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Review article

Recommendations of the Brazilian Society of Rheumatology for the induction therapy of ANCA-associated vasculitis

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ABSTRACT

The purpose of these recommendations is to guide the appropriate induction treatment of antineutrophil cytoplasmic antibody-associated vasculitis (AAV) patients with active disease. The recommendations proposed by the Vasculopathies Committee of the Brazilian Society Rheumatology for induction therapy of AAV, including granulomatosis with polyangiitis, microscopic polyangiitis and renal-limited vasculitis, were based on systematic literature review and expert opinion. Literature review was performed using Medline (PubMed), EMBASE and Cochrane database to retrieve articles until October 2016. PRISMA guidelines were used for the systematic review and articles were assessed according to the Oxford levels of evidence. Sixteen recommendations were made regarding different aspects of induction therapy for AAV. The purpose of these recommendations is to serve as a guide for therapeutic decisions by health care professionals in the management of AAV patients presenting active disease.

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Recomendações da Sociedade Brasileira de Reumatologia para a terapia de indução para vasculites associadas ao ANCA

RESUMO

O objetivo destas recomendações é orientar o tratamento apropriado de indução em pacientes com vasculites associadas a anticorpos anticitoplasma de neutrófilos (VAA) ativa. As recomendações propostas pelo Comitê de Vasculopatias da Sociedade Brasileira de Reumatologia para a terapia de indução para VAA, incluindo granulomatose com poliangiite, poliangiite microscópica e vasculite limitada ao rim, foram baseadas em uma revisão sistemática da literatura e na opinião de especialistas. A revisão da literatura foi feita com as bases de dados Medline (PubMed), Embase e Cochrane para consultar artigos até outubro de 2016. As diretrizes Prisma (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses* – Principais itens para reportar revisões sistemáticas e metanálises) foram usadas para a revisão sistemática e os artigos foram avaliados de acordo com os níveis de evidência Oxford. Dezesseis recomendações foram feitas em relação a diferentes aspectos da terapia de indução para VAA. O objetivo dessas recomendações é servir como um guia para decisões terapêuticas por profissionais da saúde no tratamento de pacientes com VAA que apresentem a doença ativa.

Palavras-chave:
Vasculite associada a ANCA
Granulomatose com poliangiite
Poliangiite microscópica
Vasculite limitada ao rim
Diretrizes

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of necrotizing systemic vasculitis that affects predominantly small vessels with few or no immune deposits at vessels wall, associated with ANCA as a common biomarker.[1] ANCA are antibodies against enzymes in azurophilic granules of neutrophils and lysosomes of monocytes with specificity for proteinase-3 (PR3-ANCA) and for myeloperoxidase (MPO-ANCA).[2] AAV includes granulomatosis with polyangiitis (GPA, previously known as Wegener's granulomatosis), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA, previously known as Churg-Strauss syndrome) and organ-limited AAV, for example renal limited vasculitis (RLV).[1]

Before starting therapy for AAV patients at onset especially GPA and MPA, it is necessary to determine disease extension. The European Vasculitis Study (EUVAS) classification categorizes disease extension into five different subsets as follows: localized disease, early systemic disease, generalized disease, severe disease and refractory disease (Table 1).[3] However, management of a newly diagnosed AAV patient may be also planned based on the presence of organ/life threatening disease or not or whether there is rapidly progressive renal failure or pulmonary hemorrhage.[4] The main outcome measures for the assessment of AAV disease activity are the third version of the Birmingham Vasculitis Activity Score (BVAS) and the BVAS-WG which was adapted for GPA patients.[5,6]

The AAV treatment is divided in induction and maintenance therapy. Induction therapy is prescribed for patients with active disease, either at disease onset or at disease relapses during follow-up; its purpose is to attain complete remission and to avoid damage accrual. After achieving remission, maintenance therapy is started and its goal is to prevent disease relapses.[7]

Table 1 – EUVAS disease categorization for AAV according to different levels of severity.[3]

Categories	Definition
Localized	Disease restricted to upper and/or lower respiratory tract without systemic involvement or constitutional symptoms
Early systemic	Involvement of any organ or system, without organ-threatening or life-threatening disease
Generalized	Renal or other organ-threatening disease, serum creatinine <500 μmol/L or 5.6 mg/dL
Severe	Renal failure or other organ-threatening disease, serum creatinine >500 μmol/L or 5.6 mg/dL
Refractory	Progressive disease unresponsive to therapy with glucocorticoids and cyclophosphamide

AAV, antineutrophil cytoplasmic antibody associated vasculitis; EUVAS, *European Vasculitis Study*.

The purpose of these recommendations is to guide the management of AAV patients according to current evidence from literature, facilitating the access to available therapies as well as minimizing permanent damage due to uncontrolled disease activity. These recommendations addressed aspects of induction therapy in patients with AAV, including GPA, MPA and RLV.

Methods

A systematic review of the literature from 1992 to October 2016 was performed using the following databases: Medline (Pubmed), Embase and Cochrane. Search strategy was done according to each PICO (Patient, Intervention, Control and Outcome) question elaborated by ten rheumatologists with experience in the management of AAV. The PICO questions were based on the different aspects of the induction treatment

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