

Electrolyte contents of serum and erythrocytes of patients with a tetanic syndrome before and after oral treatment with magnesium

R. Fehlinger¹⁾, C. Kemnitz¹⁾, K. Seidel¹⁾ and T. Günther²⁾

Zusammenfassung

Bei unbehandelten Patienten mit tetanischem Syndrom (Gruppe A; n=30) und nach 4wöchiger oraler Mg-Behandlung mit 375 mg Mg/die (Gruppe B, n=15) wurden der Na⁺-, K⁺-, Ca²⁺- und Mg²⁺-Gehalt in Serum und Erythrozyten sowie die klinische Symptomatik bestimmt: Nach Mg-Therapie war eine signifikante Verbesserung der klinischen Symptome festzustellen. Nach der Mg-Zufuhr waren die K⁺- und Mg²⁺-Konzentration im Serum geringfügig angestiegen. Der Na⁺- und Ca²⁺-Gehalt der Erythrozyten blieb erhöht und wurde durch orale Mg-Behandlung nicht beeinflusst. Der erhöhte Na⁺- und Ca²⁺-Gehalt der Erythrozyten wird als zusätzliches diagnostisches Kriterium beim tetanischen Syndrom empfohlen.

Summary

Na⁺, K⁺, Ca²⁺ and Mg²⁺ contents in serum and erythrocytes as well as clinical symptoms were compared in untreated patients with tetanic syndrome (group A; n=30) and in patients 4 weeks after Mg medication of 375 mg Mg/d (group B; n=15). After Mg therapy, there was a significant amelioration of the clinical symptoms and brain performance (concentration of mind) as proved by psychometric tests.

After the Mg medication, there was a small significant increase of serum K⁺ and Mg²⁺. The Na⁺ and Ca²⁺ contents in erythrocytes were increased in patients with tetanic syndrome but were not influenced by oral Mg treatment. The increased Na⁺ and Ca²⁺ contents of erythrocytes are proposed to be an additional diagnostic criterion in tetanic syndrome.

¹⁾ Clinic of Neurology and Psychiatry, Dept. Med. (Charité), Humboldt-University, DDR-1040 Berlin/GDR

²⁾ Institute of Molecular Biology and Biochemistry, Free University, D-1000 Berlin/FRG

Résumé

Les auteurs ont comparé les taux sériques et érythrocytaires de Na⁺, K⁺, Ca⁺⁺ et Mg⁺⁺ ainsi que les symptômes cliniques observés chez des patients atteints de spasmophilie, non traités (groupe A, n=30) ou ayant reçu 375 mg/j de magnésium pendant 4 semaines (groupe B, n=15). Le traitement par le Mg a entraîné une amélioration significative de la symptomatologie et des performances intellectuelles (concentration) évaluées à l'aide de tests psychométriques.

Le Mg a légèrement, mais significativement, augmenté la kaliémie et la magnésémie. Les taux érythrocytaires de Na⁺ et de Ca⁺⁺ ont augmenté chez tous les patients atteints de tétanie, mais n'ont pas été influencés par le traitement oral par le Mg. Les auteurs proposent d'inclure cette augmentation des taux intra-érythrocytaires de Na⁺ et de Ca⁺⁺ parmi les critères diagnostiques de la spasmophilie.

Introduction

A preceding paper reported on patients with chronic hypomagnesemic tetany who had been chronically treated with Mg for some years and who showed normal serum electrolytes but increased Na⁺ and Ca²⁺ contents in erythrocytes [6]. In order to get a better insight into the pathogenesis of this disease, we investigated serum and erythrocyte electrolytes of untreated patients and after 4 weeks of oral Mg therapy.

Methods

Patients

Including criteria

Only patients with a tetanic syndrome were taken who showed the classic symptoms with frequent and spontaneous muscle cramps and carpopedal spasms. In some of the patients a tetanic syndrome had already been diagnosed. However, these patients remained untreated for at least 3 months so that the tetanic symptoms appeared again.

Excluding criteria

Borderline cases of tetanic syndrome; patients with psychotropic therapy, with accompanying vitamin therapy or a mineral substitution; pregnancy; patients with severe concomitant diseases.

