Serum Level of Macrophage Migration Inhibitory Factor in Helicobacter pylori-Infected Patients

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Key words: Helicobacter pylori, macrophage migration inhibitory factor

(DOI: 10.2169/internalmedicine.46.6242)

Helicobacter pylori (H. pylori) are known to be bacteria residing in stomach and causing acute and chronic gastric inflammation. In molecules associated with H. pylori-induced gastric inflammation, proinflammatory cytokines such as TNF-α and IL-8 particularly play an important role in the development of H. pylori-induced gastric inflammation (1). However, there have been a few investigations on the serum level of cytokines in H. pylori infected patients (2, 3), and the results are controversial.

Macrophage migration inhibitory factor (MIF) is known to be one of the proinflammatory cytokines and is crucial in the regulation of immune response and the development of inflammation including gastrointestinal disorders (4). A recent study has shown the critical role of MIF in H. pylori infection, but has not clearly shown that H. pylori infection affects circulating MIF level in human (5). In this study, to further clarify the role of MIF in H. pylori infection, we investigated the serum level of MIF in H. pylori positive and negative patients.

Fifty-seven H. pylori positive patients (age 20-79, male: female =36: 21) and 43 H. pylori negative patients including peptic ulcer and gastritis caused by non-steroidal anti-inflammatory drugs (age 25-75, male: female = 26: 17) were enrolled into the study. There was no significant statistical difference between these two groups in an age- and sex-adjusted analysis. Each patient gave informed consent. The presence of H. pylori infection was diagnosed with histological examination in corpus and antrum, urease-test and 13C-breath test. Participants who had been treated with anti-ulcer drugs or received anti-bacterial treatment within 1 month were excluded from this study. Serum samples were obtained from each patient after overnight fasting. Serum MIF level was measured with MIF enzyme-linked immunosorbent assay (ELISA) kit (Sapporo Immunodiagnostic Laboratory, Sapporo, Japan) according to the protocol. Results were expressed as mean ± standard error. *P<0.01. H. pylori (+), H. pylori-positive patients; H. pylori (-), H. pylori-negative patients; GU, gastric ulcer; DU, duodenal ulcer.

Figure 1. (A) The serum level of macrophage migration inhibitory factor (MIF) in Helicobacter pylori (H. pylori)-infected patients and non-infected patients. (B) The serum level of MIF in the H. pylori-infected patients with gastric, duodenal ulcer and gastritis. Results are expressed as mean ± standard error. *P<0.01. H. pylori (+), H. pylori-positive patients; H. pylori (-), H. pylori-negative patients; GU, gastric ulcer; DU, duodenal ulcer.

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Received for publication September 16, 2006; Accepted for publication February 1, 2007

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were statistically analyzed using Mann-Whitney U-test, and those in comparison between gastric ulcer, duodenal ulcer and gastritis in *H. pylori*-infected patients were using ANOVA (Stat View, SAS Institute, Cary, North Carolina, USA). P<0.05 was considered statistically significant. This study has been approved by the local Ethical Committee.

The level of MIF in serum was significantly (P<0.01) increased in *H. pylori* positive patients compared with *H. pylori* negative patients (6.49 ± 1.01 and 3.02 ± 0.36 ng/mL, respectively) (Fig. 1A). However, there was no statistically significant difference in serum level of MIF among the patients with gastric ulcer (n=18), duodenal ulcer (n=15) and gastritis (n=24) in *H. pylori* positive patients (6.65 ± 1.00, 6.50 ± 1.13 and 6.02 ± 1.06 ng/mL, respectively) (Fig. 1B).

Xia et al recently reported the increased expression of MIF in epithelial cells, T cells and macrophages of gastric mucosa in *H. pylori*-infected gastritis (5). It has been reported that bacterial infection increases the secretion of MIF from cells and tissues (4). Although our current study did not clarify the reasons why *H. pylori* infection increases the serum MIF level, it is suggested that secretion of MIF from MIF positive cells infiltrating into gastric mucosa may affect the serum level of MIF. On the other hand, we found no difference in the serum level of MIF among gastric ulcer, duodenal ulcer and gastritis. This suggests that the serum level of MIF depends on the increase in the numbers of MIF positive cells in gastric mucosa independently of tissue destruction.

Although our study was preliminary and further study is needed to conclude the association of serum MIF level with *H. pylori* infection, our data suggest that MIF might be related to the status of *H. pylori* infection.

**References**