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Pentoxifylline influences acute-phase response in acute myocardial infarction

P. Lechleitner[1], N. Genser[1], J. Mair[2], J. Maier[1], M. Herold[1], H. Beimpold[1], B. Föger[1], F. Dienstl[1], B. Puschendorf[2], and H. Tilg[3]

[1] Abteilung für Innere Medizin, [2] Abteilung für Chemie und Biochemie der Universität Innsbruck
[3] Department of Medicine, New England Medical Center, Boston

The aim of the present study was to investigate the effect of pentoxifylline (POF) on the acute-phase response by C-reactive protein (CRP) and tumor necrosis factor alpha (TNF-α) and on the release of creatine kinase (CK) in patients with acute myocardial infarction (AMI). POF is effective in modulating cytokines, for example, in suppressing TNF-α [2], which induces acute-phase protein synthesis in the liver [1].

Forty patients with confirmed AMI were investigated (29 men and 11 women, aged 40–83 years, mean 61 years). Immediately after admission 20 patients were randomized to receive the commercially available form of pentoxifylline at a dosage of 400 mg orally four times daily until day 3 after admission. Of the total, 30 patients received thrombolytic therapy. No patient received lidocaine, steroids, or other drugs with known anti-inflammatory effects. Localization of the infarcted area was determined by electrocardiogram (anterior, 17; inferior wall, 23).

Blood samples were drawn on admission and 16, 24, 48, and 72 h thereafter. CRP serum concentration was measured by a nephelometric method (QM 300, Kallestad, Austin, USA). TNF-α was assessed by a commercially available radioimmunoassay (RPA 532, Amersham International, Amersham, UK). The median TNF-α concentration in 34 healthy volunteers was 37.5 pmol/l (interquartile range 33.8–40.0 pmol/l). Data are presented as median values and interquartile range. Differences between groups were assessed using the Mann-Whitney *U* test. A *P* value of less than 0.05 was considered significant.

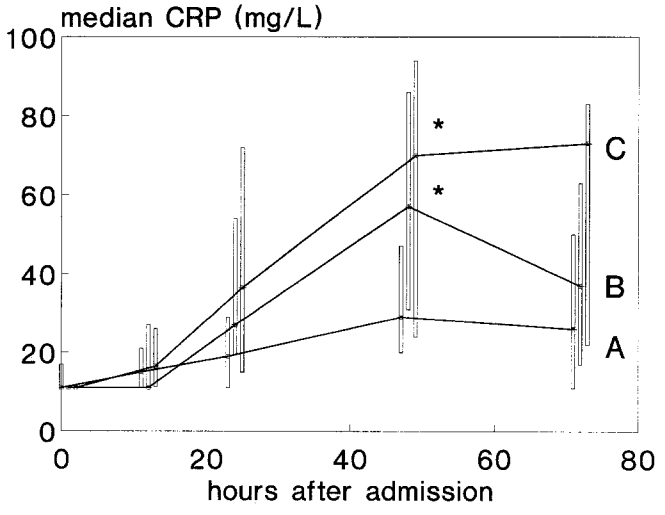

Fig. 1. CRP concentrations in patients with pentoxifylline (*A*) versus controls with (*B*) and without (*C*) thrombolytic therapy. Only one patient in the POF group did not receive thrombolytic therapy (data not included). Data are presented as median (*lines*) and interquartile range (*bars*). *Asterisks*, significant differences from POF patients ($P<0.05$)

Eight persons had to be excluded from data analysis: four POF patients and two controls because of inflammation at the site of the intravenous line ($n=3$) or pneumonia ($n=1$), and two further POF patients because of gastrointestinal side effects. The remaining patients (14 POF patients and 18 controls) were comparable in age, sex, delay, and localization of the infarcted area. Only one patient died, of severe pneumonia.

Results are presented in Fig. 1.

In the POF-treated group, maximum CK activity was significantly lower (median 464 U/l; interquartile range 216–734 U/l) than in controls (903 U/l; 535–1795 U/l; $P<0.05$).

Low CRP serum concentrations may indicate decreased inflammatory response and a reduced extension of myocardial infarction. POF suppresses lipopolysaccharide-induced, macrophage-derived TNF-α and interleukin 1 (IL-1) synthesis [2] without affecting interleukin 6 (IL-6) production [3]. Although we found no significant differences in TNF-α plasma levels between groups, it is most likely that reduced CRP concentrations in POF-treated patients are due to diminished TNF-α and/or IL-1 synthesis, as the other regulator of CRP synthesis, IL-6, is not influenced by POF [3]. A possible limitation of this study is our relatively small sample size. These preliminary findings, however, justify the further evaluation of POF effects in AMI patients with regard to infarct size and mortality.

References

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Dr. P. Lechleitner
Medizinische Universitätsklinik
Anichstrasse 35
A-6020 Innsbruck
Austria