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Etanercept withdrawal in JIA

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ABSTRACT

Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease in children. The use of biologic therapy has improved prognosis and quality of life for these patients. Remission is more easily achieved and pediatric rheumatologists started to question if, when and how this expensive and potentially dangerous treatment might be withdrawn. To date, few studies have addressed these questions and results are divergent, more research being needed. As the latest Romanian protocol for biologic therapy in JIA includes it, and because Etanercept is the most prescribed biologic drug in our country, we propose an Etanercept treatment withdrawal protocol for JIA patients in remission.

Keywords: JIA, biologic treatment, withdrawal, etanercept, protocol

INTRODUCTION

Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease in pediatrics. This chronic illness affects life quality and can lead to severe articular ankylosis. The use of biologic therapy has substantially improved the prognosis and life quality of these children, many of them achieving remission. However, biologic therapy is expensive, has potential severe adverse effects (infectious and allergic) and long-term usage is associated with some concerns regarding safety. This is why pediatric rheumatologists started to wonder if, when and how could this treatment be withdrawn. Etanercept is the most popular and prescribed biologic drug used in JIA (dosage: 0,4 mg/kg sc twice a week). Few studies regarding biologics withdrawal were made, most of them being retrospective and concerning Etanercept tapering. Unfortunately their results are often divergent and not able to predict disease flare (3,5).

ETANERCEPT WITHDRAWAL IN JIA – LITERATURE REVIEW

Studies in which Etanercept was terminated abruptly (6,7) showed that one-third of patients were in remission for at least 12 months, but the other two-thirds relapsed. When Etanercept was tapered gradually half of the patients maintained remission for 12 months (3,5). The latest studies suggest that Etanercept should be discontinued after a minimum 2 years remission (1-4) and before synthetic DMARDs (Methotrexate). Systemic onset JIA patients with polyarticular evolution are more likely to maintain remission after Etanercept withdrawal (3,4). ANA positivity raises the chance of flare (2,4). Most of the studies could not find a correlation between age, sex, JIA subtype, total length of treatment, or disease duration, and risk of flare (2,3). More research is needed to identify the most effective strategy to discontinue biologic therapy.

In the light of these studies results and as the latest Romanian protocol for biologic therapy in JIA includes it (8), we propose the following method of Etanercept treatment withdrawal for JIA patients in remission.

ETANERCEPT WITHDRAWAL PROTOCOL IN JIA

- Inclusion Criteria
  - Patients diagnosed with JIA and treated with Etanercept

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- Remission for minimum 2 years, defined as:
  - Absence of clinically active arthritis, defined as:
    - Joint swelling or
    - Inflammatory joint pain and morning stiffness longer than 15 minutes
  - Absence of MRI sacroiliitis for JIA-ERA (enthesitis-related arthritis)
  - ESR and CRP within normal limits
  - Physician's visual analogue scale <10 mm
- Signed informed consent by a parent (or legal guardian) or by the patient (if over 18).

● Exclusion criteria
- ANA positivity
- Uveitis (switch)
- N.B. an early attempt of Etanercept withdrawal does not represent an exclusion criteria, even if failed (flare)

● Method
- Maintaining pediatric dosage of 0,4 mg/kg
- Gradual increase of dose interval:
  - 1 administration every 1 week for 3 months
  - 1 administration every 2 weeks for 3 months
  - 1 administration every 4 weeks for 3 months
  - STOP

● Follow-up
- Clinical (including patient's and physician's visual analogue scale) and biological reassessment (including ESR and CRP)
  - Monthly during Etanercept tapering
  - Depending on the evolution thereafter
- Imagistic reassessment (only for JIA-ERA):
  - Pelvic MRI when stopping Etanercept, at 6 months, 1 year and 2 years

REINTRODUCTION OF ETANERCEPT

● Criteria:
- Relapse during tapering, defined as:
  1. Joint swelling or
  2. Inflammatory joint pain and morning stiffness longer than 15 minutes
  3. Lack of other known causes for 1 and 2
  4. MRI sacroiliitis (only for JIA-ERA)
- Relapse at more than 3 months from the last etanercept dose
  - Health Ministry and National Health Assurance System Order nr 192/142/2017 (or later settlement) will apply

● Method:
- restart etanercept at 0,4 mg/kg twice a week

CONCLUSIONS

Biologic therapy improved prognosis and life quality of JIA patients, inducing remission in many of these children. However, the costs and potential severe adverse effects of biologic drugs raised the questions of when and how to withdraw this therapy. Unfortunately, few studies were able to answer, sometimes the results were divergent, more research being needed to identify the most effective strategy. As the latest romanian protocol for biologic therapy in JIA allows it and because Etanercept is the most prescribed biologic drug in our country, we propose an Etanercept withdrawal protocol for JIA patients in remission.

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