



A Clinical study on Ophthalmic Manifestation of Rheumatoid Arthritis based on patients attending Rheumatology Department of Medical College Hospital, Thiruvananthapuram, South Kerala

Authors

S. Rema Devi¹, Jacob Antony²

¹Assistant Professor, Regional Institute of Ophthalmology, Government Medical College, Thiruvananthapuram, Kerala 695 035, India

²Associate Professor, Department of Rheumatology, Government Medical College, Thiruvananthapuram, Kerala 695 011, India

Abstract

Background: Rheumatoid Arthritis (RA) is an auto Immune chronic Inflammatory disorder of worldwide distribution and it causes painful and destructing articular conditions. Extra articular manifestation in RA are more common in sero +ve patients. The extra articular manifestations includes, epicarditis, pleuritis, major cutaneous, vasculitis, ophthalmic manifestations, glomerulo nephritis, and other type of vasculitis. Ophthalmic manifestation caused by RA causes severe ocular morbidities if not screened at an early stage.

Materials and Methods: A hospital based prospective observational study on patient attended at Rheumatology Department of Medical College, Thiruvananthapuram who have diagnosed as Rheumatoid arthritis were examined and called for detailed ocular evaluation at RIO Clinic. A total of 198 cases were screened during August 2019 to January 2021. All patients were subjected to detailed history, pertaining to age, duration of the disease systemic manifestation of RA, drug history and its duration and symptoms related to ophthalmic manifestation were collected. Protocol based treatment were offered after detailed ophthalmic evaluations tests and effect of treatment was studied during follow up periods. Data of the patients were recorded on a pre-fabricated proforma. Data was statistically analysed by chi-square analysis odds ratio and Logistic regression analysis.

Results: 115 (58.08%) patients of RA (Rheumatoid arthritis) showed Ophthalmic manifestations KCS. (dry eye manifestations) was the most common complications which responds well to artificial tear substitutes on daily application. Complications like episcleritis scleritis and iridocyclitis and keratitis were noted out and active emergency strategies were given to avoid ophthalmic morbidities and this helped to alleviate the problems of severe Vn Impairment. Drugs related to ocular complications like quinolen toxicity and posterior sub capsular opacity due to steroid toxicity were ruled out and strict follow up measures were given along with the guidance of the Rheumatologist.

Conclusion

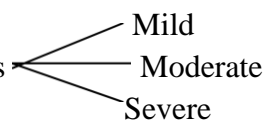
1. Rheumatoid arthritis is also a systemic auto immune disease have signs and symptoms of the eye.
2. KCS (Dry Eye manifestation) were the commonest complication.
3. Early Ophthalmologic interference and active treatment regimen can reduce further extent of ocular morbidities and thus Vn threatening conditions.

Keywords: Rheumatoid arthritis, peripheral Ulcerative keratitis, hydroxy- chloroquine, kerato conjunctivitis sicca, Non steroidal anti inflammatory drugs, posterior sub capsular cataract.

Background

RA is a common chronic systemic Inflammatory disorders of unknown etiology that primarily involve joints. Approximately more than 25% of patients with RA will have ocular manifestation. Hence in the present study indicated the urgent need of the RA patients for ophthalmic Screening and management to avoid Vision impairment and severe sight threatening conditions.

RA confirmed cases were studied at RIO (Regional Institute of Ophthalmology, Thiruvananthapuram) prospectively and the data obtained were statistically analysed commonly noted ophthalmic manifestation are:-

Dry Eye Manifestations 

Episcleritis, scleritis, scleritis with PUK, Iridocyclitis, Quinolen maculopathy and posterior subcapsular opacity (Posterior-subcapsular Cataract) in relation with systemic therapy related complications.

DRY eye manifestations were the commonest. Adequate treatment measure were offered to those patients who have showed abnormal Schirmer test and diminished corneal tear meniscus. Among the episcleritis, the simple diffuse type was noted commonly. Scleritis was mainly of the diffuse anterior type in which ocular surface edema and chemosis was noted only in doubtful cases phenylephrine test with 2% drops are used for differentiation between episcleritis and scleritis patients. Most of the scleritis patients were treated with oral and topical steroids and NSAIDS. Nodular scleritis was noted in few cases with complaints of intense pain on palpation. Yet with starting of intense therapy had brought change in reduction of symptoms like pain and redness. Topical steroid and NSAID resistant cases were responds well to immuno suppressive like cyclosporine drops.