Treatment of patients

Blood was taken from all patients at the beginning of the study. Thereafter, 15 patients (5 males, 10 females) remained untreated, 15 patients (5 males, 10 females) received orally 3 × 125 mg Mg/day (pyrrolidone-carbonacid-magnesium-salt, Mag-2, Laboratories Meram, Paris France) for 4 weeks. Subsequently, again blood was taken from all patients. The average age of all patients of each group was 34 years.

Psychometric tests

Therapy was controlled by psychometric tests as described in detail (3, in preparation).

Determination of Na⁺, K⁺, Ca²⁺, and Mg²⁺ content

Two ml heparinized blood was washed twice with cold isotonic sucrose. Erythrocytes were freeze-dried and ashed in a Plasma Processor 200 E (Technics, GmbH). The ash was solubilized in 0.1 N HCl. After dilution, Na⁺ and K⁺ were measured by flame photometry (Beckman) and Mg²⁺ by atomic absorption spectrophotometry (Pye Unicam, SP9). Ca²⁺ was measured by flameless atomic absorption spectrophotometry (Pye Unicam, SP9).

Na⁺, K⁺ and Ca²⁺ contents in serum were measured by flame photometry (FCM 6341 Eppendorf), Mg²⁺ in serum by atomic absorption spectrophotometry (AAS 1, Zeiss Jena/GDR).

Results

Clinical observations before and after Mg treatment

After the 4 weeks of Mg medication, the frequency of tetanic attacks and the degree and frequency of paraesthesia and dizziness, as was found by self assessment of the patients were reduced significantly. Additionally the same observation was made by a medical specialist. Likewise we found with psychometric methods an improvement of brain performance (an increased number of substituted symbols in the "Symbol-Digit-Substitution-Task" and a reduced number of mistakes on the Vienna determination instrument after long-time-stress of 30 minutes with 600 signals) (in preparation).

Tab. 1: Mineral content in serum (mM) of untreated tetanic patients (group A) and after 4 weeks of oral Mg medication (group B). Mean ± SEM

	Na ⁺	K ⁺	Ca ²⁺	Mg ²⁺
Group A (n=30)	143,0 ± 0,7	4,16 ± 0,007	2,50 ± 0,04	0,80 ± 0,01
Group B (n=15)	143,3 ± 0,9	4,63 ± 0,10**)	2,50 ± 0,16	0,84 ± 0,01*)

Significant difference to untreated patients as revealed by Student's unpaired t-test
 *) p < 0,01
 **) p < 0,001

Serum electrolytes before and after Mg treatment

No differences in serum and electrolytes were observed between the untreated and the placebo groups. Therefore, both groups were considered together (group A). The mineral concentrations in serum are summarized in Tab. 1. All mean values were in the normal range before and after treatment. There was only a small increase of K⁺ and Mg²⁺ concentration at the end of the therapy.

Erythrocyte electrolytes before and after Mg therapy

Patients with freshly diagnosed tetanic syndrome show increased erythrocyte Na⁺ and Ca²⁺ contents (Tab. 2). The values were identical to those found in patients with chronic hypomagnesemic tetany who had been treated with Mg for some years [6]. In agreement with this result, erythrocyte Na⁺ and Ca²⁺ contents in the patients were not changed by Mg therapy. Other erythrocyte electrolytes were not significantly different from normal values.

Tab. 2: Mineral content in erythrocytes (mmol/kg dry weight) of untreated tetanic patients (group A) and after 4 weeks of oral Mg medication (group B). Mean ± SEM

	Na ⁺	K ⁺	Ca ²⁺	Mg ²⁺
Group A (n)	22,22 ± 1,56 (29)	261,7 ± 2,7 (24)	0,050 ± 0,008 (30)	6,43 ± 0,11 (30)
Group B (n)	21,27 ± 1,80 (15)	259,4 ± 2,9 (12)	0,059 ± 0,011 (15)	6,66 ± 0,15 (15)

Discussion

Clinical observations

The clinical and psychometric data we obtained with this study are in accordance with preceding clinical investigations [3]. In other clinical trials the positive effect of oral Mg medication in tetanic syndrome could be demonstrated by various symptoms and indications: decrease of neuromuscular irritability with a reduced frequency of cramps and tetanic attacks, increase of muscle strength, improvement of brain performance (concentration of mind, stress tolerance), improvement of electronystagmographic parameters [3].

