



GRAVES' OPTHALMOPATHY

Rituximab appears to be effective in the treatment of severe thyroid eye disease

WHAT IS THE STUDY ABOUT?

Thyroid eye disease (TED), also known as Graves ophthalmopathy, is an inflammatory disorder most often associated with Graves' disease but also can be seen with Hashimoto's thyroiditis. Mild TED can be treated relatively easily but treatment of severe disease is difficult. Fortunately, severe TED with marked inflammation of the eye and eye muscles, bulging of the eyes and double vision is rare. Although steroid therapy can help to control the inflammation around the eyes and long-term treatment is effective, there can be significant side effects from this treatment. External radiation can improve the mobility of the eye muscles, but does not help with the double vision and bulging of the eyes in these patients. Many immunosuppressive drugs have been tried in patients with severe TED with minimal or no effect. Rituximab is a selective immunosuppressive drug that specifically targets B lymphocytes, a major cause of inflammation in Graves' disease and in TED. This drug has been used in other autoimmune diseases. The goal of this study was to evaluate the safety and effectiveness of rituximab in the treatment of TED.

THE FULL ARTICLE TITLE:

Silkiss RZ, et al. Rituximab for Thyroid Eye Disease. *Ophthal Plast Reconstr Surg* 2010. DOI: 10.1097/IOP.0b013e3181c4dfde.

WHAT WAS THE AIM OF THE STUDY?

The aim of this study was to evaluate the safety and efficacy of rituximab in the treatment of TED.

WHO WAS STUDIED?

The study group included 12 patients from 2 centers in the United States. All patients were 18 years of age or older and had active TED that had not improved with a short course of steroids.

HOW WAS THE STUDY DONE?

Demographic data on all patients was collected, including age, sex, smoking status at time of presentation, whether 1 or 2 eyes were affected and serum autoantibody levels, including thyroid stimulating immunoglobulin, TSH receptor and TPO antibodies. All patients who had

TED which had not improved with a short course of glucocorticoids and who had negative tests for infections with hepatitis B, C and HIV were offered rituximab as an alternative to long-term steroid treatment. Patients were given 2 doses of 1000 mg of rituximab intravenously 2 weeks apart. The severity of the eye disease was calculated at the start of the study and at 4, 8, 16, 24, 36 and 52 weeks according to 2 different scores, the Clinical Activity Score (CAS) and the Thyroid Associated ophthalmopathy scale (TAOS), each of which measures the severity of different parameters of disease activity.

WHAT WERE THE RESULTS OF THE STUDY?

Twelve patients with active TED were treated with rituximab. There were no acute or long term adverse effects of the rituximab infusions. There was a significant improvement in CAS scores beginning 1 month after infusion of rituximab that was maintained during the 12-month observation period. There also was a significant improvement in the TAOS score during the course of the study. All patients had some improvement in their severe TED. The thyroid antibody and TSH levels did not change at any point during the study.

HOW DOES THIS COMPARE WITH OTHER STUDIES?

This is a first study examining the effect of rituximab on TED. One case report showed that rituximab produced marked improvement in the eye symptoms in a patient with severe TED. Two studies in patients with Graves disease showed that rituximab was effective in inducing remission in some of the patients.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Rituximab appears to be a promising, safe and effective alternative to long-term steroid treatment in patients with severe TED. More studies with larger numbers of patients are needed.

— M. Regina Castro, MD

ATA THYROID BROCHURE LINKS

Graves disease: http://thyroid.org/patients/patient_brochures/graves.html

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GRAVES' OPTHALMOPATHY, continued

ABBREVIATIONS & DEFINITIONS

Graves' disease — the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Hashimoto's thyroiditis — the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy the gland.

Thyroid eye disease (TED) — also known as Graves ophthalmopathy. TED is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

TSH — thyroid stimulating hormone – produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

TPO antibodies — these are antibodies that attack the thyroid instead of bacteria and viruses, they are a marker for autoimmune thyroid disease, which is the main underlying cause for hypothyroidism and hyperthyroidism in the United States.

Rituximab — a selective immunosuppressive drug that is administered intravenously and which is directed against B lymphocytes (cells of the immune system).

Steroids/Glucocorticoids — general antiinflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation.

CAS — Clinical Activity Score, a scoring system used to evaluate patients with Graves' ophthalmopathy. It is based on classical signs of inflammation (pain, redness, swelling and function) and helps predict which patients will benefit from certain medications.

TRAb — antibodies often present in the serum of patients with Graves disease that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism.

Thyroid stimulating immunoglobulin /TSI — antibodies often present in the serum of patients with Graves' disease that are directed against the TSH receptor, that cause stimulation of this receptor resulting in increased levels of thyroid hormones in the blood and hyperthyroidism.

Antibodies — proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.

Autoimmune disorders — a diverse group of disorders that are caused by antibodies that get confused and attack the body's own tissues. The disorder depends on what tissue the antibodies attack. Graves' disease and Hashimoto's thyroiditis are examples of autoimmune thyroid disease. Other Autoimmune disorders include: type I diabetes mellitus, Addison's disease (adrenal insufficiency), vitiligo (loss of pigment of some areas of the skin), systemic lupus erythematosus, pernicious anemia (B12 deficiency), celiac disease, inflammatory bowel disease, myasthenia gravis, multiple sclerosis and rheumatoid arthritis.