

Sulfasalazine Reduces the Number of Flares of Acute Anterior Uveitis Over a One-Year Period

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ABSTRACT. Objective. To evaluate the efficacy of sulfasalazine (SSZ) in the prevention of recurrent flares of acute anterior uveitis (AAU).

Methods. We included patients seen from June 1997 to October 2000 in this prospective, open, longitudinal study who fulfilled the following inclusion criteria: either (1) ≥ 3 flares of AAU in the previous year or (2) ≥ 2 recurrences of uveitis within 3 months before starting the trial. We excluded uveitis of infectious or malignant origin or patients with contraindications to the drug. The response criteria were defined as absence of symptoms and the presence of a normal ophthalmologic examination. The major outcome was the number of flares of uveitis over a one-year period compared in the same group of patients with the flares along the previous year without SSZ.

Results. Three hundred ninety-four patients with uveitis were evaluated during the period of the study and 10 patients fulfilled the inclusion criteria. The mean number of flares in the pre-SSZ year was 3.4 (SD 0.5), which was significantly reduced to 0.9 (SD 1.1) in the year of treatment ($p = 0.007$).

Conclusion. SSZ treatment seems to reduce the number of flares over a one year period in patients with recurrent AAU. (J Rheumatol 2003;30:1277-9)

Key Indexing Terms:

ACUTE ANTERIOR UVEITIS

TREATMENT

SULFASALAZINE

It is well established that noninfectious and nonmalignant uveitis with involvement of the posterior area, or with a chronic course, or uveitis associated with an autoimmune disease should be treated with systemic corticosteroid and/or immunosuppressive drugs. Patients with anterior uveitis usually respond well to local topical treatment, and systemic drugs are usually not necessary. However, it has been reported that 34% of patients with uveitis have acute anterior recurrent uveitis (AARU)^{1,2} that recurs in a variable period of time.

When we started our study, the only publication that had investigated how to prevent recurrence of attacks was a retrospective study suggesting sulfasalazine (SSZ) prevents flares of AARU in patients with spondyloarthropathies (SpA)³. We hoped to confirm, by a prospective study, those preliminary results.

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Submitted July 16, 2002; revision accepted November 15, 2002.

MATERIALS AND METHODS

Study design. To evaluate the role of SSZ, a prospective, open, longitudinal study comparing a group of patients before and after a therapeutic intervention was designed. Our objective was to decrease the number of flares of AARU over a one-year period. The inclusion criteria were the presence of ≥ 3 flares of anterior uveitis in the previous year or a recurrence of a flare within 3 months of the previous one. We excluded infectious or malignant uveitis and patients with contraindications to SSZ.

Diagnosis. Anterior uveitis was diagnosed by an ophthalmologist according to the International Uveitis Study Group classification system⁴. The major outcome measure was the reduction of the number of flares of AARU over a one-year period of treatment, in comparison with the previous pretreatment year. The response criteria were defined as the absence of symptoms and a normal ophthalmologic examination.

Patient selection. Patients were selected from June 1997 to October 2000 from a multidisciplinary uveitis clinic composed of a team of ophthalmologists and rheumatologists. All patients included in the study were visited monthly after starting SSZ during the first 3 months and every 3 months thereafter. However, they were instructed to inform us as soon as possible if they had a new flare.

Treatment. Flares were treated with local standard treatment plus SSZ, and the patient was seen every 2 weeks after the resolution of the flare and cessation of the ocular therapy. No patients received treatment with oral corticosteroids or any disease-modifying drug other than SSZ.

The drug was started at a dose of 500 mg/day and increased 500 mg/wk to achieve a stable dose of 2 g/day (1 g bid) that was maintained during the study period of one year. In cases of a new flare, the dose was increased 500 mg/wk up to a total dose of 3 g/day.

Routine laboratory measurements included complete blood count, and hepatic and renal biochemistry were performed monthly for the first 3 months and every 3 months thereafter.

Statistical analysis. The Wilcoxon test was applied to compare the number of flares in the pretreatment year with those in the one-year treatment period.

RESULTS

Three hundred ninety-four patients with uveitis attended our specialized uveitis clinic during the study period and clinical data were included in our database.

