


Comparative study between Corticosteroid and Methotrexate treatment for patients with orbital pseudo tumor

Estudio comparativo entre el tratamiento con corticosteroides y metotrexato en pacientes con pseudo tumor orbitario

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205

Abstract

Orbital pseudotumor (OST) is a chronic inflammatory disease affecting Orbital tissue around the eye in a behavior just like a tumor but it does not invade or metastasize. Treatment of OST may be conservative in mild cases while in patients with significant moderate to severe course need treatment that may be medical or surgical. **Objective:** Compare between corticosteroid and methotrexate effectiveness and less complications in treatment of OST. **Method:** A case series study (47 females and 28 males) with proptosis of one or both eyes, redness of the eye or periorbital pain either alone or in combination. Patients having clinical feature suggestive of OST with threat to the eye function or its surrounding muscles and neurovascular tissue that need medical treatment included in this study while others that need surgical treatment excluded from this study. Results: This study made on 75 patients having clinical feature rise the suspension of OST, all ages involved with high incidence at 6th decade followed by the 2nd decade. Group A patients get response to treatment progressively in the 1st three months but later after one year of follow up the percentage decrease to about 45% while in group B although there is slow response to the treatment but with follow up after one year about 87.5% have a good response to treatment. Conclusion: This study suggest that Methotrexate is a well-tolerated medication in patients with Orbital Pseudotumor disease to avoid Corticosteroid therapy failure.

Key word: Orbital Pseudotumor, Corticosteroids, Methotrexate.

Resumen

El pseudotumor orbitario (OST) es una enfermedad inflamatoria crónica que afecta al tejido orbitario alrededor del ojo con un comportamiento similar al de un tumor, pero que no invade ni hace metástasis. El tratamiento de la OST puede ser conservador en los casos leves, mientras que en los pacientes con un curso significativo de moderado a grave se necesita un tratamiento que puede ser médico o quirúrgico. **Objetivo:** Comparar entre la efectividad de los corticosteroides y el metotrexato y menos complicaciones en el tratamiento de la TSO. **Método:** Estudio de una serie de casos (47 mujeres y 28 hombres) con proptosis de uno o ambos ojos, enrojecimiento del ojo o dolor periorbitario solo o en combinación. Los pacientes con características clínicas que sugieran OST con amenaza para la función ocular o los músculos circundantes y el tejido neurovascular que necesitan tratamiento médico se incluyen en este estudio, mientras que otros que necesitan tratamiento quirúrgico se excluyen de este estudio. **Resultados:** Este estudio realizó en 75 pacientes que presentaban aumento de características clínicas la suspensión de OST, todas las edades involucradas con alta incidencia en la 6^a década seguida de la 2^a década. Los pacientes del grupo A obtienen una respuesta al tratamiento progresivamente en los primeros tres meses, pero más tarde, después de un año de seguimiento, el porcentaje disminuye a aproximadamente el 45%, mientras que en el grupo B, aunque hay una respuesta lenta al tratamiento, pero con un seguimiento después de un año, aproximadamente el 87,5%. tener una buena respuesta al tratamiento. Conclusión: Este estudio sugiere que el metotrexato es un medicamento bien tolerado en pacientes con enfermedad de pseudotumor orbitario para evitar el fracaso de la terapia con corticosteroides.

Palabras clave: pseudotumor orbitario, corticosteroides, metotrexato

Orbital pseudo tumor (OST) is a chronic inflammatory disease affecting Orbital tissue around the eye in a behavior just like a tumor but it does not invade or metastasize. This disease may need surgery or it may resolve spontaneously¹. The cause for this disease is unknown but some inflammatory condition may associate like inflammatory bowel disease or in children with recent upper respiratory tract infection^{1,2}. Orbital Pseudo tumor usually unilateral, can affect all ages mostly young women (mean 45years old, pediatric 17%)^{1,2}. It is the second cause of orbital proptosis after Thyroid eye disease (TED) and the 3rd in the incidence of Orbital disorder after TED and lymphoproliferative disease accounting 5-17%¹. Patients with OST usually presented with periorbital pain and swelling although other may experience decrease, or double vision, restricted eye movement each separately or as a combined manifestation². OST may be missed with TED or Orbital cancer which necessitate a test for differentiation which include blood investigations, orbital computed tomography, MRI, ultrasound, and biopsy may be needed². Treatment of OST may be conservative in mild cases while in patients with significant moderate to severe course need treatment that may be medical or surgical². Main medical treatment includes corticosteroid, reduce or stop release the substance in the body that lead to inflammation, it may break the immune system of the body allowing for getting or flourishing the already exist infection. Common Corticosteroids side effects may include body edema, hyperplasia, and depression; disturb sleep, skin rash, skin bruises, acne, increased sweating, hirsutism, headache, dizziness, stomach ulcer, and changes in menstrual cycle, nausea, vomiting³. While in some patients other medication used like cytotoxic drugs (cyclophosphamide) or immunosuppressant (methotrexate) which cause sclerosing the pseudo tumor¹. Methotrexate interfere with the growth of cells that reproduce very quickly. Common side effects may include: fever, chills, tiredness, mouth sores, nausea, upset stomach, dizziness; or abnormal liver function tests⁴. OST complication develop due to long time proptosis of the eye that probably lead to corneal opacity or ulceration while in other double vision can be recognized². The aim of study is compare between corticosteroid and methotrexate effectiveness and less complications in treatment of OST.

