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Adalimumab in combination with methotrexate is more effective than methotrexate alone for treatment of uveitis associated with juvenile idiopathic arthritis

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Uveitis is defined as an intraocular inflammation and classified based on its anatomical location in the eye. Uveitis is closely associated with juvenile idiopathic arthritis (JIA). Although all types of uveitis can occur in association with JIA, the one observed most frequently (83%) is chronic anterior uveitis. Girls aged less than 7 years and who are antinuclear antibody (ANA) positive constitute the group of patients at highest risk. Uveitis may give rise to serious complications, such as cataract formation, band keratopathy, glaucoma or synechiae. In severe cases, it can produce total loss of vision.

Corticosteroids, either topical in the form of drops or systemic, are the first line of treatment, but in cases in which they do not suffice to control inflammation, methotrexate continues to be the drug of choice.[1]

In recent years, there has been an increasing number of clinical trials focused on the treatment of uveitis. However, applying the findings of these studies is not always easy. First, because most of these studies have been conducted in adults. Also, because the cases of uveitis included in these studies are of a highly diverse aetiology, and those associated with JIA constitute a small percentage of the total.[2]

The SYCAMORE trial, reviewed in the current issue of *Evidencias en Pediatría*,[3] is a randomised controlled trial comparing the efficacy of adalimumab combined with methotrexate versus methotrexate alone for the treatment of uveitis associated with JIA.

The trial was stopped early because children that received adalimumab in combination with methotrexate exhibited a significantly lower risk of uveitis compared to those that received placebo with methotrexate. On the other hand, there was a higher incidence of adverse events (although most were mild) in children that received adalimumab compared to those that received placebo.

The SYCAMORE trial is of considerable clinical relevance for two reasons. The first is that few clinical trials of drugs for the treatment of uveitis in children have been conducted to date. Secondly, unlike other studies with samples that were substantially heterogeneous as regards the type of uveitis, this trial focused on forms of uveitis associated with JIA.

However, the study also has significant limitations. One of them, which must be taken into account on interpreting the results of the study, is that its conclusions cannot be generalised to all patients with JIA-associated uveitis, as the study only included patients that continued to have uveitis despite ongoing treatment with methotrexate, who probably corresponded to the most severe forms of disease. However, this limitation is also an element of interest, as it is precisely for patients with uveitis refractory to methotrexate that we need effective therapeutic options like adalimumab.

Another limitation of the study that was also intrinsic to its design is that it did not explore the efficacy of adalimumab as monotherapy in these patients, as all children who were randomly assigned to treatment with adalimumab were also treated with methotrexate.

Last of all, we ought to reflect on the comparison of the adverse effects in each arm of the trial. The combined use of methotrexate and adalimumab was associated with a greater number of adverse effects compared to methotrexate alone. However, we have no way of knowing whether this was due to adalimumab itself or to the use of drugs in combination.

It should also be noted that both the duration of followup and the size of the trial preclude reaching conclusions on the risk of developing serious adverse effects such as cancer or demyelinating disease.[4]

To conclude, the SYCAMORE trial has produced evidence on the efficacy of adalimumab in combination with methotrexate in JIA-associated uveitis. The use of adalimumab was associated with an increased incidence of adverse events, but most of them were mild. Uveitis carries a high risk of morbidity, and there is little evidence of the efficacy of other drugs, including biologic agents.

Taking all these aspects into account, we recommend adalimumab for the treatment of children with uveitis refractory to methotrexate with the purpose of preventing serious sequelae, but under strict monitoring to watch for the development of serious adverse events.

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