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Recent therapeutic advances in juvenile idiopathic arthritis

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A B S T R A C T

Over the past two decades, the management of juvenile idiopathic arthritis (JIA) has been revolutionized by the increased tendency toward early aggressive interventions and the availability of the novel biologic medications. In 2017, three novel randomized controlled trials have evaluated the effectiveness and tolerability of golimumab and tocilizumab in polyarticular JIA, and shown that methotrexate may increase and prolong the effect of intra-articular corticosteroid injection in children with oligoarthritis. A more rational approach to the management of JIA is being fostered by the recent publication of therapeutic recommendations, consensus treatment plans, and advice for the optimal care. A few months ago, an international consensus effort has led to the development of the recommendations for the treat-to-target in JIA. The application of this strategy in routine care may improve disease outcome. Because the potential of attaining inactive disease in children with JIA has markedly increased, there is an urgent need for randomized controlled trials, analyses of clinical data sets, and expert advice to guide discontinuation of medications once complete disease quiescence has been achieved.

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Introduction

The term juvenile idiopathic arthritis (JIA) embraces a heterogeneous group of illnesses, all displaying joint inflammation but with distinct clinical phenotypes, disease courses, outcomes, and, presumably, genetic background and pathophysiology [1]. The current disease classification, based on the criteria created by the Pediatric Task Force of the International League of Associations for Rheumatology (ILAR), outlines seven disease categories defined on the basis of the clinical and laboratory features present in the first 6 months of illness [2]. JIA is the most common rheumatic disease of childhood and a leading cause of acquired disability in the pediatric age group.

Over the past two decades, the management of JIA has been revolutionized by the tendency toward earlier introduction of methotrexate (MTX), the more widespread use of intra-articular corticosteroids (IACs), and, most importantly, the availability of biologic disease-modifying antirheumatic drugs (DMARDs) [3]. This advance has made disease remission an achievable objective for most children with JIA. Complete disease control is regarded as the ideal therapeutic goal because its attainment was found to lead to better long-term outlook [4].

In recent years, information on the efficacy and safety of drug therapies for JIA has been enriched through the accomplishment of new randomized controlled trials (RCTs) of traditional medications and biologic DMARDs. In addition, a more rational therapeutic approach has been fostered by the promulgation of therapeutic recommendations and consensus treatment plans (CTPs). Most recently, a multinational collaborative effort has led to the development of the recommendations for the treat-to-target (T2T) strategy in JIA. There is currently an increasing interest for an international consensus and evidence-based information to establish the optimal time for discontinuation of medication therapies in children with JIA, who achieve sustained clinical remission.

The aim of the present review is to summarize the results of the RCTs conducted in the past year in oligoarticular and polyarticular JIA, to examine the therapeutic recommendations and CTPs proposed for the same disease subsets, and to discuss the rationale that underlies the implementation of the T2T strategy in JIA. In addition, the results of a recent survey that aimed to assess the attitudes and strategies of pediatric rheumatologists toward withdrawing medications in children with clinically inactive JIA are discussed.

Recent RCTs in oligoarticular and polyarticular JIA

Oligoarthritis, which is defined as an arthritis that affects four or fewer joints during the first 6 months of illness, is the most common JIA category in Caucasian children in North America and Europe [5]. Although articular damage and physical disability in oligoarthritis are generally less common and severe than those seen in other forms of JIA, children with this disease may develop significant musculoskeletal abnormalities such as flexion contractures, valgus deformities, and localized disturbance of bone growth [1]. Furthermore, a sizeable proportion of them experience a spread of joint disease over time (so-called extended oligoarthritis). In this subgroup, the prognosis is guarded [6,7].

In contrast to the numerous RCTs that have been performed in polyarticular and systemic JIA [3], only a few evidence-based data are available to guide the treatment of oligoarthritis [8–11]. As a result, the management of this condition is largely empirical and likely variable among pediatric rheumatologists [12].

IAC injections are widely used in the treatment of children with oligoarthritis [13]. However, the role of MTX, which is a key medication in the therapeutic regimen of polyarticular JIA, in this disease subset remains unclear. Ravelli and co-workers [14] addressed the question of whether concomitantly administered MTX augments the frequency and duration of remission of joint disease in children with oligoarticular JIA who undergo IAC therapy. This multicenter RCT conducted in Italy compared IAC injections alone versus IAC injections along with oral MTX in children with oligoarticular JIA. Although in the intention-to-treat analysis of the primary outcome (remission of arthritis symptoms in all injected joints at 12 months) the difference between the two therapeutic groups was not significant, post hoc multivariable analysis and Cox proportional hazards model suggested that concomitantly administered MTX may prolong and, to a lesser extent, augment the effectiveness of IAC therapy. The assessment of safety did not show an appreciable increase in serious toxicity.

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