

Original Research

Post-Cholecystectomy Syndrome and Magnesium Deficiency

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Key words: post-cholecystectomy syndrome, functional biliary symptoms, magnesium deficiency

Background and Objective: In 20%–30% of cholecystectomised patients a biliary syndrome (called Post-Cholecystectomy Syndrome: PCES) reappears after some weeks or months. Its etiology, in certain cases, is an anatomic one: (choledochal lithiasis or stricture, obstructive papillitis, pancreatic duct stenosis), but there are many cases in which all organic causes are excluded.

Methods: The aim of this study was to analyze the correlation between these functional disturbances and magnesium (Mg) deficiency (MD). We analysed 52 patients with PCES and MD, in which organic lesions of the remaining bile ducts were excluded by imaging and endoscopic methods.

Results: MD was confirmed by serum and erythrocytic low Mg levels. 82% of patients were women. Supplemental therapy was provided with Tiomag (Mg gluconate and methionine), vitamin B₆ and Ca lactate for 6 weeks or more. In 50 patients, PCES symptomatology disappeared after this treatment. In 14 cases some symptoms reappeared after a few weeks-months, but after repetition of the same therapy they completely disappeared.

Conclusions: Our results demonstrate the dependence of PCES functional manifestations on MD, especially the recurrence of symptoms, which again subsided after Tiomag therapy was reinstated.

INTRODUCTION

According to published data, 20–30% of cholecystectomized patients develop a post-cholecystectomy syndrome (PCES) after weeks or months [1]. The etiopathogenesis of this syndrome is clear in certain cases (choledochal lithiasis, choledochal stricture, cholesterolosis, obstructive papillitis, pancreatic duct stenosis) [2], but there are other instances in which there is no evidence of anatomic lesions [3–5]. This fact suggests functional disturbances. According to Durlach, functional disturbances of the digestive tract and biliary tree are magnesium (Mg)-dependent [6]. Mg catalyzes over 360 biochemical reactions, among which are synthesis of gastric juice-enzymes and mucins and of digestive polypeptide hormones such as pancreozymin-cholecystokinin, the role of which in the bile-ducts physiology is well known [4,6,7]. Mg is indispensable for synthesis of macroergic compounds and release of the energy stored in these compounds, as well as for the synthesis of hydrogen and electron transporter [8–22]. This is evidence of the cytoprotective role of this ubiquitous intracellular ion. Disturbance of its homeostasis entails many functional imbalances. Starting from these considerations, in this study we investigated the extent to which Mg deficiency (MD) is involved in PCES etiopathogenesis.

MATERIAL AND METHODS

The study included 52 cholecystectomised patients with PCES and MD, in which organic lesions of the remaining bile ducts were excluded by imaging and endoscopic methods. The patients were followed up for a mean period of 12,7 months, using test-sheets on which was recorded: age, gender, levels of serum and erythrocytic Mg, serum calcium (Ca), disturbances of the central and peripheral nervous system, digestive, trophic and functional disturbances. All the patients received substitution therapy with Tiomag (Mg-gluconate + methionine), according to a regimen devised in the 3rd Medical Clinic of Cluj-Napoca. Mg and Ca levels were determined by a photocomplexometric method.

RESULTS

Mean age of the study group was 43.6 years (Fig. 1), with 82.69% of the patients being women. Cholecystectomy was performed for the conditions presented in Table 1.

MD, alone, was diagnosed in 60% of the patients; the other 40% of the patients had deficiencies of both Mg and Ca.

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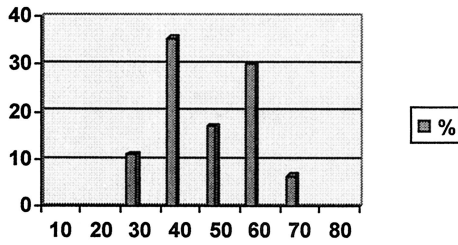


Fig. 1. Distribution by age decades of the patients with PCES.

Table 1. Diseases That Indicate Cholecystectomy

Disease	No of patients	Percentage
Biliary lithiasis	44	84.64
Choledochal lithiasis	3	5.76
Gallbl. cholesterosis	1	1.92
Gallbl. malformation	1	1.92
Non-lith. cholecystitis	3	5.76

Normal Ca/Mg balance was restored by standard Tiomag therapy (Table 2).

