Lupus/Rheumatoid Arthritis (Auto Immune Disorders) Research Directory

Magnesium deficiency in systematic lupus erythematosus

Subject(s): MAGNESIUM deficiency diseases; SYSTEMIC lupus erythematosus -- Diagnosis
Source: Journal of Nutritional & Environmental Medicine, Jun97, Vol. 7 Issue 2, p107, 5p, 1 chart
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Abstract: Discusses the effects of reduced erythrocyte magnesium (Mg) deficiency in patients with systematic lupus erythematosus (SLE). Common symptom of the disorder; How to determine if SLE patients are also prone to hypomagnesemia; Results of the study.
AN: 9711141130
ISSN: 1359-0847
Full Text Word Count: 2470
Database: Academic Search Elite
Section: ORIGINAL RESEARCH

MAGNESIUM DEFICIENCY IN SYSTEMIC LUPUS ERYTHEMATOSUS

Reduced erythrocyte magnesium (Mg) levels have been reported in fibromyalgia syndrome (FS), chronic fatigue syndrome (CFS), myofascial pain syndrome (MPS) and eosinophilia myalgia syndrome (EMS). These disorders have chronic pain as a common symptom. Chronic pain also affects some patients with systemic lupus erythematosus (SLE). To determine if SLE patients are also prone to hypomagnesemia, red blood cell (RBC) and plasma Mg levels were measured in all SLE patients seen in a general rheumatology practice in a 3-year period. There were 25 such patients with a mean age of 47 years. Thirteen SLE patients had FS and 12 did not have either FS or MPS. The mean RBC Mg level for the SLE patients was 4.60 mg dl-1, statistically significantly lower than that of the reference controls and 12 osteoarthritis controls. It did not matter whether the SLE patients had ES or MPS. This finding has implications for diagnosis and treatment.

Keywords: magnesium, myalgias, lupus, pain.

INTRODUCTION

Reduced erythrocyte magnesium (Mg) levels have been reported in fibromyalgia syndrome (FS) [1], chronic fatigue syndrome (CFS) [2], myofascial pain syndrome (MPS) [3] and eosinophilia myalgia syndrome (EMS) [4]. These four disorders have chronic pain and/or fatigue as a common denominator. Furthermore, it has been proposed that low Mg levels predispose patients to myalgias [5] and that low muscle Mg levels correspond to a low pain threshold [6]. Systemic lupus erythematosus (SLE) is also a condition that can be characterized by chronic pain in some patients. Lupus patients have often been described as having myalgias, arthralgias and pain resulting from inflammation of such structures as the lung pleura and/or pericardium [7-9]. If patients experience pain because of a flare of this systemic inflammatory connective tissue disease the treatment would typically be medications such as glucocorticosteroids or even immunosuppressants [10, 11]. However, if low Mg is causing or contributing to increased pain in SLE patients without any concomitant increase in inflammatory activity, the use of these medications would not be expected to ease the pain and could perhaps be counterproductive because of side-effects. With this in mind the Mg levels were checked in SLE patients in a general rheumatology practice.

PATIENTS AND METHODS

Patients

During the period September 1992 to May 1995 inclusive, 25 SLE patients were evaluated and treated in a general rheumatology practice. All the patients fulfilled 1982 American College of Rheumatology (ACR) criteria for SLE [12]. There were four males and 21 females with a mean age of 47 years (range 18-64 years). Thirteen SLE patients (one male and 12 females) fulfilled the ACR criteria for FS [13]. The remaining 12 patients (three males and nine females) had neither FS nor MPS.

