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ORIGINAL RESEARCH ARTICLE

MYCOPHENOLATE MOFETIL THERAPY IN SCLERITIS: ANALYSIS OF SEVEN CASES IN TERTIARY EYE HOSPITAL IN INDIA.

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ABSTRACT

To evaluate the effectiveness of immunomodulatory mycophenolate mofetil in the treatment of scleritis. A retrospective non comparative review of seven cases of scleritis managed with mycophenolate mofetil at a tertiary eye hospital. The following information was extracted from the patients folders; socio-demographics, causes, type of scleritis, duration of scleritis, previous treatment on before commencement of mycophenolate mofetil (MMF), any systemic association, visual acuity (VA) at presentation and at the last hospital visit, laterality of the scleritis and the side effects experienced during the use of mycophenolate mofetil.Two patients with anterior nodular and four patients with diffuse anterior scleritis were identified. The mean follow up was 6 months. Six patients had the same pre-treatment VA and one patient had improved VA. No patient reported any side effect. All the inflammations were controlled in all the patients and no case of relapsed during the usage of MMF was reported. And no patient needed any additional immmunosupressive agents.Mycophenolate mofetil appears to be an effective drug in the management of anterior scleritis. The absence of side effects following its use is remarkable. It holds promise to reducing the blinding complication of scleritis. A further study with large sample size may be required to confirm our findings.

Key words: *Corticosteroids, India, Mycophenolate mofetil, Scleritis.*

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INTRODUCTION

Ocular inflammation is a common cause of ocular morbidity worldwide.[1, 2] Scleritis is an inflammation of sclera the tissue and usually associated with pain. Scleritis is characterized by cellular infiltration and sclera oedema. Improper management of scleritis may result in visual impairment/ blindness. Scleritis affects women more often than men, with a peak incidence in the fifth decade[3], it frequently starts in one eye and becomes bilateral in more than half of the cases.[3] Bilaterality is more commonly encountered in scleritis associated with systemic rheumatic disorders. The causes of scleritis include; idiopathic, infectious, collagen vascular disorders, drugs and surgery induced scleritis which was first described by Arensten et al. [4] in 1976. The diagnosis of scleritis is almost always clinical; however when the posterior sclera is involved, clinical signs may be less obvious and imaging studies are required to confirm the diagnosis.

One of the mainstay of management of scleritis is the use of steroid (topical and oral), however, ocular and systemic complications following long duration usage of steroids lead to introduction of more potent and less side effect immunosuppressant drugs such as azathioprine, methoterate,

cyclophosphamide, chlorambucil, cyclosporine and Mycophenolate mofite (MMF). Indication for the use of immunosuppressant drugs in the treatment of scleritis include anterior necrotizing scleritis, posterior scleritis and scleritis associated with a systemic autoimmune disease or collagen vascular disease.

MMF is an immunosuppressive agent, an ester morpholinoethyl of mycophenolic acid, with effective mode of action, by preventing the replication of T- and B-lymphocytes by inhibiting the de novo pathway of purine synthesis.[5] Since introduction of MMF in early 70's it has been used as immunomodulatory agents in prevention of acute renal grafting rejection[6] and treatment of many autoimmune systemic disorders.[7-11] Recently its use in the treatment of scleritis has been reported.[12-17] However no such report has been reported in India population hence the purpose of this study is to describe our experience with the use of MMF in the treatment of patients with scleritis.

MATERIALS AND METHODS

This was a retrospective review of seven patients who had scleritis and were treated between 1st September 2012 – 30th April 2013 (8-month-period) at Sankara Nethralaya hospital Chennai, India. The hospital is a tertiary eye centre and receives referral from across India and other countries. The case records of all consecutive patients, treated with mycophenolate mofetil (CellCept, Roche Laboratories Inc., Nutley, NJ) at uveitis unit of the hospital for scleritis were retrieved from the medical records unit of the hospital. The following information were extracted from their folders; demographics (age, sex, occupation, tribe, education), causes, type of scleritis, duration of scleritis, previous treatment on before commencement of mycophenolate mofetil (MMF), any systemic association, visual acuity (VA) at presentation and at the last hospital visit, laterality of the scleritis, side effects experienced during the use of mycophenolate mofetil, any additional drugs apart from mycophenolate mofetil and follow up. Scleritis classification was assigned based on the Watson and Hayreh classification.[18]

All the patients under went ocular assessment with slit lamp examination and binocular indirect ophthalmoscope (BIO). Each patient was given tablets MMF 1000 mg 12 hourly for two weeks, and thereafter 500 mg 12 hourly for two weeks. Additionally, the following adjuvant was given to each patient: tablets predinisolone 40 mg daily and then tailed down to 10 mg daily and tablet Ranitidine 150 mg 12 hourly daily.

