Methotrexate for the treatment of noninfectious scleritis

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ABSTRACT ●

Objective: To assess corticosteroid-sparing and inflammation control in patients with noninfectious scleritis treated with methotrexate.

Design: Retrospective review.

Participants: Patients who received methotrexate treatment for noninfectious scleritis and who had 12 months of follow-up after treatment initiation were included in this review.

Methods: The clinical records of noninfectious scleritis patients presenting at the University of Ottawa Eye Institute between September 1, 2010 and December 31, 2014 treated with methotrexate were retrospectively reviewed. Seventeen patients (21 eyes) were included in the study. Main outcome included inflammation control and corticosteroid-sparing success. Secondary outcomes were reduction of immunosuppression load and best-corrected visual acuity.

Results: The proportion of eyes with corticosteroid-sparing success was 69.2% at 3 months and 92.3% at 12 months. The proportion of eyes that achieved inflammation control was 61.9% at 3 months and 90.5% at 12 months. The corticosteroid immunosuppression load at treatment start was 1.9 ± 2.07 and at 12 months was 0.48 ± 1.03 ($p < 0.01$). There was no statistically significant difference in best-corrected visual acuity.

Conclusions: The treatment of noninfectious scleritis with methotrexate appears to be effective at both achieving steroid-sparing success and controlling inflammation during 12 months of therapy. Immunosuppression load decreased significantly over 12 months of therapy while best corrected visual acuity was stable.

Scleritis is an ocular inflammatory disease that often presents as a painful inflammation of the sclera with acute scleral redness. It is associated with several ocular complications including scleral thinning, keratitis, uveitis, glaucoma, cataract, macular edema, serous retinal detachment, and papilledema. Sight-threatening disease or vision loss can occur due to these complications.[1,2] Scleritis is associated with an underlying systemic disease in approximately 50% of patients.[1,3] Several common autoimmune conditions associated with scleritis include rheumatoid arthritis, relapsing polychondritis, inflammatory bowel disease, granulomatosis with polyangiitis, and systemic lupus erythematosus. Less common autoimmune conditions associated with scleritis include Cogan syndrome, reactive arthritis, polyarteritis nodosa, psoriatic arthritis, Behçet disease, ankylosing spondylitis, and giant cell arteritis.[2] Additionally, there are infectious and malignant causes of scleritis, but these are less common.[1]

The first line treatment of noninfectious scleritis is typically nonsteroidal anti-inflammatory drugs (NSAIDs) and the administration of high-dose oral corticosteroids for a short duration if NSAID treatment is unsuccessful.[1] Corticosteroids can be administered topically, locally, or systemically and have proven to be the mainstay of treatment.[2,4] Although corticosteroid therapies are excellent at reducing ocular inflammation, they are associated with many negative side effects that increase in incidence and severity proportionally with duration of use.[2]

The addition of immunomodulatory therapies can be considered if corticosteroid therapy fails to control inflammation or when corticosteroid-sparing therapy is needed to reduce the risk of systemic side effects when corticosteroid is used long term.[5] The 3 most commonly used antimetabolite agents in treating ocular inflammation are methotrexate, azathioprine, and mycophenolate.[6]

Because noninfectious scleritis is a rare condition with a low incidence and prevalence, a limited number of studies has effectively assessed corticosteroid-sparing immunomodulatory agents such as methotrexate.[1,2,5,7–9] A recent study surveyed uveitis specialists and rheumatologists and found that these 2 specialties show some differences in treatment preference for the management of idiopathic scleritis.[8] Although these differences existed, methotrexate was still the most commonly selected agent chosen by both specialties.

The goal of this study is to assess the level of corticosteroid-sparing success and inflammation control in patients with noninfectious scleritis treated with methotrexate to better define the role of methotrexate in the treatment of noninfectious scleritis and help guide clinicians in their approach to treatment. Assessing both corticosteroid-sparing success and inflammation control will help determine if methotrexate is an effective treatment for noninfectious scleritis and will encourage clinicians to consider methotrexate as a safe alternative to long-term corticosteroid use.