Ten out of the 394 patients fulfilled the inclusion and exclusion criteria with a mean age of 47 years (range 30–84 yrs). Sex, age, diagnosis, the number of flares of AARU in the year before and after starting SSZ, and HLA-B27 status are shown in Table 1. Informed consent was obtained from all patients prior to starting SSZ treatment.

Of the 10 patients, 3 were men, 7 had some type of SpA (4 ankylosing spondylitis, one reactive arthritis, one undifferentiated SpA, and one inflammatory bowel disease), and 3 had idiopathic uveitis.

The mean number of flares in the pretreatment year was 3.4 (SD 0.5, range 3–4). During the one-year SSZ treatment period, the mean number of flares decreased to 0.9 (SD 1.1, range 0–3). These differences were significant ($p = 0.007$).

Only one patient, who had an undifferentiated SpA, was considered a nonresponder. In 4 patients (2 with ankylosing spondylitis and 2 with idiopathic uveitis) the number of flares was reduced and in the remaining 5 patients there were no flares during the year of treatment (Table 1).

Two adverse events were recorded, both consisting of a mild and transitory elevation of transaminases, neither of which required discontinuation of the therapy.

DISCUSSION

AARU, the most common form of uveitis, is frequently associated with the HLA-B27 haplotype and SpA^{1,2}, and has a tendency to recur in a variable period of time. AARU usually responds to topical ocular treatment, and systemic

corticosteroids or immunosuppressive drugs are usually not indicated⁵. However, immediately after starting our specialized uveitis clinic, we observed that some patients had a high number of flares, and also that recurrences were seen in some cases close to cessation of the ocular treatment.

To our knowledge, when we started this work in 1997, there was only one published retrospective study³, in which the authors recorded the number of flares in 22 patients with some type of SpA during SSZ treatment for their rheumatic symptoms. They compared the number of flares in a period of the disease without this treatment and showed a significant reduction of flares during SSZ treatment.

Based on these data, a prospective study using SSZ was designed. The inclusion of patients with 3 or more flares during a one-year period was chosen based on the accepted opinion that occasional flares do not justify treatment other than topical ocular therapy. However, in patients with 3 or more episodes of uveitis in one year, it could be of interest to attempt the improvement of the disability that the continuous ocular disease produces.

Our results show that there is a significant reduction in the number of flares after starting SSZ treatment in patients with 3 or more episodes in the previous year. Of the 10 patients in the study, only one did not respond, 4 had a reduction in the number of flares, and the remaining 5 patients had no new flares during the year of treatment with SSZ.

Although this was a prospective study, it has the limitations of being open and not controlled. However, while we were analyzing our data, Benitez, *et al* published a report supporting our results⁶. In their randomized, prospective, open study of 22 patients with ankylosing spondylitis (10 with SSZ and 12 with no treatment), a reduction in the number of recurrences of uveitis in the SSZ group was found ($p = 0.016$). In addition, the blood-aqueous barrier permeability of the eyes, determined by fluorophotometry, was significantly higher during acute attacks of uveitis in the group of patients without SSZ ($p = 0.019$).

Table 1. Characteristics of the patients included in the study.

Age	Sex	Diagnosis	HLA-B27	Uveitis Flares, n	
				Year Before SSZ	Year After SSZ
84	F	IBD	NA	4	0
32	M	AS	+	3	0
53	M	AS	+	3	0
45	F	Idiopathic	+	4	2
48	F	AS	–	3	2
40	F	Reactive	+	4	0
57	F	AS	+	3	1
39	F	Idiopathic	+	4	0
50	M	Idiopathic	+	3	1
30	F	US	–	3	3

IBD: inflammatory bowel disease; AS: ankylosing spondylitis; US: undifferentiated spondyloarthritis; NA: not available.

Our results show that SSZ seems to reduce the number of flares of AARU over a one-year period in selected patients with a high number of recurrences. Our study, in addition to the 2 others published, provides the justification for a more extensive investigation to confirm the results. Until then, patients with AAU and frequent recurrences should be treated with SSZ.

ACKNOWLEDGMENT

The authors thank to Dr. R. Madero and M.E. Miranda for the statistical assessment and the corrections made to the original manuscript.

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