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Letters to the Editor

Efficacy of Mycophenolate Associated With Methotrexate as a Maintenance Treatment for Systemic Sclerosis-Associated Interstitial Lung Disease☆

Eficacia del micofenolato asociado a metotrexato como tratamiento de mantenimiento de la enfermedad pulmonar intersticial asociada a la esclerosis sistémica

Dear Editor,

We have read with great interest the recently published article by Espinosa et al.[1] about the effectiveness of cyclophosphamide (CPM) as a maintenance treatment in interstitial lung disease (ILD) associated with systemic sclerosis (SS). This paper demonstrates the effectiveness of CPM for controlling the evolution of the decline in lung function present in these patients with treatments longer than 12 months. Currently, CPM is a potent immunosuppressant and is considered a first-line treatment in ILD associated with systemic sclerosis.[2] Nevertheless, CPM has a considerable list of adverse effects, among which we should highlight infections, due to their frequency, and hemorrhagic cystitis and infertility, due to their severity. This latter effect is one of the most important, as SS affects predominantly women of reproductive age. Mycophenolate mofetil (MMF), however, an excellent immunosuppressant with a better adverse effect profile than CPM, has been demonstrated to be effective in ILD associated with SS.[3,4] Methotrexate (MTX) is a drug that is useful in the skin and joint manifestations of autoimmune diseases and it is a double-edged sword in interstitial lung diseases associated with this group of pathologies: one the one hand, it has demonstrated efficacy as a maintenance treatment, but on the other hand there is a well-described dose-dependent association between the use of MTX and lung toxicity.

We would like to provide our experience with 5 patients with SS-associated ILD who received an initial treatment with boluses of intravenous CPM at a dose of 750 mg monthly for the first 6 months, followed by a trimester regime with mean treatment duration of 19.2±6.6 months. At the start of treatment with CPM, forced vital capacity (FVC) was below 70% in 4 of the 5 patients and the carbon monoxide diffusing capacity (DLCO) was severely depressed, with means of 59.8%±10.7% and 31.8%±12.3%, respectively. After one year of treatment with CPM, the mean difference in FVC and DLCO was 1.8±6.9 and 6.6±2.7, respectively. Although CPM stabilized the lung function of these patients, either the clinical progression or the presence of skin and joint manifestations led us to a change in the treatment regime, substituting CPM for associated MMF at a dosage between 1.5 and 2.5 g/day and MTX in a single weekly dose of between 5 and 10 mg, orally. After one year of treatment, the mean difference in FVC was 3.2%±4.6%, while the mean difference in DLCO was 2.2%±3.9%. Unlike with CPM monotherapy, the patients presented a clinical improvement in the skin and joint manifestations. None of the patients presented severe adverse effects requiring the medication to be suspended.

Therefore, the association of MMF at full doses and MTX at low doses stabilized the deterioration in respiratory function with an effectiveness similar to the CPM boluses, in addition to improving the extrapulmonary symptoms of these patients with a good profile for tolerance and safety.

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