.J. et al.*: Magnesium, zinc and copper status in women involved in different sports. Int. J. Sport. Nutr., 9, 295, 1999.
12. Starobrat-Hermelin B.: The effect of deficiency of selected bioelements on hyperactivity in children with certain specified mental disorders. Ann. Acad. Med. Stetin., 44, 297, 1998.

13. *Stending-Lindberg G. et al.*: Serum *Mg* in acute viral disease in man. In: Cantin M., Seeling M.S.: Magnesium in health and disease. Spectrum Press, 935, 1980.
14. *Zargar A.H. et al.*: Copper, zinc, and magnesium levels in non-insulin dependent diabetes mellitus. Postgrad. Med. J, 74, 665, 1998.

STRESZCZENIE

Celem niniejszej pracy była ocena poziomu magnezu (*Mg*) w surowicy krwi u chorych na odrę w ostrym okresie choroby i po trzech tygodniach od ustąpienia objawów klinicznych, w porównaniu z grupą kontrolną. Badania dotyczyły 26 chorych na odrę w wieku od 14 do 34 r. ż., hospitalizowanych z powodu odry w Klinice Chorób Zakaźnych AM w Lublinie. Analizowaną grupę stanowili pacjenci bez chorób współistniejących, u których uzyskano poprawę kliniczną po przeprowadzonym leczeniu. U wszystkich badanych oznaczono dwukrotnie stężenie *Mg* w surowicy w okresie hospitalizacji oraz jednorazowo w okresie rekonwalescencji.

Grupa kontrolna obejmowała 24 osoby zdrowe w wieku od 15 do 19 lat, u których stężenie *Mg* w surowicy krwi oznaczono jednorazowo.

Uzyskane dane liczbowe poddano analizie statystycznej. Nie stwierdzono statystycznie istotnych różnic w poziomie *Mg* w surowicy krwi w ostrym okresie odry i w rekonwalescencji.

W ostrym okresie odry i po trzech tygodniach od ustąpienia objawów klinicznych poziom *Mg* w surowicy krwi był statystycznie istotnie niższy w porównaniu z kontrolą.