

Gender-related effects of chronic non-malignant pain and opioid therapy on plasma levels of macrophage migration inhibition factor (MIF)

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Macrophage migration inhibitory factor (MIF) is a cytokine produced by neuroendocrine and immune tissues that possesses several characteristics of a neuroendocrine mediator. Chronic pain is known to affect and to be affected by neuroendocrine and immune mechanisms. In the present study, the plasma levels of MIF and several hormones (cortisol, estradiol, testosterone) were determined to evaluate their mutual behaviour in controls and in chronic pain patients. Blood samples were collected from males and females divided into groups depending on their age (younger or older than 55) and health condition: 1) pain-free control subjects; 2) chronic non-malignant pain subjects. Moreover, two additional groups were added to evaluate the effects of short- and long-term opioid administration: 3) short-term opioid-treated chronic pain patients and 4) long-term opioid-treated chronic pain patients (longer than 6 months). MIF in control/younger men was higher than in all the other control and chronic pain groups. MIF was lower in pain patients than in controls of both sexes. MIF was not changed by morphine administration; its levels remained lower in opioid-treated subjects than in controls after both short- and long-lasting administration. Chronic pain changed hormone plasma levels differently in male and female patients. MIF was positively correlated with testosterone and negatively with estradiol. These results demonstrate sex differences in the younger men and women and a strong pain-induced decrease of MIF availability. These findings suggest the involvement of this cytokine in the sex differences observed in chronic pain conditions.