Pheripheral Ulcerative Keratitis was noted in five cases.

Treatment modality included were topical preparation of 1% medroxyprogesterone or 20% N, acetylcysteine along with lubricating gel, antibiotic drops, or ointment, and cycloplegic drops in favour of aiding re-epithelization. Anterior, uveitis patients were treated with protocol based drugs and were responded to treatment very effectively. Many patients referred from Rheumatology Department for evaluation of quinoline and steroid induced toxicity. Some patients were using quinoline for more than five years without any follow up or ophthalmic evaluations while on screening they were presented with drop in vision acuity and scotomas on macular function tests. Hence urgent regular ophthalmic follow up evaluations and monitoring was suggested to these patients. Some patients receiving systemic steroids were having postering subcapsular cataracts were presented with decreased vision on both eye on Vn acuity screening tests. Hence to these patients also we had given instructions like an urgent need of attending the Rheumatology clinic on regular intervals to receive new suggestions of any change in the prescribed dose schedule of systemic drugs.

Aim

1. To find out the ophthalmic manifestation of patients with Rheumatoid arthritis attending a tertiary eye hospital in southern Kerala and their management.
2. Treatment outcomes of those patients who receiving treatment.

Settings: Regional Institute of Ophthalmology Government Medical College Hospital, Thiruvananthapuram, South Kerala.

Materials and Methods

The study was designed as a hospital based prospective observational study and patients presented at Rheumatology Department of Government Medical College hospital, Thiruvananthapuram, identified as RA were examined and called for detailed ocular evaluations at RIO. A total of 198 patients were

screened during August 2019 to January 2021. After getting consent from the Institutional Human Ethical Committee all patients were subjected to detailed evaluation include history taking as to age, the duration of illness, drug history (history of treatment taking) and systemic illness and ocular symptoms were collected and subjected to detailed ocular examination was done using torch light and slit lamp, visual acuity test and detailed fundus examination was done. Patients who is on plaquenil (HcQ) were subjected to macular functions tests like Amsler Grid test, colour Vn tests, field analysis and B Scan evaluations. DRY eye Evaluation tests was done in almost all the patients protocol based treatment was given to all patients with ophthalmic manifestations and effect of treatment was evaluated during the 1st visit and later follow up periods. Data of the patients were recorded on a pre fabricated proforma. Data was statistically analysed by chi-square analysis, odds ratio and Logistic regression analysis.

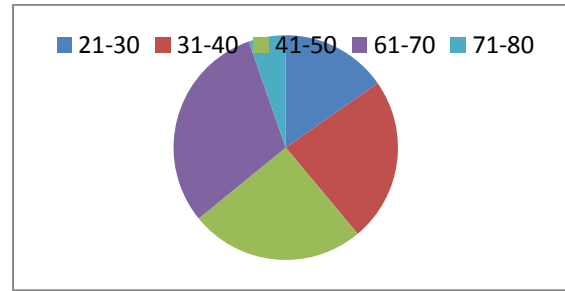
Results

198 patients with Rheumatoid factor positivity were screened from August 2019 to January 2021. Out of 198 patients 115 patients were showed Ophthalmic manifestation Results are as given below.

Age Distribution

Age (Years) group Analysis of the population revealed majorly of the subjects were in the age group of 5th decade ie between 51 – 60 years (Table 1) followed by 6th decade (61-70 years).

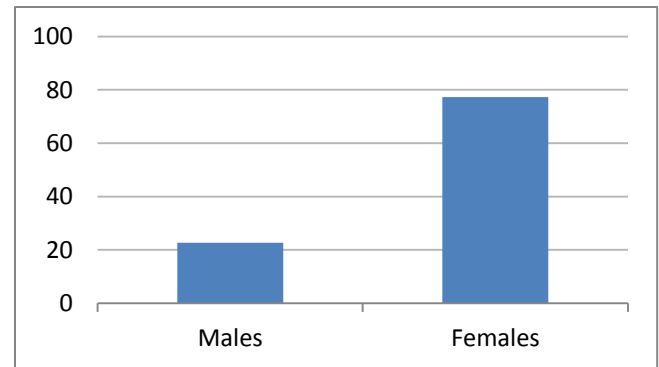
%	Frequency	Age
10.10	20	21-30
15.65	31	31-40
16.66	33	41-50
20.20	40	61-70
3.53	7	71-80



Sex Distribution

About the sex distribution (Table 2) majorly of the patients were females. 153 (77.27%) and males were 45 (22.72%). Female predominance was noted in this study.

