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Title: Methotrexate vs azathioprine in chronic sarcoidosis

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Body: Background Although steroids remain the mainstay of therapy in sarcoidosis, chronic use is associated with toxicity. Evidence is missing on which second line therapy is most appropriate. Aim To compare the effect of methotrexate (MTX) and azathriopine (AZA) in second line treatment of chronic sarcoidosis patients regarding steroid use, lung function and side effects. Methods This is a retrospective cohort study, reviewing all patients who started MTX or AZA in two Dutch/Belgian tertiary referral centres. Demographic data, steroid use, lung function tests and side effects were noted from initiation until 2 years after or discontinuation. Treatment effect was calculated with a linear mixed model with FEV1, VC, DLCO and prednisone dose changes over time as endpoints. Differences in side effects were calculated with χ2-tests. Results 200 patients were included, 145 received MTX and 55 received AZA. Prednisone daily dose decreased with 6.32 mg/year ($p<0.0001$) while on therapy, with no difference between MTX and AZA. FEV1 showed a mean increase of 52 ml/year ($p=0.006$) and VC of 95 ml/year ($p=0.001$), with no difference between drugs for both. DLCO (% predicted) increased with a mean of 1.23%/year ($p=0.018$). Mean DLCO was 5.12% lower in the AZA group ($p=0.05$), but this difference was constant over time. There were significantly more patients with infections in the AZA group (26.5 vs 16.0% $p=0.01$). No significant differences were found regarding other side effects. Conclusions This is the first study comparing the effect of MTX and AZA in sarcoidosis treatment. Although more infections occurred in the AZA group, this study shows both drugs were equally effective in terms of lung function improvement and had a significant steroid sparing effect.