THU0013 BIOLOGICAL AND IMMUNOLOGICAL PROFILES OF THE DELTA-SELECTIVE OPIOID RECEPTOR ANTAGONIST HS 378

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10.1136/annrheumdis-2001.522

Background Immuno-hyperreactivity is a fundamental process in inflammatory conditions such as rheumatoid arthritis. Delta-selective opioid receptor antagonists have been shown to exhibit inhibitory effects on inflammation. Therefore, the development of such compounds is highly promising with regard to selective action and is also of potential clinical relevance for human inflammatory diseases. HS 378 is a recently developed indolomorphinan with high selectivity and antagonist potency at the delta-opioid receptor.

Objectives The present study was performed to characterise the opioid binding properties and pharmacological and immunological activity of HS 378 and to compare them with those of two well-known delta-opioid receptor antagonists, naltrindole and naltriben.

Methods In vitro opioid receptor binding profiles were determined in rat brain homogenates. Agonist/antagonist potency of HS 378 was determined in the [³⁵S]GTPγS functional assay using membranes from CHO cells transfected with cloned human opioid receptors. In order to assess immunological activity, HS 378 was tested on concanavaline A stimulated rat T-lymphocytes.

Results HS 378 showed 4.7- and 2.4-fold higher mu/delta selectivity compared to naltrindole and naltriben, respectively. In the [³⁵S]GTPγS functional assay, HS 378 resulted in an apparent dose-related suppression of concanavaline A induced rat T-lymphocyte proliferation with an IC₅₀ value of 0.54 μM. The IC₅₀ of HS 378 was 13 times lower than that of naltrindole and 8 times higher than that of cyclosporine A.

Conclusion Taken together, our findings indicate that the small molecule HS 378 has properties that may be of therapeutic value in the setting of human inflammatory diseases.

THU0014 INCREASED SOLUBLE INTERCELLULAR ADHESION MOLECULE 1 LEVELS AND DECREASED ERYTHROCYTE SUPEROXIDE DISMUTASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POSSIBLE ASSOCIATION WITH THE DISEASE ACTIVITY

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10.1136/annrheumdis-2001.523

Background

Objectives We investigated the serum levels of soluble intercellular adhesion molecule-1 (sICAM-1) and the activity of erythrocyte superoxide dismutase (SOD) in rheumatoid arthritis (RA). We also sought whether there was a correlation between sICAM-1 and erythrocyte SOD and whether the levels of sICAM-1 reflected disease activity.

Methods Levels of sICAM-1 were measured in serum of 42 patients with active RA and 30 control subjects by an enzyme-linked immunosorbent assay. SOD activity was determined in erythrocytes isolated from patients with active RA and from controls.

Results The serum levels of sICAM-1 were significantly higher in the patients with RA than in the control subjects ($p < 0.001$). In contrast, the activities of erythrocyte SOD were significantly lower in RA patients than those in healthy controls ($p < 0.001$). A significant negative correlation was found between the levels of sICAM-1 and erythrocyte SOD activity ($r = -0.39$, $p < 0.01$). There was a statistically significant positive correlation between sICAM-1 levels with Ritchie articular index (RAI) score and C-reactive protein (CRP) ($r = 0.32$, $p < 0.05$; $r = 0.44$, $p < 0.01$, respectively), whereas no significant correlation was observed between sICAM-1 and erythrocyte sedimentation rate (ESR) ($r = 0.21$, $p > 0.05$).

Conclusion These results show that the increased levels of sICAM-1 present in active RA patients might be due to the decreased activity of erythrocyte SOD, and increased levels of sICAM-1 may also reflect disease status or activity.

THU0015 NA⁺, K⁺, ATPASE, INTERCELLULAR ADHESION MOLECULE-1 AND RHEUMATOID ARTHRITIS: A STUDY ON THE ERYTHROCYTE MEMBRANE

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10.1136/annrheumdis-2001.524

Background

Objectives We measured serum levels of soluble intercellular adhesion molecule-1 (sICAM-1) and erythrocyte membrane Na⁺, K⁺, ATPase activity and the correlation of these parameters in patients with rheumatoid arthritis (RA), and investigated whether the levels of sICAM-1 were correlated with the disease activity.

Methods Serum sICAM-1 levels were determined with sandwich enzyme-linked immunosorbent assay (ELISA) and erythrocyte membrane Na⁺, K⁺, ATPase activity with spectrophotometric method in sera from 42 patients with RA and in 30 healthy controls. Erythrocyte sedimentation rate (ESR) was determined according to the Westergren method and C-reactive protein (CRP) by nephelometric method. Disease activity was assessed by disease activity criterias.

Results Although decreased erythrocyte membrane Na⁺, K⁺, ATPase activity, serum levels of sICAM-1 were significantly higher in patients with RA than in healthy controls. Significant negative correlations between sICAM-1 levels and erythrocyte membrane Na⁺, K⁺, ATPase activity ($r = -0.678$, $p < 0.001$) were observed. There was a weak but statistically significant positive correlation between sICAM-1 levels with Ritchie articular index (RAI) score and CRP ($r = 0.32$, $p < 0.05$; $r = 0.44$, $p < 0.01$, respectively), whereas no significant correlation was observed between sICAM-1 levels with ESR, age and disease duration. There was no correlation between values of CRP, RAI and ESR with erythrocyte membrane Na⁺, K⁺, ATPase activity.

Conclusion From these data, it is concluded that the decreases in erythrocyte membrane Na⁺, K⁺, ATPase activity and increases in sICAM-1, ESR and CRP levels are present in RA, and that the decrease in erythrocyte membrane Na⁺, K⁺, ATPase activity in RA might be due to increased sICAM-1, and increased levels of sICAM-1 and correlations with other parameters may be a significant and novel marker for evaluating the disease status and the activity of RA.