Clinical Update

Treating obsessive–compulsive and tic disorders

Perlmutter SJ, Leitman SF, Garvey MA, Hamburger S, Feldman E, Leonard HL, Swedo SE. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive–compulsive disorder and tic disorders in childhood. *Lancet* 1999; 354:1153-8.

Background

Obsessive–compulsive disorder (OCD) and tic disorders are common in childhood, affecting 1% to 2% of school-aged children and adolescents. Treatment with serotonin-reuptake inhibitors, behaviour therapy, or both, helps more than 75% of these patients, but most show only partial response and relapse when medication is discontinued. The cause of OCD and tic disorders is unknown. Poststreptococcal autoimmunity has been postulated as a possible environmental trigger, raising the possibility that some children might respond to immunomodulatory therapy.

Question

Is plasma exchange or intravenous immunoglobulin (IVIG) better than placebo in decreasing neuropsychiatric symptoms in children with exacerbations of OCD or tics triggered by streptococcal infection?

Design

The study was a randomized, placebo-controlled trial with follow-up at 1 month and 1 year. Children between the ages of 5 and 14 years, with an existing severe exacerbation of OCD or tic disorder and a history of exacerbations associated with streptococcal infection, were randomly assigned to treatment with plasma exchange (5 single-unit exchanges over 2 weeks), IVIG (1g/kg on 2 consecutive days) or placebo (intravenous saline). Symptom severity was rated on standard scales at baseline, 1 month and 12 months (active treatment groups only) after treatment. Neuropsychiatric medications were maintained at constant doses over the first month and were then adjusted as needed.

Results

Thirty children participated in the study; 10 received plasma exchange (2 subjects were lost to follow-up at 12 months), 10 received IVIG (1 subject withdrew within a month) and 10 received placebo. At baseline patient characteristics and symptom severity were similar, with the exception that tics were more severe among children in the plasma-exchange group. Mild-to-moderate adverse reactions were experienced by 12 of the 19 subjects in the active treatment groups (e.g., nausea, vomiting and headache) and by 2 in the placebo group (e.g., stomach ache and headache). At 1 month the IVIG and plasma-exchange groups showed a mean improvement from baseline of 45% (OC scale score reduction of 12) and 58% (OC scale score reduction of 13) respectively, while children in the control group improved a mean of 3% (OC score reduction of 0.9); overall function scores were 2.9 (33% improvement), 2.8 (35% improvement) and 0 (no change) for the respective groups. Symptom improvement usually occurred by 1 week in the plasma-exchange group and by 3 weeks in the IVIG group. Tic symptoms improved significantly in the plasma-exchange group only. At 12 months 14 of the 17 children who had received active treatment were much or very much improved.

Commentary

Postinfectious autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) are believed to be mediated by antibodies formed after group A β-hemolytic streptococcal infection that cross-react with neuronal tissue.[1] Sydenham's chorea, the neurological manifestation of rheumatic fever, has been proposed as a potential model of pathophysiology.[2] The original hypothesis of the study was that either IVIG or plasma exchange would reduce symptom severity by blocking (IVIG) or removing (plasma exchange) the antibodies that are cross-reacting. Despite limitations, such as the lack of blinding to treatment assignment,[3] the study demonstrated that both interventions effectively reduced symptoms in a select population of children with a history of streptococcal-induced symptom exacerbation. According to this hypothesis, however, the rate of symptom improvement should be directly proportional to the rate of antibody removal. Most of the children receiving plasma exchange did not show immediate improvement, suggesting that the mechanism of immunomodulation is not well understood.

Clinical implications

This study does not support the routine use of immunomodulatory agents to treat OCD and tic disorders but does prompt intriguing questions for further study and review.[4] — *Erica Weir*, CMAJ

References

1. Swedo S, Henrietta L, Barbara M, Allen A, Rapoport J, Dow S, et al. