

TNF inhibitors: A magic bullet for juvenile idiopathic arthritis-uveitis treatment?

On November 27, 2020, Sanna Leinonen defended her thesis, "Treatment and complications of juvenile idiopathic arthritis-related uveitis," at the Faculty of Medicine, University of Helsinki and Helsinki University Hospital in Finland. Her main supervisor was Professor Kaisu Kotaniemi, PhD, University of Helsinki with co-supervisor Professor Tero Kivelä, Helsinki University Hospital.



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Juvenile idiopathic arthritis (JIA) and related uveitis is a persistent childhood-onset inflammatory disease affecting one or more joints and one or both eyes. The origin of JIA-related uveitis is unknown. Uveitis in JIA presents typically as a chronic and relapsing anterior uveitis without inflammatory symptoms. Persistent uveal inflammation can cause vision-impairing complications, such as cataract, glaucoma, edema, and scarring of the macula.

The focus of uveitis treatment is to improve the visual prognosis by controlling the inflammation. Topical glucocorticoids reduce inflammation in the eye but do not control the systemic joint disease. Additionally, they tend to induce cataract formation, high intraocular pressure, and related glaucoma. This is why children with JIA-related uveitis are treated with systemic antirheumatic drugs. Methotrexate is the gold-standard treatment of JIA and related uveitis. If methotrexate does not control the inflammation, a tumor-necrosis factor (TNF) inhibitor, such as adalimumab or infliximab, is introduced. These antirheumatic drugs reduce inflammation in the eyes and joints, improve visual prognosis, are associated with fewer ocular complications, and delay the need for ocular surgery in JIA-uveitis. There is increasing evidence to support that the early introduction of antirheumatics is crucial in controlling JIA-uveitis and related complications.

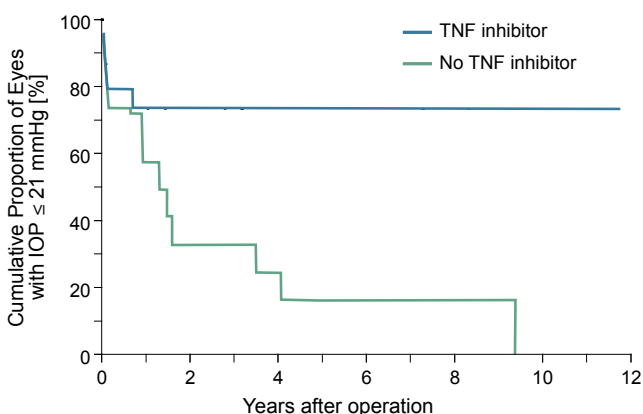


Figure 1. Survival of MMC-trabeculectomy with and without TNF inhibition

Key points:

- Long-term visual acuity remains high after cataract surgery in eyes with well-controlled uveitis.
- Trabeculectomies are more successful in eyes treated with TNF inhibition.
- Better outcomes in juvenile idiopathic arthritis-uveitis and related complications can be achieved with antirheumatic treatment and meticulous control of inflammation.

This thesis focused on the variables contributing to treatment success when managing the inflammation and complications of JIA-related uveitis. The first study showed that antirheumatic treatment may improve the results of trabeculectomy in JIA-related uveitis. Intraocular pressure was better controlled in patients who were treated with TNF inhibitors during surgery compared to patients without TNF inhibition (Figure 1). TNF inhibition was not associated with a higher rate of postoperative complications.

In the second study, better control of uveitis was achieved when methotrexate was combined with adalimumab. The absence of methotrexate was associated with a higher grade of inflammation and immunization against adalimumab. Remission was achieved only among patients without immunization against adalimumab.

The third study concluded that if macular edema does not respond to antirheumatics and systemic glucocorticoids, a sustained-release glucocorticoid implant (Retisert™) may help in controlling macular edema and improving visual acuity. In addition to the intraocular glucocorticoid treatment, all patients needed antirheumatic treatment to control their JIA-uveitis. The complication rate was high, and 7 of 8 eyes required further surgery.

In the fourth study, better control of inflammation 3 to 12 months prior to cataract surgery was associated with a better postoperative visual outcome. Twenty-six cataract extractions with primary intraocular lens implantations were performed. The median visual acuity remained high (0.9–1.0) during 5 to 10 years of follow-up.

Articles in the dissertation

- Leinonen S, et al. Potential effect of tumor necrosis factor inhibitors on trabeculectomy with mitomycin C for patients with juvenile idiopathic arthritis-related uveitic glaucoma: a retrospective analysis. *JAMA Ophthalmol.* 2015;133(11):1323-1328.
- Leinonen ST, et al. Anti-adalimumab antibodies in juvenile idiopathic arthritis-related uveitis. *Clin Exp Rheumatol.* 2017;35(6):1043-1046. Epub 2017 Nov 14.
- Leinonen S, et al. Fluocinolone acetonide intravitreal implant (Retisert®) in the treatment of sight threatening macular edema of juvenile idiopathic arthritis-related uveitis. *Acta Ophthalmol.* 2018;96(6):648-651.
- Leinonen S, et al. Results 5 to 10 years after cataract surgery with primary IOL implantation in juvenile idiopathic arthritis-related uveitis. *J Cataract Refr Surg.* 2020;46(8):1114-1118.