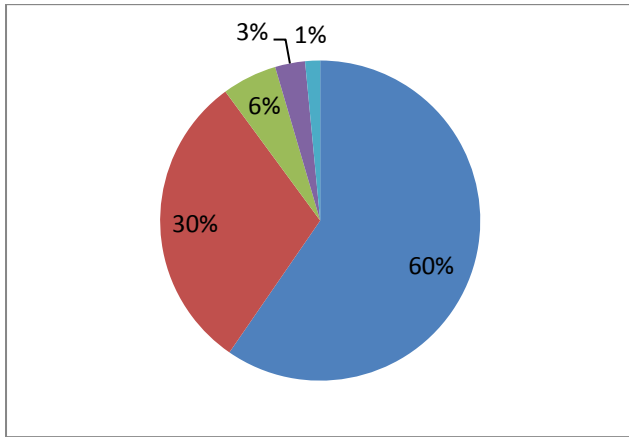
%	Number	Patients
22.72	45	Males
77.27	153	Females
99.99	198	Total



Duration of Disease

Majorly of the patients ie 118 in our study had RA for about 0-5 years in the range followed by 6-10 yrs in 60 patients only. 20 patients had disease duration more than 10 years. Hence severe vision threatening conditions were not much in this study.

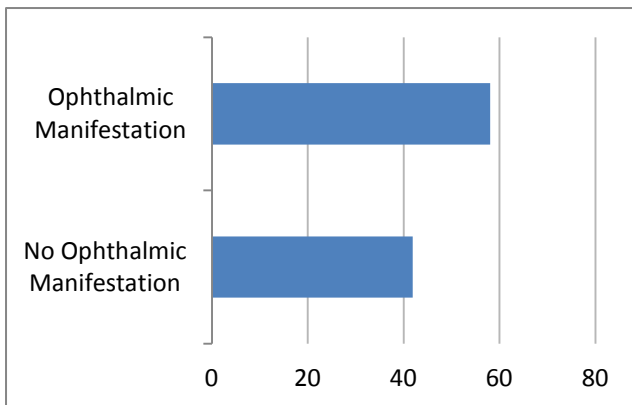
%	Number	Duration (Years)
59.59	118	0-5
30.30	60	6-10
5.55	11	11-15
3.03	6	16-20
1.51	3	21-25



Incidence of Ophthalmic Manifestation

Results on ophthalmic manifestations were revealed as out of 198 patients 115 patients were showed. Hence Ophthalmic involvement was very high in this study.

%	Number	Parameter
58.08	115	No. of Patients having Ophthalmic Manifestation
41.91	83	No. of Patients not having Ophthalmic Manifestation



Incidence of dry eye Manifestations

Main manifestations detected were dry eyes (mild, moderate, severe) followed by episcleritis, scleritis, Iridocyclitis and peripheral Ulcerative keratitis.

%	Frequency	Dry eye Manifestations
		Types
40.90	18	Mild
36.36	16	Moderate
22.72	10	Severe
1.51	44	Total

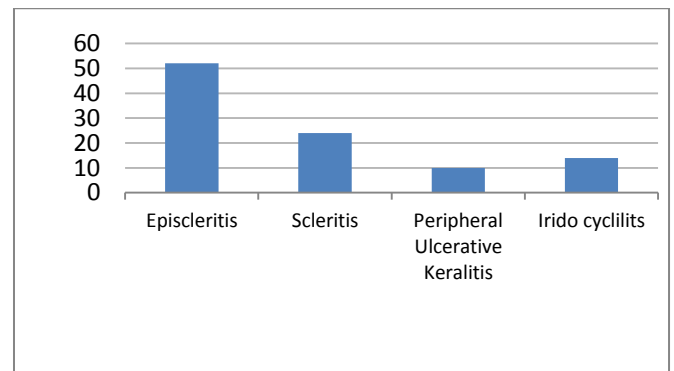
44 Patients showed different grades up dry eyes. Most of the patients were symptomatic. Those

with severe dry eye were presented with Corneal punctuate erosions also. Diagnosis was made by schirmer test I and II and TBUT.