All the patients had physician assessment clearance for steroid and immunomodulatory use.

The baseline investigations included a full blood count (FBC), anti-nuclear antibody, RPR/VDRL (rapid plasma reagin/ veneral disease research laboratory), angiotensin-converting enzyme, antinuclear antibody (ANA), rheumatoid factor, anti-neutrophil antibodies, chest x-ray, urinalysis, liver and renal function test. Ocular ultrasound was done to confirm cases of posterior scleritis. The patients were reviewed at two weeks after commencement of MMF and thereafter every four weeks. At each visit patients came with repeated full blood count (FBC) and erythrocyte sedimentation rate (ESR) tests.

Each patient was given questionnaire (Table 1) home to fill about the possible side effect she/he experienced during the ingestion of MMF.

At each hospital visit each patient was asked for any history of side effect, state of vision and each patient underwent VA assessment, slit lamp examination and BIO. In this study necrotizing scleritis was diagnosed if the scleral inflammation was associated with thinning or loss of scleral tissue. Success rate

in this study was measured in term of improvement in symptoms and signs of ocular inflammation (level of redness and swelling), reduction in predinisolone dosage and adverse effect of MMF therapy. Snellen visual acuity was converted to LogMAR visual acuity for analysis and change in VA before commencement of MMF and VA at the last hospital visit was compared. In a patient with bilateral scleritis visual acuity in the better eye was considered for interpreting result. Simple frequency analysis was done.

Ethical clearance for the study was obtained from ethical and researcher committee of Sankara Nethralaya hospital Chennai, India.

RESULTS

Of the seven patients 2 were males and 5 were females (71.4%) with mean age of 46.9years (range 23-61years). Table 2 showed patients demographics. Only one of the cases was a bachelor undergraduate. The scleritis are caused mainly by autoimmune diseases (n= 3). The mean duration of scleritis before referral to the hospital was 1year. There were 2 cases of anterior scleritis and the rest were diffuse anterior scleritis. Before commencement of MMF 3 patients had being receiving combination of steroids and methotrexate while the rest were only on steroids therapy. The above 3 patients commenced MMF because of failure of methotrexate to ameliorate the patients symptoms. Five patients had associated systemic diseases (2 each diabetic mellitus and rheumatic arthritis; and 1 pulmonary tuberculosis and diabetic mellitus). The scleritis mostly affects left eye (57.1%). Three of the patients had VA $6/6^{-2}$ at presentation while, at last hospital visit the VA in 6 patients remain the same and improvement in one patient was noticed. Table 3 visual acuity of the patients. The means follow-up of the patients following MMF usage was 6 months.

No side effect of MMF was recorded. And no patient needed any other immunosuppressive agents.

Table1: Questionnaire for patients on Mycophenolate mofetil

SN	Questions	Answer	
		Yes	No
1	Did you develop diarrhoea?		
2	Did you have vomiting?		
3	Did you get your blood counts done?		
4	If yes, is the white blood cells count bellow 3000/cubic mm?		
5	Did you develop any fever?		
6	Did you develop any respiratory or urinary tract infection?		
7	Any other side effect, please mention here:		

Table 2: Socio-demographic of the patients

Demographics	Frequency	%
Age (years)		
20 -30	2	28.6
31 -40	2	28.6
40+	3	42.8
Sex		
Male	2	28.6

Female	5	71.4
Occupation		
House wife	3	42.8
Civil servant	2	28.6
Farmer	2	28.6

Table 3: Visual acuity of the patients

	Premedication VA	VA at last hospital visit
3 patients	6/6-2	6/6-2
3 patients	6/9	6/9
1 patient	6/18+2	6/9+3

DISCUSSION

Scleritis whether acute or chronic if not properly managed may lead to visual impairment/blindness. The main stay of management of scleritis still remain steroids (topical and oral) however, because of complication arising from their long time used, lead to the introduction of various immunosuppressant drugs[15, 16]. MMF has been reported to be effective in the treatment of ocular inflammatory disease.[12, 16, 19-22]

All the case series responded well to MMF therapy with dose of 2 g daily for 2 weeks and thereafter 1g for 2 weeks this was similar to previous reported [23]. But was different from Nida et al[12] who have to use 3 g of MMF to get maximal effect in their 4 patients. The reason might be because of less severity of scleritis in our patients.

The studied case series did not report any side effect (both ocular and systemic) compared to other studies [12, 13, 22]. The reason may be because of short duration of our follow-up, possible genetic makeup in our patients and patient afraid of not receiving co-operation and attention of the eye care team if they report side effect. However this bias may be eliminated by prospective study at this centre.

Our study is limited because of retrospective nature of the study, small numbers of the patients and short duration of follow up.

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