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INVITED REVIEW

Why are glucocorticoids recommended at a high dose in the Takayasu arteritis guidelines?

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ABSTRACT

Takayasu arteritis is one the large vessel vasculitis affecting the aorta and major branches. Glucocorticoid treatment plays an important role in the treatment of this disease, as in all vasculitis.According to the most recent evidence, theguidelines suggested initiating GCs at high dosages, particularly in patients who had just received a diagnosis. This review aims to analyze this research and identify the rationale behind the current guidelines' recommendations.

Keywords: glucocorticoids, large vessel vasculitis, Takayasu arteritis.

Introduction

Takayasu arteritis (TA) is a large vessel vasculitis that often affects women and involves the aorta and its major branches. Although it is predominantly an insidious disease, it can escalate to fatal complications in some patients (myocardial infarction, stroke, etc.) [1]. The treatment of TA is challenging, because of the rarity and heterogeneity of the disease. The disease can present with a range of clinical symptoms, including fever, weight loss, malaise, and vascular problems [2]. Additionally, observational studies involving a small number of patients provide the majority of the data for management of the disease [3].

Glucocorticoid Therapy in Takayasu arteritis

In the management of TA, glucocorticocorticoids (GCs) consistently served the main role. Nevertheless, there is insufficient data to determine the optimal GC dose and duration in TA treatment [4].

GC monotherapy is a treatment option that has been previously examined in TA [5, 6]. In a systematic review and meta-analysis which included 28 observational studies and totally 1098 patients with TA assessed the clinical response, normalization of acute phase reactants (APRs), relapses and adverse events after GC monotherapy [5]. The study concluded, nearly 60% of the patients experienced clinical response, 84% of the patients had normalization of the APRs, and 66% of the patients had relapses under GC monotherapy. High relapse rates during GC tapering seem to be a major concern with GC monotherapy. In a study, TA patients who received high dose GCs for remission induction and continued with GC tapering after remission had a relapse incidence of 96%. The median GC dose at the time of relapse was reported as 10 mg/day [7].

In the systemic literature review of The European Alliance of Associations for Rheumatology (EULAR) guideline, no research has centered on

the role of GCs in TA; so they mentioned the GC recommendations as low level of evidence (LoE) 1b [3]. When tocilizumab versus GC monotherapy (0.2 mg/kg/day) given to TA patients presenting with relapse was evaluated, relapse was observed in 80% of patients receiving GC monotherapy during dose reduction between 8-16 weeks [8]. In this study, starting in week 4, the GC dose was reduced by 10% every week until it was at least 0.1 mg/kg/day. Similarly, in the randomized double-blind study of abatacept, in patients with TA, a 60% relapse rate was seen in the GC monotherapy group, in which treatment was initiated with 40-60 mg/day GC and gradually reduced [9]. This 60% relapse rate was reported in the 12th week, when the GC dose was decreased to 20 mg/day and in the study protocol the GC dose was reduced to 0 mg in the week 28.

Currently, immunosuppressive therapies, conventional synthetic (cs), and biological (b) disease modifying anti-rheumatic drugs (DMARDs) are recommended in addition to GCs in *American College of Rheumatology* (ACR) Vasculitis Foundation Guideline for the Management of LVV which is the most recent guideline for LVV management [10]. According to recent studies, the majority of the patients in high experienced vasculitis clinics are treated with immunosuppressive therapies in addition to GCs.In a study from National Institutes of Health (NIH) and the Vasculitis Clinical Research Consortium 86% of the TA patients received csDMARDs and 52% of the TA patientsreceived bDMARDs [2]. However, evidence supporting prioritization of a specific DMARD for the management of TA is an unmet need [11].

In the EULAR recommendations for the management of LVV, starting the therapy with 40-60 mg/day high dose GCs with a csDMARD was recommended in TA with LoE of 4 [12]. According to the ACR Vasculitis Foundation Guideline for the Management of LVV [10], for the patients with active, severe TA initiating therapy with high-dose GCs was recommended over low-dose (very low level of evidence). This recommendation is based on the aforementioned study [4], which highlights the substantial risk of relapse with low dose GC treatment. In this study, it was also shown that lower GC dose during active disease is a predictor for future relapses. So they concluded that a starting dose of GC monotherapy below 30 mg/day should be avoided even if disease activity seems mild at the time of diagnosis, according to the results of the study [4]. Studies that report the reverse also exist. In a Chinese cohort including 566 patients with TA, the treatment was started with a moderate dose of GC monotherapy in 85% of the patients and [6] authors, recommended moderate doses of GC therapy for the initial management of TA. In another study, starting with 1mg/kg/day or 0.5 mg/kg/day GC in addition to immunosuppressives was compared in patients with TA, and the cumulative risk of relapse was found to be similar [13]. Another study [14] reported that, adding bDMARD allows the GC dose to be reduced in relapsing TA patients.

Conclusion

Regarding the dosage of GC in the treatment of TA, further research is needed. Current guidelines including both the ACR and the EULAR, are based on a limited number of studies. According to the latest data, these guidelines recommended starting GCs with high doses, especially in newly-diagnosed patients ; in order to control the disease activity, reduce relapses, get possible positive effects on certain outcomes such as mortality.

Author contribution

Study conception and design: GKA; draft manuscript preparation: GKA. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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