

LETTER TO THE EDITOR

Dietary factors and endocrine consequences of multiple chemical sensitivity

Factores dietéticos y consecuencias endocrinas de la sensibilidad química múltiple

Dear Editor:

In a recent cross-sectional study, Aguilar-Aguilar et al.¹ found that patients with newly diagnosed of multiple chemical sensitivity (MCS) followed an exclusion diet in 57.7 percent.¹ Similarly, it was estimated that approximately half of all cases (52.1 percent) were taking daily dietary antioxidants and/or supplements.¹ Aguilar-Aguilar and colleagues¹ should be congratulated for providing new nutritional clinical data among patients with MCS.^{1,2} As the investigators correctly state in the Discussion section, elimination diets may lead to a low muscle mass (sarcopenia),¹ along with frailty/fragility, weakness, and impair mobility.¹ The interesting study by Aguilar-Aguilar and colleagues¹ helps further the connection between low micronutrient consumption and MCS. We would like to share our perspective on MCS and metabolic abnormalities of micronutrients.

In the case series to which we refer,^{3–5} it has now been expanded to include more than 164 patients with MCS. Further analyses are now under way. Therefore, in our own clinical experience with MCS patients, 41.5 percent of patients (68 of 164) presented with hormonal disorders, a larger percentage than that reported in our previous retrospective MCS study,³ in which the overall prevalence of hormone-related disorders was 31.7 (13 of 41) percent.³

The mean ($\pm SD$) age of MCS patients was 48.9 ± 12 years (range, 22–78). The female to male ratio is approximately 6:1. At this time, amongst 164 patients who received diagnosis of MCS between 2000 and 2019, 10 of 164 (6.1 percent) had adrenal gland dysfunction (8 had hyposurrenalism and 2 had Cushing's syndrome). As was seen in a previous trial of MCS,³ hyperprolactinemic disorders are recognized diagnostic entities that are associated with MCS.³ Amongst MCS patients, 11 of 38 (28.9 percent) had a diagnosis of hyperprolactinemia. Patients were not taking any anxiety medications.



From a nutritional standpoint, in our clinical experience, zinc deficiency is one of the most important metabolic alterations with existing MCS syndrome.⁶ In fact, zinc is often displaced and/or replaced due to long term exposure to metal toxicants.⁶ Also, hypozincemia may be a marker of other hormonal as well as metabolic abnormalities (i.e., adrenal gland dysfunction, liver metabolic response, and malabsorption syndrome).^{3,6,7}

In patients with severe MCS ($n=54$), four patients had coexisting genetic and rare diseases (4 of 54, 7.4 percent): one patient received a diagnosis of porphyria, one patient had systemic mastocytosis, one had Ehlers–Danlos syndrome, and one had sickle cell anemia. Neuropathy (axonal) – predominantly related to small-fiber involvement – occurred in 39 (39 of 164, 23.8 percent) of the subjects in our MCS cohort.³ Small-fiber neuropathy is a well-recognized entity and may be associated with auto- and/or dysimmune reactions induced by toxic metals.³

Metabolically, in patients with MCS caused by retention of toxic metals (long-term body burden of toxic metals)³ there was an impairment of vitamins (mainly vitamins B) and trace elements activities, which in turn lead to destabilization of delicate hormonal balance.^{3,8}

Interestingly, none had clinical manifestations of MCS originating from molds^{9,10} to date. Currently, we have follow-up data on undesirable side effects relating to antioxidant supplements among individuals who have suffered with MCS. Combining acute and late adverse effects owing to antioxidant therapy (mainly reduced glutathione, GSH) had been reported in our initial study to account for about 60–70 percent.³ Now, the rate of patients with adverse effects to antioxidants was moderately increased to 72.7 percent (24 of 33).

Lastly, that 7 of 164 patients with MCS (4.3 percent) had anorexia nervosa emphasizes the high prevalence of anorexia and/or eating disorders in patients with chemical sensitivity.¹¹ Physicians treating patients with multiple chemical sensitivity (also termed MCS) should monitor their patients' hormone levels as well as micronutrients.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.endinu.2019.09.008](https://doi.org/10.1016/j.endinu.2019.09.008).

References

1. Aguilar-Aguilar E, Marcos-Pasero H, de la Iglesia R, Espinosa-Salinas I, Ramírez de Molina A, Reglero G, et al. Characteristics and determinants of dietary intake and physical activity in a group of patients with multiple chemical sensitivity. *Endocrinol Diabetes y Nutr.* 2018;65:564–70.
2. Loria-Kohen V, Marcos-Pasero H, de la Iglesia R, Aguilar-Aguilar E, Espinosa-Salinas I, Herranz J, et al. Multiple chemical sensitivity: genotypic characterization, nutritional status and quality of life in 52 patients. *Med Clin (Barc).* 2017;149:141–6.
3. Pigatto PD, Minoia C, Ronchi A, Brambilla L, Ferrucci SM, Spadari F, et al. Allergological and toxicological aspects in a multiple chemical sensitivity cohort. *Oxid Med Cell Longev.* 2013;356235.
4. Guzzi G, Ronchi A, Barbaro M, Spadari F, Bombecari G, Brambilla L, et al. Multiple chemical sensitivity and toxic metals. *Toxicol Lett.* 2016;258 Suppl.:s113.
5. Pigatto PD, Ronchi A, Dolcetta D, Brambilla L, Ferrucci S, Passoni M, et al. Exposure to metals, multiple chemical sensitivity and neurogenic inflammation. *J Clin Toxicol.* 2018;8:86.
6. Pigatto P, Ronchi A, Brambilla L, Ferrucci S, Spadari F, Passoni M, et al. Serum zinc levels, allergy to metals, and multiple chemical sensitivity. *Contact Dermat.* 2014;70:90.
7. Baines CJ, McKeown-Eysen GE, Riley N, Cole DEC, Marshall L, Loescher B, et al. Case-control study of multiple chemical sensitivity, comparing haematology, biochemistry, vitamins and serum volatile organic compound measures. *Occup Med (Chic Ill).* 2004;54:408–18.
8. Tan SW, Meiller JC, Mahaffey KR. The endocrine effects of mercury in humans and wildlife. *Crit Rev Toxicol.* 2009;39:228–69.
9. Pall ML, Anderson JH. The vanilloid receptor as a putative target of diverse chemicals in multiple chemical sensitivity. *Arch Environ Health.* 2004;59:363–75.
10. Valtonen V. Clinical diagnosis of the dampness and mold hypersensitivity syndrome: review of the literature and suggested diagnostic criteria. *Front Immunol.* 2017;8:951.
11. Guzzi G, Falabella V, Brambilla L, Ferrucci S, Legori A, Pigatto PD. Mercury sensitization and anorexia mercurialis. *Contact Dermat.* 2018;79:71.

Paolo D. Pigatto^a, Valentina Rossi^b, Gianpaolo Guzzi^{c,*}

^a *Clinical Dermatology, IRCCS Istituto Ortopedico Galeazzi, Department of Biomedical, Surgical and Dental Sciences, University of Milan, 20161 Milan, Italy*

^b *IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy*

^c *Italian Association for Metals and Biocompatibility Research – A.I.R.M.E.B., Milan, Italy*

* Corresponding author.

E-mail address: gianpaolo_guzzi@fastwebnet.it (G. Guzzi).