A case series study was conducted between June 2010 and Oct. 2018 on 75 patients (47 females and 28 males) with proptosis of one or both eyes, redness of the eye or periorbital pain either alone or in combination. Patients having clinical feature suggestive of OST with threat to the eye function or its surrounding muscles and neurovascular tissue that need medical treatment included in this study while others that need surgical treatment excluded from this study. Those patients included regardless of the age. Clinical, laboratory and radiological evaluations was done for all patients. After confirmation of the diagnosis mainly by CT scan which was the most valuable tool for diagnosis through its ability to show the tissue characterization and localization without the need for surgical intervention, some (group A) patients 35 use corticosteroids CS (Dexamethasone injection 8mg and tablet 0.5mg) while (group B) 40 patients use Methotrexate (MTX) tablet 2.5mg. The choice of drug depending on the patient preference or tolerance after explaining the side effects of each drug, some patients have medical disease like Diabetes mellitus or they are overweight that warrant the use of CS. The patients that use the CS started with Dexamethasone injection 8mg/day for the 1st five days then shifted to the tablet collectively 6mg/day in a tapering manure, decreasing the dose 1mg/week depending on the improvement until we reach a dose of 1mg/day then we stabilize the dose and continue such dose. On the other hand, patients utilize MTX started with 8tab. (20mg) in one day/week while folic acid 2 tab./day for the rest of the week to reduce MTX side effects with monitoring of blood electrolytes and complete blood count every month. The patients during follow up started to feel relieving of the symptoms supported by the laboratory and radiological examinations. Patients were followed for at least one year. The improvement recorded here refer to complete resolving of symptoms apart of loss of vision once it happened no recovery recorded at all. Statistical analysis done using Pearson Chi-square test. All study participants provided informed consent.

This study made on 75 patients having clinical feature rise the suspension of OST, all ages involved with high incidence at 6th decade followed by the 2nd decade (tab. 1). The male are more affected by the disease (47) than the female (28) in ratio of about 2:1 (tab.1). The most common clinical feature was redness of the eye (32) then proptosis (30), Periorbital pain (22) followed by diplopia (13) and last one visual loss

3 in patients (tab. 1). Group A patients get response to treatment progressively in the 1st two months but later after six months of follow up the percentage decrease to about 45% while in group B although there is slow response to the treatment but with follow up one year about 87.5% have a good response to treatment (tab.1).

Table1. Distribution of Age, Gender, Clinical feature and response to treatment.

	Group A Corticosteroids (n=35)		Group B Methotrexate (n=40)		
	No	%	No	%	
Age (years) 10---19	10	28.6	5	12.5	0.450
20---29	3	8.6	7	17.5	
30---39	2	5.7	4	10.0	
40---49	5	14.3	8	20.0	
50---59	11	31.4	12	30.0	
=>60 years	4	11.4	4	10.0	
Gender Male	20	57.1	27	67.5	0.355
Female	15	42.9	13	32.5	
Clinical feature					
Periorbital pain	12	34.3	10	25.0	0.378
Proptosis	13	37.1	17	42.5	0.637
Diplopia	8	22.9	5	12.5	0.237
Eye redness	15	42.9	17	42.5	0.975
Vision lost	2	5.7	1	2.5	0.479
Response to treatment 1 st week	10	28.6	3	5.0	0.005*
1 st month	16	45.7	8	20.0	0.017*
3 rd month	23	65.7	17	42.5	0.044*
6 th month	25	71.4	23	57.5	0.210
1 year	14	40.0	35	87.5	0.0001*

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Patients treated with CS develop many side effects like dermatological, hormonal, headache, gaining weight and peptic ulcer. (tab. 2). While patients treated with MTX develop side effects in about 25% of the total patients in this group which was less harm to the patients and can be managed with dose manipulation (tab.2).

Table 2. Side effects develop in patients treated with Corticosteroids and MTX.

