

Hypomagnesemia and bronchial hyperreactivity

A case report

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In a 37-year-old woman, a heavy smoker and an alcoholic, bronchial hyperreactivity to histamine (PC_{20} FEV_1 0.8 mg/ml) was related to hypomagnesemia (0.55 mmol/l). After acute magnesium repletion (24 h i.v. infusion $MgSO_4$ 6 g, serum magnesium 1.05 mmol/l), histamine PC_{20} FEV_1 increased up to 9.8 mg/ml. The role of magnesium in modulating smooth muscle contractility is discussed and the importance of checking serum magnesium in patients with airway obstruction is suggested.

Key words: bronchial hyperreactivity; chronic airway obstruction; magnesium.

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Many symptoms of magnesium deficiency reflect increased neuromuscular excitability. The effect of a reduced magnesium concentration on smooth muscle contractility has been extensively investigated in the vascular system (1). Vascular spasms have been shown to occur *in vitro* when magnesium concentration is lowered (1) and many clinico-epidemiological observations have suggested a role of magnesium deficiency in cardiovascular disease (2).

We do not know of any published observation concerning hypomagnesemia and bronchial reactivity.

We recently noted bronchial hyperreactivity related to a low serum magnesium level in a patient who was also a heavy smoker and an alcoholic.

CASE REPORT

A 37-year-old woman was evaluated for moderate effort dyspnea. She had a 3-year history of occasional episodes of wheezing during acute airway infection. She was a heavy smoker (40 pack/year) and her alcoholic intake had increased up to 200 g/day in the last 2 years.

On examination she appeared thin and pale, and wheezing was heard over her chest during forced expiration. Blood pressure was 120/80 mmHg/80 mmHg. Brisk tendon reflexes were present.

Spirometry (see Table) showed mild airway obstruction. She denied recent airway infection in the last 2 months. X-ray film of the chest showed increased markings. Hb was 10.2 g/100 ml, the mean corpuscular volume (MVC) was 104 μ m³/cell, white cell count was 5,700, with 71 % neutrophils, 22 % lymphocytes, 6 % monocytes, 1 % eosinophils; folic acid was 1.7 ng/ml (normal > 3), B_{12} vitamin 620 pcg/ml (normal 200-900 pcg/ml), urea nitrogen was 12 mg/100 ml (4.3 mmol/l), glucose 99 mg/100 ml (5 mmol/l), phosphorus 2.0 mg (0.5 mmol/l), magnesium 0.55 mmol/l (normal 0.7-1.0 mmol/l); protein 7.6 g (albumin 4.3 g and globulin 3.3 g)/100 ml; potassium 3.9 mmol/l, sodium 131 mmol/l and calcium 2.30 mmol/l. Skin tests for common allergens were negative.

Histamine bronchial challenge was performed using a standard method (3), by intermittent aerosol generation, five breaths at each doubling histamine concentration, starting

Table 5

Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), maximal expiratory flow at 50 (MEF₅₀) and at 25 % (MEF₂₅) of FVC, histamine concentration causing 20 % reduction of baseline FEV₁ (PC₂₀ FEV₁) and serum magnesium concentration baseline, after glucose and MgSO₄ infusion, and 6 months after first examination

	Baseline	% pr	Glucose	MgSO ₄	6 months
FVC (l)	2.97	91	2.95	3.26	2.85
FEV ₁ (l)	1.94	77	1.97	2.20	1.90
MEF ₅₀ (l)	1.78	40	1.75	1.82	1.75
MEF ₂₅ (l/s)	0.59	24	0.63	0.59	0.60
PC ₂₀ FEV ₁ (mg/ml)	0.80		0.78	9.30	1.2
Mg serum (nmol/l)	0.55		0.52	1.05	0.55

from 0.25 mg/ml. The histamine concentration causing a 20 % fall of forced expiratory volume in 1 s (PC₂₀ FEV₁) was 0.8 mg/ml, i.e. a high degree of bronchial hyperreactivity.

We investigated whether bronchial hyperreactivity could be related to magnesium deficiency. To this aim, after obtaining the patient's informed consent, we determined histamine PC₂₀ FEV₁ on 2 consecutive days, after 24 h continuous infusion of elemental magnesium (0.6 mmol/kg, 6 g MgSO₄) dissolved in 1000 ml of isotonic glucose on day 2, in a single blind fashion. Measurements of serum electrolytes were repeated at the end of each infusion.

No side effects were reported during the study. At the end of MgSO₄ infusion magnesium serum level rose to 1.05 mmol/l, with no change in sodium, potassium and calcium. A mild increase in both vital capacity (VC) and FEV₁ was observed at the end of MgSO₄ infusion (see Table). PC₂₀ FEV₁ after glucose infusion was similar to baseline value (0.75 mg/ml) and rose to 9.8 mg/ml after MgSO₄ infusion. The patient was discharged with prescription of vitamins and magnesium supplementations.

Six months later she came to the outpatient office for a scheduled visit. She had continued to drink and smoke. Her serum Mg level was still low (0.55 mmol/l), as well as histamine PC₂₀ FEV₁ (1.2 mg/ml).

DISCUSSION

Heavy alcohol consumption has many deleterious effects, among these increased prevalence of chronic airway obstruction (6), and magnesium

and folic acid deficiencies (13) are pertinent to the case under discussion.

The finding of bronchial hyperreactivity in a heavy smoker is not surprising and it is generally ascribed to a decreased airway caliber (5). However, the high degree of bronchial hyperreactivity shown by our patient could hardly be due only to her mild airflow limitation, neither could it be related to other common causes of bronchial hyperreactivity, such as recent airway infection or atopy. We suggest that hypomagnesemia was related to bronchial hyperreactivity in our patient, since magnesium repletion greatly attenuated bronchial reactivity to histamine. After magnesium infusion, FVC and FEV₁ increased slightly (9%) in comparison to pre-infusion values. This effect of magnesium on lung volumes could depend on improvement of respiratory muscle power, as previously reported (4), or on a direct bronchodilation (8, 9). The small increase in FEV₁ after MgSO₄ infusion may explain part of the increase in histamine bronchial threshold.

A low magnesium concentration can enhance the contractility of smooth muscle *in vitro* and it may increase the vascular contractile response to humoral agents, such as norepinephrine, prostaglandins and angiotensin II (1). In the respiratory system, magnesium inhibits the mechanical response of guinea pig trachea smooth muscle to leukotrienes (12), and recently we found that aerosol administration of magnesium decreased bronchial reactivity to histamine (10) and to methacholine (11) in asthmatics in clinical remission.

Magnesium, the second most prevalent intracellular cation, is considered a special physi-

ological kind of calcium channel blocker (7). As intracellular influx of calcium is the final common path of bronchial smooth muscle contraction, and calcium channel blockers have some protective effect on bronchoconstriction induced by several stimuli (14), it is conceivable that magnesium may modulate bronchial reactivity. In conclusion, we suggest that serum magnesium concentration should be checked in patients with chronic airway obstruction and hypomagnesemia should be promptly treated, not only for its deleterious effect on respiratory muscle power, but also for its possible contribution to bronchial hyperreactivity.

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