The mean time necessary to restore equilibrium is presented comparatively with two groups (Fig. 2), one with spasmophilia with digestive (but not biliary) manifestations and another with spasmophilia without digestive manifestations.

In 14 of the patients, who discontinued Tiomag treatment for two months or more, digestive disturbances and MD recurred. After resumption of treatment and MD correction, these disturbances again resolved.

DISCUSSION

The Tiomag preparation is composed of Mg-gluconate and methionine [23]. This association is based on the metabolic interaction of Mg with methionine and its metabolites, which supply 80% of the sulfur requirement of the body [24]. In order to establish an adequate therapeutic regimen, it is necessary to know the Mg levels and the Mg/Ca ratio, because in the case of an associated hypocalcemia Ca deficiency must also be corrected. This can be done simultaneously with Mg supplementation, by co-administering a mean dose of 186 mg Ca²⁺/day. Providing this amount of Ca is very important, for the range in which Ca-Mg antagonism does not manifest is very narrow [25]. The time required for restitution of normal Mg/Ca equilibrium was prolonged in the group studied. The cause of this prolonged time is probably the absence of gall bladder and

Table 2. Supplementation Regimen

Mg ²⁺	300–600 mg
Ca ²⁺	185 mg
Vitamin B ₁	60–100 mg
Vitamin B ₆	250–750 mg

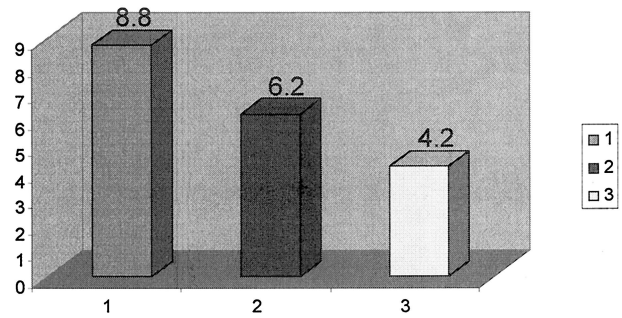


Fig. 2. Duration of therapy (weeks). 1 = PCES group, 2 = spasmophilia with digestive manifestation, 3 = spasmophilia without digestive manifestation.

intermittent bile evacuation into the duodenum, with possibly impaired intestinal Mg absorption.

The results obtained show that functional hepato-biliary and gastrointestinal disturbances in the group studied are Mg-dependent. Tiomag treatment eliminates these disturbances, re-establishing normal function of hepatocytes and bile ducts. Discontinuation of treatment for more than two months leads to recurrence of the above-mentioned symptoms. Resumption of Tiomag therapy makes the symptoms subside again. Systematic Mg administration, in amounts that meet requirements, under clinical and biochemical evaluation, prevents recurrence of PCES manifestations.

These findings demonstrate the cytoprotective role of this therapeutic regimen on the hepatocyte and bile ducts [26–29].

CONCLUSIONS

1. Functional manifestations of PCES subsided after Mg and methionine (Tiomag) supplementation, with vitamins B1 and B6, and Ca lactate.
2. Discontinuation of the supplements allowed for recurrence of clinical symptoms, which subsided again after the treatment was resumed.
3. The findings demonstrate the dependence of PCES functional manifestations on MD.
4. Maintenance of Mg and supportive nutritional supplementation prevents recurrence of PCES symptoms.

REFERENCES

1. Duca S: Sindromul biliarelor operati. Ed. Genesis Cluj, 1992.
2. Blumgart TM, Lygidakis NJ: The post-cholecystectomy patient. In Blumgart LM (ed): "The Biliary Tract." Edinburgh: Churchill Livingstone, pp 143–156, 1982.
3. Moody FG: "Advances in Diagnosis and Surgical Treatment of Biliary Tract Disease." New York: Masson, 49–56, 1981.
4. Geenen J: Intraluminal pressure recording from the human sphincter of Oddi. Gastroenterol 78:317–324, 1980.