Ophthalmic Manifestation other than systemic therapy

Ophthalmic Manifestation Types

%	Number	Manifestation
52	26	Episcleritis
24	12	Scleritis
10	5	Peripheral Ulcerative Keralitis
14	7	Irido cyclilits
100	50	Total

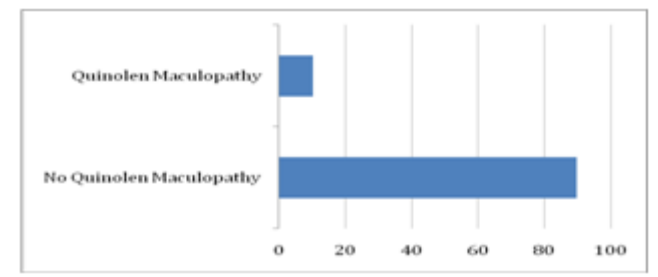


In this study Episcleritis was noted in 26 (52%) patients. Scleritis as 12 (24%) was mainly of the diffuse anterior type.

PUK were noted in 5 (10%) patients only.

Anterior uveitis was noted in 7 (14%) persons.

Systemic therapy related ophthal complications
Systemic therapy related complication were noted in 11 persons. 9 persons were having PSC and 12 persons were having Quinolen (plquenil) maculopathy.



A. Quinolen Maculopathy

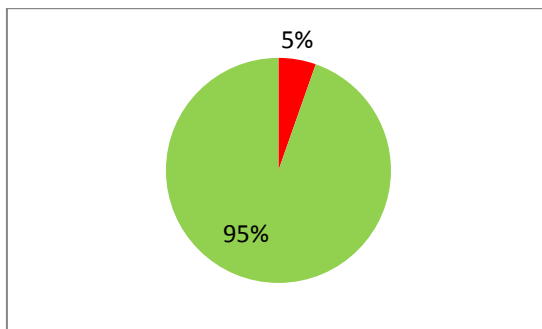
117 persons were using Hydroxychloroquine (Plaquenil) Out of which only 12 patients showed Quinolen Maculopathy (bull's eye) with lower

corneal deposits they were having HCQ more than 5½ years.

Complication due to Steroid

Steroid toxicity in form of posterior sub capsular opacity were noted in 9 out of 115. They were presented with symptoms like decreased, vision glare and decreased sensitivity to contrast.

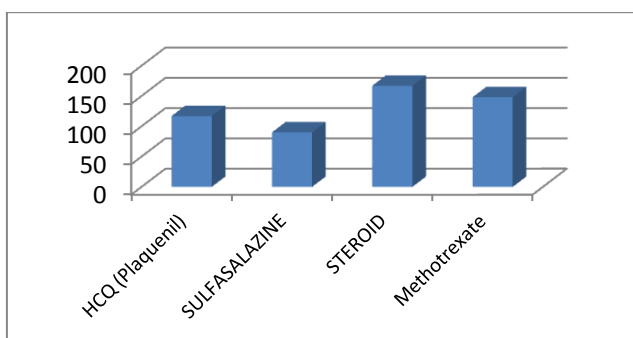
%	No. of patients not having PSC	%	No. of Patients showed PSC	Total No. of Patients on Steriod
94.61	158	5.38	9	167



Commonly Used Anti Rheumatoid Drug

In this study commonly, used anti rheumatoid drugs prescribed from Rheumatology Department were noted as (HCQ) plaquenil, sulfasalazine, steroid (Methyl prednisolone) and methotrexate.

No. of Patients	Drugs
117	HCQ (Plaquenil)
90	SULFASALAZINE
167	STERIOD
148	Methotrexate



Discussion

RA has a worldwide distribution with an estimated prevalence of 1 to 2% a frequency that has been reported from several European and