Serum electrolytes

In untreated patients with a tetanic syndrome, one can expect the following statistic alterations in serum electrolytes: hypocalcemia in 33 %, hypomagnesemia in 20 % and hypokalemia in 10 % of the patients. Such reduced concentrations can be found as singular pathological data or in

various combinations. A statistically significant differentiation between tetanic patients and controls via Ca^{2+} and Mg^{2+} concentration in serum [1, 4] or Mg^{2+} in erythrocytes [2] is successful only with larger groups. From the therapeutical point of view the results are contrary. Irrespective of the electrolyte pattern in serum a positive therapeutic effect of oral Mg medication was reported by only 60–70% of unselected tetanic patients [1, 2, 3]. In comparable clinical studies (outdoor tetanic patients, oral application of $3 \times 125 \text{ mg Mg/d}$ as citrate salt over 4 weeks) we were able to prove the clinical effects mentioned above, but we found practically no change of electrolyte concentrations in serum [3, 5], only a slight tendency towards an increase of K^+ [5]. With pyrolydione-carbonacid-Mg-salt there was a small increase of the K^+ and Mg^{2+} concentration in serum. The small increase of K^+ in serum in a group of unselected tetanic patients after single oral Mg-medication had not as yet been described.

Erythrocyte electrolytes

The most significant result was the increased Na^+ and Ca^{2+}

content in erythrocytes. The altered electrolyte content in patients' erythrocytes may be caused by an increased membrane permeability, whose biochemical mechanism has not yet been defined.

From the clinical symptoms of latent tetany it can be concluded that other cells, such as nerve cells or muscle cells, may have a similar alteration in membrane permeability. However, in the cells contrarily to erythrocytes, an increase in extracellular Mg^{2+} concentration may reduce the intracellular Na^+ or Ca^{2+} content, as can be concluded from the remarkable therapeutic effect of Mg supplementation. Probably, only voltage-gated Ca^{2+} channels may be influenced by increased extracellular Mg^{2+} . In agreement with this suggestion, in experiments with lymphocytes, Ca^{2+} influx induced by concanavalin was insensitive to increased extracellular Mg^{2+} and verapamil [7]. The increased Na^+ and Ca^{2+} content of erythrocytes in combination with clinical symptoms may be taken as an additional diagnostic criterion for latent tetany. However, it is not helpful in controlling the therapeutic effect.

References

- [1] Durlach, J.: Tetanie durch Magnesiummangel. Münch. Med. Wschr. **104** (1962) 57–60.
- [2] Durlach, J.: Aspects cliniques et biologiques du déficit magnésique chronique primaire. Feuilles de Biologie **23** (1982) 61–64.
- [3] Fehlinger, R., Franke, L., Glatzel, E., Meyer, E., Michalik, M., Rapoport, S. M., Rüstow, M., Schulze, Ch. and Schumann, G.: Klinische Studien zur Mg-Behandlung des tetanischen Syndroms. Mag.-Bull. **3** (1981) 298–306.
- [4] Fehlinger, R. and Seidel, K.: The Hyperventilation Syndrome: A Neurosis or a Manifestation of Magnesium Imbalance? Magnesium **4** (1985) 129–136.
- [5] Fehlinger, R., Mielke, U., Faulk, D. and Seidel, K.: Rheographic indications for reduced cerebral vasoconstriction after oral magnesium medication in tetanic patients, a double-blind, placebo-controlled trial. Magnesium **5** (1986) 60–65.
- [6] Günther, T., Höllriegel, V., Vormann, J., Fehlinger, R. and Seidel, K.: Electrolyte metabolism in erythrocytes from patients with chronic hypomagnesemic tetany. Mag.-Bull. **8** (1986) 288–292.
- [7] Vormann, J. and Günther, T.: Effect of concanavalin A and extracellular magnesium on the concentration of intracellular free Ca^{2+} in thymocytes from normal and Mg-deficient rats. Mag.-Bull. **9** (1987) 33–35.

(For the Authors: Doz. Dr. sc. med. R. Fehlinger, Clinic of Neurology and Psychiatry, Dept. Med. [Charité], Schumannstr. 20/21, DDR-1040 Berlin/GDR)