SOCIEDADE BRASILEIRA DE REUMATOLOGIA

REVISTA BRASILEIRA DE REUMATOLOGIA

www.reumatologia.com.br

Brief communication

Leflunomide in Takayasu arteritis – A long term observational study

*Alexandre Wagner Silva de Souza**, *Renan de Almeida Agustinelli*, *Hemerli de Cinque Almeida*, *Patrícia Bermudes Oliveira*, *Frederico Augusto Gurgel Pinheiro*, *Ana Cecilia Diniz Oliveira*, *Emilia Inoue Sato*

Rheumatology Division, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil

ARTICLE INFO

Article history:
Received 18 June 2015
Accepted 25 September 2015
Available online 2 March 2016

Keywords:
Systemic vasculitis
Takayasu arteritis
Leflunomide
Therapy

ABSTRACT

Objective: To evaluate the extended follow-up data on efficacy and toxicity of leflunomide therapy in Takayasu arteritis (TA) patients previously enrolled in the original open-label study of short-term effects of leflunomide in TA.

Methods: An open-label long-term longitudinal study was performed in TA patients who fulfilled the 1990 American College of Rheumatology criteria for TA and had participated in a previous study that evaluated short-term efficacy of leflunomide in TA. Complete follow-up information could be retrieved from 12 out of 15 patients enrolled in the original study. Disease activity was evaluated by Kerr's criteria and by the Indian Takayasu Activity Score 2010 (ITAS2010).

Results: The mean follow up time was 43.0 ± 7.6 months and 5 (41.6%) TA patients remained on leflunomide therapy while 7 (58.3%) TA patients had to change to another therapy due to failure to prevent relapses in 6 patients and toxicity in one patient. No significant differences were found between patients who remained on leflunomide therapy and those who changed to another agent regarding age at study entry, time since diagnosis, prednisone daily dose at study entry, baseline ITAS2010, mean or maximum ESR and CRP, and cumulative prednisone dose at study end. Among TA patients who had changed leflunomide to another agent, two had an additional clinical relapse and needed to change therapy.

Conclusion: Leflunomide led to sustained remission in approximately half of patients at a mean time of 12 months and was well tolerated by TA patients.

* *Corresponding author.*
E-mail: alexandre_wagner@uol.com.br (A.W.S. de Souza).

http://dx.doi.org/10.1016/j.rbre.2016.02.003

Leflunomida na arterite de Takayasu – Estudo observacional de longo prazo

Palavras-chave:
Vasculites sistêmicas
Arterite de Takayasu
Leflunomida
Tratamento

RESUMO

Objetivo: Avaliar os dados de seguimento em longo prazo em relação à eficácia e toxicidade do tratamento com leflunomida em pacientes com arterite de Takayasu (AT) previamente recrutados no estudo aberto original dos efeitos de curto prazo da leflunomida na AT.

Métodos: Fez-se um estudo longitudinal aberto de longo prazo com pacientes que preencheram os critérios para AT da American College of Rheumatology de 1990 e que participaram de um estudo anterior que avaliou a eficácia em curto prazo da leflunomida na AT. Obtiveram-se informações completas de seguimento de 12 dos 15 pacientes incluídos no estudo original. A atividade da doença foi avaliada pelos critérios de Kerr e pelo Indian Takayasu Activity Score 2010 (ITAS2010).

Resultados: O tempo médio de seguimento foi de 43,0 ± 7,6 meses. Cinco (41,6%) pacientes com AT permaneceram em tratamento com leflunomida, enquanto sete (58,3%) tiveram de mudar para outro tratamento em razão da falha em prevenir recidivas em seis pacientes e toxicidade em um paciente. Não foram encontradas diferenças significativas entre os pacientes que continuaram o tratamento com leflunomida e aqueles que mudaram para outro agente em relação à idade no início do estudo, tempo desde o diagnóstico, dose diária de prednisona no início do estudo, ITAS2010 inicial, valor médio ou máximo de VHS e PCR, e dose de prednisona cumulativa no fim do estudo. Entre os pacientes com AT que mudaram de leflunomida para outro agente, dois tiveram nova recidiva clínica e precisaram mudar de tratamento.

Conclusão: A leflunomida levou à remissão sustentada em aproximadamente metade dos pacientes por um período médio de 12 meses e foi bem tolerada pelos pacientes com AT.

Introduction

Takayasu arteritis (TA) is a large vessel vasculitis that is characterized by granulomatous inflammation involving the aorta, its main branches and pulmonary arteries.[1] TA affects more frequently females and the onset of symptoms usually occurs during the second and third decades of life. Although TA is described in all ethnic groups, it is more prevalent in Asians.[2] The assessment of disease activity in TA is usually problematic, because arterial inflammation may progress to fixed vascular injury even in the absence of overt signs and symptoms of disease activity.[3,4]

In patients with active disease, medical therapy of TA includes high dose prednisone (0.5–1 mg/kg/day) or equivalent as the first line. However, relapses occur in up to 50% of TA patients during corticosteroid tapering and thus immunosuppressive agents are usually added to corticosteroid therapy in order to halt disease progression and to spare corticosteroid use.[1,5] Conventional immunosuppressive agents used to treat TA include methotrexate, azathioprine, mycophenolate mofetil, leflunomide and cyclophosphamide. Recently, biological agents such as TNFα antagonists, tocilizumab and rituximab were added as treatment options for TA patients with refractory or severe disease.[6]

Our group showed a favorable short-term response (mean follow-up of 9.1 months) to leflunomide 20 mg/day in TA patients with active disease despite therapy with prednisone and immunosuppressive agents, mainly methotrexate.[7] However, data about long-term efficacy and toxicity of leflunomide in TA are lacking. Therefore, the aims of this study are to describe the extended follow-up data of efficacy and toxicity of leflunomide therapy in TA patients previously enrolled in the original open-label study of short-term effects of leflunomide in TA.

Patients and methods

This study is an open-label long-term longitudinal study to evaluate leflunomide in TA. TA patients included in this study fulfilled the 1990 American College of Rheumatology criteria for TA[8] and had participated in a previous study that evaluated short-term efficacy of leflunomide in TA.[7] From 15 TA patients enrolled in the original study, complete follow-up information could be retrieved from 12 patients, since 3 patients were lost to follow-up.

TA patients were divided into two groups: (A) TA patients who continued long-term use of leflunomide and (B) TA patients who had to change therapy to another immunosuppressive or biological agent. Disease activity was evaluated by the Kerr's criteria[1] and by the Indian Takayasu Activity Score 2010 (ITAS2010).[9] Acute phase reactants used to evaluate systemic inflammation included the Westergren erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Arterial lesions were assessed by magnetic resonance angiography (MRA) or by computed tomography angiography (CTA) of the entire aorta and its main branches. Cumulative prednisone dose during the follow-up period was calculated for each study participant. Adverse events attributed to leflunomide therapy