5. Paun R: *Tratat de medicina interna. Bolile aparatului digestiv*, Ed Med Bucuresti 2:527–587, 1984.
6. Durlach J: *Le magnesium en pratique clinique*. *Med Int* 11:17, 1985.
7. Durlach J, Cachin M: *Magnesium et appareil digestif*. *Vie Med* 54:4327–4334, 1973.
8. Aikawa JK: The biochemical and cellular functions of Mg. *Proc. 1st Int Sympos on Mg deficit in human pathology*, Vittel, 39–54, 1971.
9. Aikawa JK: *Biochemistry and physiology of Mg*. *Wld Rev Nutr Diet* 28:112–142, 1978.
10. Aikawa JK: *Mg—its biological significance*. Boca Raton: CRS Press, p129, 1980.
11. Cantin M, Seelig MS: *Magnesium in health and disease*. New York: Spectrum Press, p 965, 1980.
12. Classen HG, Fischer G, Dobler L, Guigas C, Herold B, Hirneth H, Jacob R, Rieg CT: Modification of acute stress reactions by the actual Mg status and synthetic Ca antagonists. In *Proc. 1st Europ Congr on Mg*, Lisbon, 125, 1983.
13. Durlach J: *Controles neurohormonaux du metabolisme du Mg et leurs consequences clinique*. *Rev Franç Endocrinol Clin* 21:507–524, 1980.
14. Durlach J: *Aspects cliniques et biologiques du deficit magnesique chronique primaire*. *Feuillets de Biologie* 23:61–84, 1982.
15. Durlach J: *Speculations on hormonal controls of magnesium homeostasis: a hypothesis*. *Magnesium* 3:109–131, 1984.
16. Ebel H, Gunther T: *Mg metabolism—a review*. *J Clin Chem Clin Biochem* 18:257–270, 1980.
17. Gunther T: *Biochemistry and pathobiochemistry of Mg*. *Magnesium Bull* 3:91–101, 1981.
18. Kiss SA: *Mg trágyázás, Mg a biológában*. *Mezőgazdasági Kiadó*, Budapest, 140, 1983.
19. McCarty MF: *Magnesium taurate and fish oil for prevention of migraine*. *Med Hypotheses* 47:461–466, 1996.
20. Schneider HJ, Anke M: *“Mg-Stoffwechsel”*. Jena: Schiller Univ, p 179, 1976.
21. Wacker WEC: *“Magnesium and Man”*. Cambridge: Harvard University Press, p 171, 1980.
22. Walser M: *Physiochemical state of magnesium in the organism*. In: *Proc. 1st Int. Sympos. on Mg deficit in human pathology*, Vittel, 55–64, 1971.
23. Szántay J: *Metabolic interrelations of Mg deficit and loss of sulphur under stress and diverse stress-conditions in humans*. *Magnesium Bull* 3, 1981.
24. Szántay J: *Contributions to the study of methionine metabolism in some stress affections and conditions*. Ph.D.Thesis, Cluj, 1972.
25. Thomas J, Millot JM, Seville S, et al: *Free and total magnesium in lymphocytes of migraine patients—effect of magnesium in rich mineral water intake*. *Clin Chim A* 295:63–75, 2000.
26. Peikert A, Wilimzig C, Kölme-Volland R: *Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study*. *Cephalalgia* 16:257–263, 1996.
27. Porr PJ: *Manifestările clinice ale deficitului de magneziu la adult*. In Miu N, Drăgotoiu G (eds): *“Magneziul în biologia și patologia umană”*. Cluj: Casa Cărții de Știință, pp 88–97, 2000.
28. Porr PJ: *Psychosomatic pathology in dyselectrolytic disorders*. In Dumitrașcu DL (ed): *“Psychosomatic Medicine. Recent Progress & Current Trends”*. Cluj: Ed. Med. Univ. “I. Hațieganu,” pp 101–108, 2003.
29. Porr PJ, Mărginean C: *Digestive manifestations of magnesium Deficit*. In Nechifor M, Porr PJ (eds): *“Magnesium. Involvements in Biology and Pharmacotherapy”*. Cluj: Casa Cărții de Știință, pp 160–165, 2003.

Received August 5, 2004.