During the study period, none of the SLE patients exhibited renal insufficiency nor was there evidence of myositis. None of the SLE patients had creatine phosphokinase (CPK) or aldolase levels outside of the 'normal range'. The mean CPK level for all 25 patients was 126 U 1-1 (normal range 32-236 U 1-1). The mean aldolase level for the eight SLE patients tested was 4.8 U 1[sup -1 (normal range 1-8 U 1-1). As a control group, 12 patients with uncomplicated monoarticular osteoarthritis (OA) (four hip, six knee and two shoulder) were also studied. There were three men (ages 44, 48 and 53 years) and nine women (mean age 50 years and range 42-64 years) in the OA group (see Table 1). None of the OA or SLE patients was taking diuretics or uricosuric drugs. None was bulimic, anorexic or using laxatives inappropriately. No patient was cachetic or on a 'crash' diet at the time of the study. None was taking vitamin supplements. All had simultaneous plasma and red blood cell (RBC) Mg determinations.

Methods

All 25 SLE patients had venous blood drawn for both RBC and plasma Mg levels. The samples were drawn into a heparinized tube from a peripheral vein. They were immediately refrigerated and then transported to a reference laboratory (National Medical Services, Willow Grove, PA, USA) where the assays were performed. The plasma and RBC Mg levels using washed cells were determined by using direction dilution techniques and atomic absorption [14, 15] and the results here reported in mg dl-1.

RESULTS

The mean RBC Mg level for the SLE patients without FS or MPS was 4.50 mg dl-1 with a standard deviation of 0.72 mg dl-1 whereas the mean RBC Mg level for the SLE patients with FS was 4.63 mg dl-1 with a standard deviation of 0.68 mg dl-1. There was no statistically significant difference between these two groups. The mean RBC Mg level for all the SLE patients was 4.60 mg dl-1 with a standard deviation of 0.70 mg dl-1, which is statistically significantly different from that of the reference controls (5.5 mg dl-1 and standard deviation 0.65 mg dl-1) and 12 osteoarthritis controls (5.30 mg dl-1 and standard deviation 0.62 mg dl-1). A comparison of the means tests showed a z score of 4.60 and $p < 0.001$. The plasma Mg levels for the SLE patients were not significantly different from the reference controls and also the osteoarthritis controls. The mean plasma Mg level for the SLE patients was 2.00 mg dl-1, which is not statistically significantly different from the mean plasma Mg level for the reference controls and for the 12 osteoarthritis controls (2.05 and 2.00 mg dl-1, respectively).

Clinical Vignette

A 35-year-old white female with a history of SLE for 9 years presented with a 3-month history of gradually increasing myalgias. There was no change in diet or exercise nor was she taking any new medications. Her SLE had been well controlled on prednisone (5 mg/day) and azathioprine (150 mg/day). She required occasional prescriptions for non-steroidal anti-inflammatory medications such as Salsalate of up to 3 g/day for arthralgias. On physical examination the patient had normal blood pressure. An examination of the head, ears, eyes, nose and throat was unrevealing. In particular, there was no alopecia, oral ulcers or malar rash. A cardiopulmonary examination was unremarkable. An abdominal examination was benign. A musculoskeletal examination revealed no signs of synovitis, bony ankylosis or joint effusions. There was fairly good range of motion of all the joints: however, there was some diffuse tenderness on palpation of

the muscles. There were only four of 18 fibromyalgia tender points noted (bilateral trapezius, right second rib and left gluteus medius). She did not fulfil the ACR criteria [13] for FS. Laboratory values revealed normal renal function and normal levels of sodium, potassium, chloride and bicarbonate. Her erythrocyte sedimentation rate (ESR) was normal (10 mm). Her CPK and aldolase were also within the normal range (164 and 4.0 U 1-1, respectively). However, her RBC Mg level was noted to be 3.8 mg dl-1 (reference mean 5.5 mg dl-1 with a range of 4.2-6.8 mg dl-1). Her plasma Mg level was 1.7 mg dl-1 (reference mean 2.05 mg dl-1 with a range of 1.6-2.5 mg dl-1). The patient's dose of prednisone was not increased nor was there a change in the dose or type of immunosuppressant. Rather, she was treated with six weekly injections of magnesium sulphate (1 g intramuscularly) as had been described previously in the treatment of CFS [2]. After the first series of six injections the patient's RBC Mg level increased to 4.3 mg dl-1, barely within the normal reference range. However, the patient's myalgias improved significantly but did not completely subside. It was not until a second course of six weekly injections of magnesium sulphate (1 g intramuscularly) that the patient's myalgias almost disappeared. Her RBC Mg level increased to 5.4 mg dl-1. The patient was treated continuously with an oral magnesium supplement (magnesium chloride (Slow Mag) 64 ma, one tablet, three times a day with food). The subsequent RBC Mg level 6 months after the initiation of the oral magnesium supplementation was 5.2 mg dl-1. The patient remains free of myalgias.

