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Biological definition of multiple chemical sensitivity from redox state and cytokine profiling and not from polymorphisms of xenobiotic-metabolizing enzymes.

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Abstract

BACKGROUND: Multiple chemical sensitivity (MCS) is a poorly clinically and biologically defined environment-associated syndrome. Although dysfunctions of phase I/phase II metabolizing enzymes and redox imbalance have been hypothesized, corresponding genetic and metabolic parameters in MCS have not been systematically examined.

OBJECTIVES: We sought for genetic, immunological, and metabolic markers in MCS.

METHODS: We genotyped patients with diagnosis of MCS, suspected MCS and Italian healthy controls for allelic variants of cytochrome P450 isoforms (CYP2C9, CYP2C19, CYP2D6, and CYP3A5), UDP-glucuronosyl transferase (UGT1A1), and glutathione S-transferases (GSTP1, GSTM1, and GSTT1). Erythrocyte membrane fatty acids, antioxidant (catalase, superoxide dismutase (SOD)) and glutathione metabolizing (GST, glutathione peroxidase (Gpx)) enzymes, whole blood chemiluminescence, total antioxidant capacity, levels of nitrites/nitrates, glutathione, HNE-protein adducts, and a wide spectrum of cytokines in the plasma were determined.

RESULTS: Allele and genotype frequencies of CYPs, UGT, GSTM, GSTT, and GSTP were similar in the Italian MCS patients and in the control populations. The activities of erythrocyte catalase and GST were lower, whereas Gpx was higher than normal. Both reduced and oxidised glutathione were decreased, whereas nitrites/nitrates were increased in the MCS groups. The MCS fatty acid profile was shifted to saturated compartment and IFN γ , IL-8, IL-10, MCP-1, PDGFbb, and VEGF were increased.

CONCLUSIONS: Altered redox and cytokine patterns suggest inhibition of expression/activity of metabolizing and antioxidant enzymes in MCS. Metabolic parameters indicating accelerated lipid oxidation, increased nitric oxide production and glutathione depletion in combination with increased plasma inflammatory cytokines should be considered in biological definition and diagnosis of MCS.

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