North American Population (2002)¹. The disease is also characterised in 80% of the patients by +ve RF but there is also a group of auto – antibodies which are called anti-CCPS and are of great significance for the diagnosis of the disease (2002, 1998)^{2,3}. Extra articular manifestations in RA are more common in sero +^{ve} patients (1973, 1997)^{4,5}. If Rf is present in high titre the higher the risk for more severe systemic disease (1997)⁷. In this study also all Rf +vity patients were screened for ophthalmic manifestations RA is usually more common in women over the age of 55 Yrs with a peak incidence in the 5th decade (2015)⁶ as similar to this study. In this study population the duration of disease (RA) ranged between few months to 25 Yrs. (60%) of the patients had disease duration in the range of 0-5 Yrs. a study similar to Wanchu et al (1997)⁷. A Study conducted by S.Kalke etal (2001)¹¹ on 121 patients had disease duration in the range of 0-5 yrs. A study conducted by Reddy et al (1997)⁸ shows that 13 out of 100 patients of RA (39%) found to have eye involvement. The prevalence rate of ophthalmic manifestation in RA has been reported differently in different studies. The present study showed 115 (58%) cases out of 198 patients.

Among the ophthalmic manifestations KCS (Dry Eyes) is the most common Ophthalmic association of RA. Rheumatoid process has been considered to be an aetiologically related to KCS by a study by Thampson and Eadie²⁹. A Study by Moss etal (2000)⁹ also showed 14.4% of the patient had dry eyes. Dry eye is caused by infiltration of the Lacrimal gland by T and B lymphocytes leads to secondary atrophy of the gland which is responsible for the further decrease of tears^{5,10} (1997, 1995).

The patient complaints of burning sensation of the eye, pain and blurred vision, mucus discharge and crusts are not uncommon so the dominant findings of KCs are two: decreased corneal tear meniscus and abnormal Schirmer Test (1993)¹². KCS may progress to Stromal Ulceration and Corneal perforation (2008)¹³. Females had more incidence than males.

Schirmer Test is performed by putting a strip of Whatman's filter Paper No.41, 35 mm long, 5 mm wide is hooked over the lower eye lid. Such that 5mm is bent into the lower fornix on contact with the ocular surface. The paper absorbs tears. The length of paper wetted over a set of time of 5 minutes is an indication of tear volume (1995)¹⁵. Normal wetting is more than 15mm Reading less than 5mm. Indicates severe Kerato Conjunctivitis SICCA. Tear film break up time is done to know the stability of tear film and requires observing, the cornea using a slit lamp bio microscope with a broad, beam cobalt-blue light source set at 10 x magnification (1985)¹⁴, dye impregnated paper strip is placed on the bulbar cornea for a brief moment ask the patient to blink and then ask the patient to refrain from blinking. The time elapsing between a complete blink and the appearance of the 1st dark spot or stroke is measured and taken as break up time. 3 values are taken and mean value is calculated. The value below 10 seconds is considered abnormal. In this study 44 patients showed dry eyes and is the most common manifestation.

The commonly prescribed treatment modalities were tear substitute (preservative free) gels and emollients for majority of the patients only in 5 patients punctual occlusion by plugs and cauterisation were needed. Tarsorrhaphy was needed in one case only.

Episcleritis had noted in 26 patients (52%) out of 198. A study by Watson and Hayreh (1976)¹⁶ on a 10 years study had revealed as 207 episcleritis and 159 scleritis patients. In this study also the number of episcleritis is more than scleritis. The simple diffuse type was commonly found. Topical steroid and NSAID as well as oral NSAIDS are advocated to this patients. Initial treatment should be focused on relieving discomfort and stoppage of progression of the disease.

Scleritis is noted in 12 patients. Mostly of the diffuse anterior type.



Diffuse Anterior Scleritis

Nodular types are noted 3 persons. Nodular scleritis tends to be intermediate in severity between diffuse Anterior Scleritis and necrotizing scleritis with respect to signs and symptoms of disease and final vision outcome.

There is more pain than episcleritis and also there is tenderness on palpation (1998), (1976)^{18,19}. Hence the need of therapy is to alleviate the pain and to prevent structural damage to the eye. Oral NSAIDS and steroid drops like (Prednisolone) and systemic corticosteroids are needed in patients with moderate to severe scleritis and slowly tapered to better tolerance dose. Sub conjunctival injection of corticosteroids delivery also given in '4' cases along with topical steroids and cycloplegic and immuno suppressants like cyclosporine drops (0.05%). Immuno suppressive drops like cyclosporine which act at least in part by interfering with interleukin-2 has been used with some success in the treatment of scleritis²⁰ (1989). Patient with non-necrotising simple diffuse scleritis treated with oral steroids/topical steroids. Non-response with above therapy in 3 cases responds well to immuno suppressants therapy.