Side effects of Corticosteroids (Group A)	No	%
Total with side effects	32	91.4
Skin rash, skin bruises, Acne	24	68.6
Body edema, Hyperphagia	21	60.0
Headache	20	57.1
Nausea, vomiting	17	48.6
Changes in menstrual cycle	15	42.9
Hirsutism	5	14.3
Stomach ulcer	2	5.7
Side effects of Methotrexate (Group B)	No	%
Total with side effects	10	25.0
Nausea, stomach upset	8	20.0
Tiredness	6	15.0
Abnormal liver function tests	4	10.0
Fever, chills	3	7.5
Mouth sores	1	2.5
Bone marrow suppression	0	0

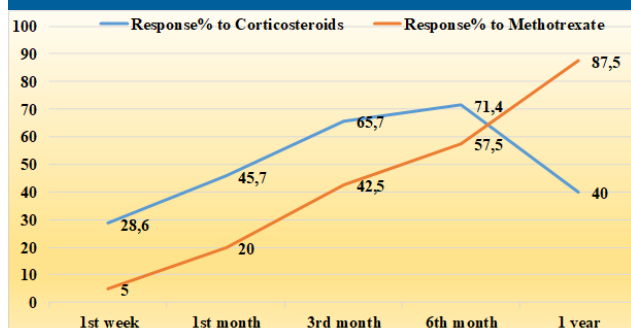
Discussion



Orbital Pseudotumor disease is the 3rd common Orbital lesion after TED and lymphoproliferative disease, its benign, non-infective lesion without definite cause^{5,6}. Pathologically there are two types that could be either sclerosing type, tend to be more aggressive one or non-sclerosing with poor therapeutic response. Underlying pathogenesis is vague that some theories supposed to be an immune-induced process with no clear cause^{7,1}. OST can be missed with other lesions involving the Orbit like TED, Sarcoidosis, Tolosa-Hunt syndrome and benign or malignant lesions, which is why it has heterogeneous presentation⁸. In this study this disease can affect any age group with female predominance (male /female ratio 2:1), Ahmed et al. also report all ages affection while male/female ratio was 3:1, also Shams PN et al found that the disease can affect any age group with slight male predominance^{9,10}. We notice that age and gender had no relation to the response to treatment and development of complications. The most common clinical features in our study were redness of the eye coming next proptosis, periorbital pain and diplopia while only three loss their vision at presentation, Avni-Zauberman et al. found that the most common clinical feature were pain and periorbital swelling in 69 and 75% of their patients respectively¹. Shams PN et al. also found that more than 50% have lid or conjunctival edema and pain with less common decrease visual acuity, proptosis and diplopia¹⁰. Diagnosis in this study made depending on the clinical criteria and the CT scan findings together with response to medical treatment, Ahmed et al. Khochtali S et al. and Tsai et al. also utilized the same criteria for diagnosis^{9,11,12}. In our study the patients use CS in a tapering manure for at least one year, they show good response to treatment but with side effects, that most of them can't tolerate it like body edema or increase body weight... etc. treatment failure occur in about 45% after one year follow up, Yamini Priya et al. report about 33-52% failure of steroid therapy while Mary K. Jacob report 37%^{6,13}. The failure with CS happened in the form of non-response, the patients could not tolerate the side effects of drug or recurrence of symptoms after secession of the drug. Khochtali S et al. have a low response rate (37%) with a high recurrence rate (52%) reported with corticosteroid therapy in their studies¹¹. Spindle J et al. also noted that 37% of their patients failed to respond to the treatment while others develop steroid dependence and steroid intolerance occurring in 33% and 13%, respectively¹⁴. However MTX therapy shown to be low coast, effective and safe drug in OST which needs close monitoring of serious complication like liver dysfunction or bone marrow suppression which are low risk to occur due to the short period of treatment. In our study 87.5% show response to therapy while only 12% show no or poor response. Sharma et al. report Two-thirds of patients had complete

resolution of their symptoms and signs¹⁵. McDonald et al. found that 72% of their patients had reduction of disease activity. Of those patients, 87.5% were able stop or decrease CS therapy. 31% patients had complete remission of their disease; 22% patients did not respond to methotrexate¹⁶. Langford CA et al. found that (71%) completed a 4 month therapeutic trial of methotrexate, they have 50% gastrointestinal disturbance, 50% fatigue, headache 14%, arthralgia 14%, hair thinning 14%, and elevated liver enzyme 43% compared to our result about 75% of our patients complete their course without significant side effects, 10% abnormal liver enzyme, 15% tiredness, 20% gastrointestinal disturbance¹⁷. In regard to statistical analysis (using Pearson Chi-square test at 0.05 level) we found that there is no significant differences between both group in relation to the age, gender and clinical feature (Table 1) but the differences found in the response of patients to treatment, P value was 0.044 in 3rd month follow up, and the response was more significant after one year of follow up (P 0.0001). (Graph 1)

Graph 1. Response to both type of drugs.



Conclusions

This study suggest that Methotrexate is a well-tolerated and suitable for long term usage medication in patients with Orbital Pseudotumor disease to avoid Corticosteroid therapy failure and also in those patients who can't tolerate, or develop serious side effects of CS. The most important additional features of MTX are less risk of opportunistic infection, cost effective, and ease of administration (single oral weekly dose).

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