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Circulating plasma cytokines, zinc, copper, vitamins A and E in multiple sclerosis patients and healthy controls

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Previous reports including our own have shown low levels of vitamins E and A[1,2] increased or decreased Zn and Cu[3–5] and elevated pro-inflammatory cytokines[6–8] in the blood and CSF of multiple sclerosis (MS) patients. The aim of this study was to investigate the relationships between the levels of circulating plasma vitamins E and A, Zn, Cu, interferon-γ (IFNγ), TNFα and IL-6 in MS patients in the remission phase of the disease compared with healthy controls. IFNγ, TNFα and IL-6 were assayed using commercially available paired antibodies (Genzyme Diagnostics Inc., UK) in an ELISA format. Vitamins A and E were extracted in ethanol and determined using HPLC (Philips PU 4100) equipped with a PU 4110 UV/visible detector and C18 reverse phase column. Determination of Cu and Zn was by ICP-MS (Perkin Elmer 5000 ICP-MS). There was no significant difference in the mean plasma levels of vitamin A, Zn, Cu, IFNγ, TNFα and IL-6 between MS patients and healthy controls (Table). There was, however, a significantly ($P<0.001$) lower plasma vitamin E concentration in patients with MS compared with controls and the mean concentrations of IFNγ, TNFα, IL-6 and copper were elevated compared with healthy controls (Table).

	Retinol (μg/l)	α-Tocopherol (mg/l)	Cu (μg/l)	Zn (μg/l)	IFNγ (pg/ml)	TNFα (pg/ml)	IL-6 (pg/ml)
MS	622±69	10.2±0.7*	1119±309	884±162	236±498	144±230	1299±1723
HC	673±84	11.2±0.8	957±189	858±131	187±90	40±26	397±775

MS, multiple sclerosis patients *n* 21 aged 22–68 years with relapse-remitting disease (expanded disability status score 2–4.5) TNF-α (*n* 16), IL-6 (*n* 8); HC, healthy controls (*n* 9) aged 25–45, IL-6 (*n* 4). *$P<0.001$.

Plasma vitamins A and E were positively correlated ($P<0.03$, $r=0.46$) in MS patients and in healthy controls ($P<0.04$, $r=0.6$). In MS patients only, a positive correlation between plasma IFNγ and TNFα ($P<0.0001$, $r=0.91$) and also between Zn and vitamin A ($P<0.07$, $r=0.4$) was observed as well as a negative correlation between Zn and IL-6 ($P<0.07$, $r=0.64$). These findings suggest that pro-inflammatory cytokines such as IL-6 may be responsible, in part, for some of the previously observed alterations in circulating nutrients in patients with MS, i.e. Zn and vitamin A. The low plasma vitamin E finding in MS compared with controls is consistent with our earlier observations in MS[1] although the present values were higher both in controls (1.7-fold) and MS (1.8-fold) than we previously reported which may indicate an increase in the intake of vitamin E in the general and MS population since the original study. Moreover, vitamin E is an important membrane lipid antioxidant and given the importance of PUFA in MS[9] it should be further investigated in patients with MS both in remission and relapse phases of the disease and in relation to membrane PUFA.

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