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Title: ACE and sIL2-R predict lung function improvement in sarcoidosis during methotrexate therapy

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Body: Introduction In sarcoidosis, the search for a disease activity marker that correlates with treatment response is ongoing. The aim of this study was to assess the course of serum angiotensin-converting enzyme (ACE) and soluble IL-2 receptor (sIL-2R) during methotrexate (MTX) therapy, and to determine the predictive value of baseline levels and change in ACE and sIL-2R for lung function improvement in sarcoidosis. Methods In this retrospective cohort study we reviewed all sarcoidosis patients who used MTX for six months. Correlation coefficients (R) and Odds ratios (ORs) were calculated to study the correlation and predictive effect of serum ACE and sIL-2R levels. Results 114 patients were included, 76 of whom had a pulmonary indication for initiating treatment. After six months of MTX treatment, mean ACE decreased with 17.2 U/l ($p < 0.0001$) and mean sIL-2R with 1850 pg/ml ($p < 0.0001$). High baseline levels of ACE correlated significantly with lung function improvement after treatment ($R = 0.45$, $p < 0.0001$; stronger in the pulmonary subgroup $R = 0.57$, $p < 0.0001$). Decrease in ACE and sIL-2R after MTX therapy correlated with improvement in lung function. The strongest correlation was found with Δ DLCO in the pulmonary group (ACE $R = 0.63$, $P < 0.0001$; sIL-2R $R = 0.56$, $P < 0.0001$). Baseline levels of ACE > 90 U/l predicted a 10% improvement in overall lung function (OR 3.55; CI 1.34-9.38), with a higher prediction level for 10% improvement in DLCO (OR 4.63; CI 1.23-17.4). Conclusion Serum ACE and sIL-2R levels correlate with lung function improvement during treatment with MTX. Serial measurements of these easily available markers could be of important value to physicians when monitoring treatment in sarcoidosis patients.