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# Failure of Methotrexate Monotherapy and Subsequent Response to Tumor Necrosis Factor Inhibitors in Pediatric Non-Infectious Uveitis

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**Research Abstract Title**
Failure of Methotrexate Monotherapy and Subsequent Response to Tumor Necrosis Factor Inhibitors in Pediatric Non-Infectious Uveitis

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**IRB Number:** STUDY00000062

**Describe role of Submitting/Presenting Trainee in this project (limit 150 words):** This is a retrospective, cross- sectional study in design. The role of the submitting trainee consists of a comprehensive retrospective review of electronic health records along with data collection and statistical assessment.

**Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words**

**Background:** Uveitis refers to inflammation of the eye and is relatively uncommon in pediatric population compare to adults, accounting for approximately %5-10 of all cases. However, early and aggressive control of disease is essential as increased risk of ocular complications and vision loss may lead to a greater psychosocial and financial burden over a child's lifespan. Etiology is grouped under two major categories; infectious and noninfectious. The most common type in the United States is noninfectious uveitis and mainly linked to autoimmune mechanisms. Even though, majority of the cases occur in isolation and classified as idiopathic; juvenile idiopathic arthritis (JIA) is the most common systemic disorder associated with childhood uveitis cases. Current evidence on pediatric uveitis treatment strategies suggest a "step-ladder approach" depending on severity of inflammation and tolerance. Initial corticosteroid therapy is the first level mainstream of inflammation control. However, additional treatment modalities is usually required in order to control further inflammation and achieve a steroid free course in order to decrease associated complications. Due to its well-established efficacy and safety profile, methotrexate (MTX) is the most widely used immune-modulatory agent as the second line therapy. In refractory cases, a third line biologic agent is usually needed. Adalimumab (ADA) and infliximab (INF) are the leading tumor necrosis factor (TNF)-alpha inhibitors that have shown efficacy, regardless of etiology. Along the complicated course of this disease a multi-disciplinary approach is crucial in patient care. Children's Mercy Hospital has a joint pediatric ophthalmology and pediatric rheumatology clinic hold once a week, where over 100 patients are followed and treated with joint decisions.

**Objectives/Goal:** This purpose of this study is to determine the rates of treatment failure with MTX monotherapy and subsequent efficacy of TNF inhibitors ADA and IFX in refractory pediatric noninfectious uveitis.

**Methods/Design:** The charts of patients evaluated with non-infectious uveitis between January 2013 and December 2017 were reviewed retrospectively. Data recored included: demographic information, site and degree of uveitis, associated systemic conditions, systemic and topical therapy. Treatment failure was defined as steroid dependence with persistent or recurrent inflammation despite maximum dose for 3 months or longer.

**Results:** Seventy-three patients (male/female=33/40) were included. Anterior uveitis (AU) was the most common presentation (n=51 total; juvenile idiopathic arthritis (JIA) associated n=23, idiopathic n=28), followed by pars planitis (n=13) and panuveitis(n=9). Mean age at diagnosis was 7.6 years. Mean follow-up period was 76.5 months (range 18-192). Overall treatment failure with MTX monotherapy was 83.5%. Of those who failed MTX monotherapy, 27 were controlled with ADA and 10 with IFX as the first additional treatment. Twenty one patients on ADA therapy were switched to IFX for persistent inflammation and %85.7 were controlled. Subgroup analysis for each type of uveitis was further performed.

**Conclusions:** There is limited data on control of various pediatric uveitis subtypes with MTX monotherapy. MTX was effective as monotherapy in less than 50% of pediatric uveitis patients with many requiring TNF inhibitors for disease control. Additional IFX and ADA were effective and safe treatment modalities to achieve steroid-free remission for pediatric uveitis.