DISCUSSION

As in the case of other painful conditions [1-3], statistically significant differences in Mg levels between SLE patients and controls tended to be seen much more readily using RBC Mg levels as the measure of total body Mg stores as opposed to the plasma Mg level. Most clinicians tend to use either serum or plasma Mg levels and in doing so may overlook Mg deficiency in some patients, a potentially reversible problem. It can be very dangerous to treat symptoms such as myalgias in SLE patients with an increase of corticosteroids and/or immunosuppressants without checking the RBC Mg level first. If an SLE patient's myalgias are due to a flare of this inflammatory connective tissue disease, it is certainly prudent to treat with medication geared towards controlling the inflammation. However, if the patient's myalgias are due to Mg deficiency, treatment with an increased dose of corticosteroids would likely be ineffective. In fact, the literature suggests that corticosteroid treatment may even intensify the Mg deficiency [16-21]. It could also cause complications such as avascular necrosis of the bone [22], osteoporosis [23], a hastening of the development of cataracts [24] and other side-effects [25]. The use of immunosuppressants is also not without risk. They can cause bone marrow suppression [26], liver toxicity [27] and other side-effects [28]. These potential problems may be acceptable if one is treating a flare of SLE. However, if the myalgias are due to hypomagnesemia, an increase in corticosteroids and/or a modification of immunosuppressants therapy could expose the patient to needless risk.

Since the pain threshold tends to decrease as the total Mg levels decrease [5], it seems only reasonable to check for hypomagnesemia in patients with an unexplained increase in chronic pain. This includes SLE patients whose myalgias may be due to different causes on different occasions. Oral Mg products suitable for supplementation are available over the counter, are relatively inexpensive and the Mg levels can be monitored to avoid potential toxicity particularly in those SLE patients with renal insufficiency.

It is not known why Mg levels tend to drop in patients with chronic pain problems such as FS, MPS, EMS and SLE. It has been suggested [3] that there may be a problem with Mg availability and/or utilization at the tissue level as opposed to a suboptimal dietary intake or an increased excretion of Mg. Whatever the mechanism, Mg deficiency should not go unnoticed. To fail to consider Mg deficiency in the differential diagnosis of neuromuscular problems in SLE might expose such patients to undue risk and expense particularly if myalgias are mistakenly attributed to inflammation.

TABLE 1. Individual RBC determination (mg dl-1)

SLE patients (n = 25)	OA controls (n = 12)(a)

-	6.8
-	6.2
5.6	-
5.4. 5.4	5.4, 5.4
5.3	5.3(c)
5.2	5.2
5.1	5.1
5.0	-
4.9, 4.9, 4.9	4.9
4.8, 4.8	4.8
4.7, 4.7	4.7
4.6, 4.6, 4.6(b)	4.6
4.5	-
4.3	-
4.0	-
3.9	-
3.8	-
3.0	-
3.0	-
2.8	-

(a) Twelve osteoarthrities patients with monoarticular disease.

(b) Mean = 4.6 mg dl-1 and standard deviation = 0.65 mg dl-1.

(c) Mean = 5.3 mg dl-1 and standard deviation = 0.62 mg dl-1.

Reference range mean = 5.5 mg dl-1.

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Source: Journal of Nutritional & Environmental Medicine, Jun97, Vol. 7
Issue 2, p107, 5p
Item: 9711141130

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