PUK was noted in five persons only.



PUK

1. PUK noted may leads to rapid corneal Keralolysis, perforation of the globe and vision failure and is associated with systemic vasculitis in more than 50% of cases (2002)²². It is a potentially divasting disorder with crescent shaped inflammation at the margin. Treatment modalities were included as topical cycloplegic, 1% medroxyprogesterone, lubricants and gels with systemic NSAIDS. I.V. (Intra venous)Cortico Steroids were also recommended in selected cases. Amniotic membrane patching done in 2 cases following the procedure less progression of the lesion and stromal Ulceration was noted post operative broad spectrum antibiotics were used for 1-2 weeks along with topical steroids for 6-8 weeks in tapering doses to reduce inflammation systemic immuno suppressants is not required²³ (2005). Anterior uveitis was noted in 7 patients but no band shaped Keratopathy was noted similar to a study done by P.G. Department of Ophthal, Chettinad Hospitals and Research Institute Chennai, T.N., South India. In 2015 for a one year study revealed 5 (20%) out of 50 patients with RA showed anterior uveitis without band Keratopathy (2015)⁶. Anterior uveitis is a sight threatening condition with long term sequale, if not diagnosed and treated early. Hence Anterior uveitis diagnosed patients were treated with proper medications and regular follow up visits also recommended.

Many patients were send for plaquenil (HCQ) toxicity ie many are using it for more than 6 years without any follow up or ophthalmologic evaluation.

Murmor et al (2011) was mentioned that substance such as chloroquine and plaquenil (HCQ) used in the treatment of RA may cause toxic maculopathy with reduced vision actuity and 'bulls eye' in the retina associated with the long

duration of treatment. (> 7 yrs administration) and the drug dose mean daily dose to minimize toxicity is 6.5 mg /kgr body mass for HCQ and 5mg/kg body mass to chloroquine (2011)²⁵.

Plaquenil (HCQ) was used in 117 patients 12 out of 117 patients were presented with bulls eye maculopathy on fundus evaluation and lower corneal deposits (Cornea verticillata) was seen in 4 patients only.

Scotoma revealed on amslers grid test to all 12 patients. Instructions like the regular follow up visits to ophthalmology clinic as well as Rheumatology clinic for seeking expert opinion upon any change in the treatment schedule of systems drugs was given. Steroid toxicity in the form of posterior sub-capsular cataract (opacity) was seen in '9' patients. A study conducted by Reddy CD etal at PGI CHANDIGARH, India on 100 patients of RA also revealed a relation and duration of steroid intake and formation of posterior sub-capsular opacity (Cataract) Duration noted as 5 months to 12 years (1977)²⁷.

Out of 167 patient's on steroids,9 showed PSCC. The presence of posterior sub-capsular opacity is noted more in patients who were on long term steroid therapy and there is absence of posterior sub capsular opacity in those who were not taking steroid. This shows the relation between steroid intake and presence of posterior sub capsular opacity the observation of posterior sub capsular opacity in patients with RA who were on long term oral steroids has been well documented by O.Glestly and Williamson^{etal 26}. In the present study the patients with the PSCC were presented with complaints of decreased Vn (Vision) glare and decreased sensitivity to contrast. Vn acuity screening tests and slit lamp evaluation for grading of the cataract was noticed. Current ocular status due to toxicity was explained to them. 4 Patients out of 9 had undergone for cataract surgery. Instructions like follow up visits on regular intervals to those patients who had undergone or not undergone for cataract surgeries were given.

Conclusion

High incidences of ophthalmic involvements are noted in this study. Therefore it is essential to seek regular Ophthalmic evaluations as a routine to detect ocular involvements early even though they are asymptomatic to avoid further sight threatening conditions. Among the ophthalmic complications dry eyes is the commonest followed by episcleritis, scleritis, PUK and Iridocyclitis (anterior uveitis) Dry eyes is directly related to the duration of the disease than the severity Routine evaluation tests help to detect the early onset of ophthalmic manifestation and to start treatment. If progressed without treatment may lead to severe vision drop due to corneal scleral involvement or due to ophthalmic complications associated with systemic therapy are evident in this study. Drugs related to this are plaquenil (HCQ) and corticosteroids.

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