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Materials and methods

Patients with a diagnosis of scleritis whose clinical records were available between September 1, 2010 and December 31, 2014 at the University of Ottawa Eye Institute were retrospectively reviewed. At the outset, 965 charts were reviewed and 27 patients had a diagnosis of scleritis and were treated with methotrexate. Out of these 27 patients, eligible patients were adult patients who received methotrexate treatment for scleritis and had 12 months of follow-up after methotrexate initiation. Patients less than 18 years of age were excluded. Patients did not have to be on current corticosteroid therapy to be included. Patients with less than 1 year of follow-up data were also excluded. Data collected included date of birth, sex, etiology, methotrexate dosage, corticosteroid and other immunosuppressive drug doses at every visit, number of periocular corticosteroid injections given, eye drops, best-corrected visual acuity, intraocular pressure, grading of scleritis according to the published criteria,[10] complications associated with treatment, and liver enzyme values. After review of all 27 patient charts over the specified time period, 17 patients (21 eyes) met the inclusion and exclusion criteria. The main outcome measures were inflammation control and corticosteroid-sparing success (see Table 1 for definitions).

The scleritis grading and clinical data recorded in the charts was performed by 1 clinician (C.G.) where the scleritis grading followed the standardized scleritis grading schema published by Sen et al.[10] The Sen et al.[10] grading scale is a photograph-based scleritis grading system that uses high-resolution colour images of the sclera that are graded from 0 to 4+, where 0 represents no scleral inflammation and 4+ represents the most severe form of scleral inflammation, necrotizing scleritis. Secondary outcomes included immunosuppressive load and best-corrected visual acuity (see Table 1 for definitions). Immunosuppressive load calculation was based on the scoring system used by Nussenblatt et al.[11] where different immunosuppressive agents received a score for each dosage level of the agent that ranged from 0–9. The sum of the individual immunosuppressive scores of each agent are then added together to calculate a total immunosuppressive grade.

Institutional review board/ethics committee approval was obtained for this study, and this research adhered to the tenets of the Declaration of Helsinki.

Results

Seventeen patients with a total of 21 affected eyes were included in the study. There were 12 females and 5 males, with a mean age of 54.2 ± 13.3 years. Two patients had rheumatoid arthritis and 1 patient had ankylosing spondylitis. One patient had a history of chronic glomerulonephritis. The remaining patients had no identifiable systemic conditions. Eighteen eyes had a diagnosis of anterior diffuse nonnecrotizing scleritis, 2 eyes had a diagnosis of anterior nodular nonnecrotizing scleritis, and 1 eye had a diagnosis of necrotizing anterior scleritis without inflammation. Only 1 eye was quiescent at the time of methotrexate initiation. The initial dose of methotrexate was 15 mg/week, and the maximum dose at any point in time over the 1-year follow-up period in any patient was 25 mg/week. Eight of the 21 eyes were not on corticosteroid at the time of methotrexate initiation. Seven patients had periocular corticosteroid injections before the treatment period with an average time of injection before treatment of 6 months. No patients received injections within the 3-month period before methotrexate initiation. Four patients (5 eyes) had periocular corticosteroid injections during the treatment period, administered at an average of 9 months after methotrexate initiation. Additionally, 4 patients had topical steroid treatment before the treatment period, and 6 patients had topical steroid treatment at some point during the treatment period. This did not have an effect on the primary and secondary outcome measures. Additionally, 1 patient had concurrent therapy during the study period with adalimumab 40 mg subcutaneously every 2 weeks and was stable throughout the follow-up duration.

The proportion of eyes that achieved steroid-sparing success was 69.2% (9/13) at 3 months, 69.2% (9/13) at 6 months, and 92.3% (12/13) at 12 months (Fig. 1). The proportion of eyes that achieved inflammation control with methotrexate was 61.9% (13/21) at 3 months, 71.4% (15/21) at 6 months, and 90.5% (19/21) at 12

Table 1—Study outcome measures

Outcome Measure	Primary or Secondary	Outcome Measure Definition
Inflammation control	Primary	Defined as a resolution (scleritis grading of 0*) in the affected eye for a duration of 3 months or longer with no increase in topical or systemic corticosteroid dose and fewer than 3 flare-ups of scleritis per year while on methotrexate therapy.
Corticosteroid-sparing success	Primary	Defined as oral prednisone ≤10 mg/day.
Immunosuppression load	Secondary	The immunosuppressive load is a calculation of immunosuppressive scores for each immunosuppressive agent used, where the sum of the individual immunosuppressive scores of each agent is used to calculate a total immunosuppressive grade. Details of this scoring system can be found in the Nussenblatt et al. article.[11]
Best-corrected visual acuity	Secondary	Snellen chart visual acuity was converted into logMAR scale acuity.

*The scleritis grading and clinical data recorded in the charts was consistent by 1 clinician (CG) where the scleritis grading followed the standardized scleritis grading schema published by Sen et al.[10]