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## Original article

# Effects of the use of growth hormone in children and adolescents with juvenile idiopathic arthritis: a systematic review

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## ABSTRACT

**Introduction:** Children with juvenile idiopathic arthritis (JIA) often have impaired growth and short stature. There is evidence that the therapeutic use of growth hormone (GH) is useful and safe in these patients.

**Objective:** To analyze the effects of GH use in patients with JIA.

**Method:** A systematic review of the literature over the last 18 years in Medline and Embase databases. The criteria were analyzed independently by the researchers. We used the following keywords: "growth hormone", "arthritis, juvenile", "arthritis, rheumatoid", "child" and "adolescent".

**Results:** Among the 192 identified articles, 20 corresponded to the inclusion criteria. Seventeen longitudinal studies and 3 case reports were found. Most studies analyzed observed increased growth, muscle mass and bone mass using GH. Adverse effects observed were glucose intolerance, diabetes, bone deformities, osteonecrosis, reactivation of the disease and low final height.

**Conclusion:** The majority of studies reported positive effects after the therapeutic use of GH, but some variability in response to treatment was observed. The combination of growth hormone with other drugs seems to be a good option.

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## Efeitos do uso do hormônio de crescimento em crianças e adolescentes com artrite idiopática juvenil: revisão sistemática

### R E S U M O

#### Palavras-chave:

Artrite idiopática juvenil  
Hormônio de crescimento  
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**Introdução:** Crianças com artrite idiopática juvenil (AIJ) frequentemente apresentam prejuízo no crescimento e baixa estatura. Existem evidências de que o uso terapêutico do hormônio de crescimento (GH) é útil e seguro nesses pacientes.

**Objetivo:** Analisar os efeitos do uso de GH em pacientes com AIJ.

**Método:** Fez-se revisão sistemática da literatura nos últimos 18 anos, nas bases de dados Medline e Embase. Os critérios foram analisados pelos pesquisadores de forma independente. Usaram-se os seguintes descritores: *growth hormone, arthritis, juvenile, arthritis, rheumatoid, child e adolescent*.

**Resultados:** Entre os 192 artigos identificados, 20 corresponderam aos critérios de inclusão. Foram encontrados 17 estudos longitudinais e três relatos de casos. A maioria dos estudos analisados observou um aumento de crescimento, massa muscular e massa óssea com o uso do GH. Os efeitos adversos observados foram intolerância à glicose, diabetes, deformidades ósseas, osteonecrose, reativação da doença e altura final baixa.

**Conclusão:** A maioria dos estudos relatou efeitos positivos após uso terapêutico do GH, porém certa variabilidade na resposta ao tratamento foi observada. A combinação do hormônio de crescimento com outros medicamentos parece ser uma boa opção.

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## Introduction

Juvenile idiopathic arthritis (JIA) is an autoimmune disease and the leading cause of chronic arthritis in pediatric patients. Its annual incidence varies from 2 to 20 cases/100,000 inhabitants, with a prevalence of 15–150 cases/100,000 inhabitants.<sup>1</sup>

Its main features are chronic arthritis, and in some cases being associated with multisystem involvement and progression to joint limitations and permanent functional disability.<sup>2</sup>

The diagnosis of JIA is based on criteria of the International League of Associations for Rheumatology (ILAR) and requires the presence of arthritis in children and adolescents aged under 16 years, that persists for at least six weeks, when excluding the presence of other causes of chronic arthritis.<sup>3</sup> According to the literature, the most frequent JIA subtypes are oligoarticular JIA (50–60%), polyarticular JIA (30–35%) and systemic JIA (10–20%).<sup>4</sup>

Children with JIA often exhibit an inadequate growth and short stature, and these effects relate to the extent of organs involved, with the activity and extent of the disease, malnutrition, malabsorption, increased catabolism, associated complications, a constant inflammatory process, and effects of the use of certain medications, being the most relevant of them the glucocorticoids.<sup>5–8</sup> Several studies have observed improved growth and height rates in patients with JIA treated with growth hormone (GH).<sup>5,9–25</sup> There are several indications of the use of GH approved for treatment of JIA; however, the use of this hormone can result in adverse events,<sup>26</sup> including negative variability in response to treatment which has been observed in some studies of patients with JIA.<sup>9,10,14,19,20,24,25,27,28</sup>

Due to the high cost and potential side effects,<sup>9,10,20,27</sup> there are controversies about the ideal indication, the dose, and

duration of the GH therapy in JIA.<sup>26</sup> An understanding the indications for therapy with growth hormone and its controversies can facilitate the evaluation of the patient and his/her referral to the best treatment.<sup>26,29,30</sup> The aim of this study is to analyze the various effects of GH use in patients with JIA, based on the literature review.

## Methods

This study consists of a systematic literature review, after a search conducted during the months of July and August 2015, of studies published in the last 18 years (1998–2015). The search of the references was conducted through an electronic database (Medline and Embase) exploration and of the reference list of identified articles by three researchers independently. References that met the inclusion criteria were evaluated, regardless of their journal. The selection of the descriptors used in the review process was conducted in consultation with DeCS (Health Sciences Descriptors byBIREME). In the search, the following descriptors in Portuguese and English were considered: “growth hormone”, “arthritis, juvenile”, “arthritis, rheumatoid,” “child” and “adolescent”.<sup>31</sup>

In the electronic database MedLine, 104 studies were identified, and Embase 88 studies were identified, totaling 192 studies. 64 matching studies were identified, and 128 articles were tabulated on a spreadsheet with data related to the title of the study, journal, year, age group studied, study idiom, evaluated diseases, disease duration, treatment time, therapeutic dose, and possible use of growth hormone as a therapy.

The inclusion criteria were as follows: (1) Original articles; (2) Articles in Portuguese or in English idiom; (3) Articles which used growth hormone as a therapy; (4) Articles that

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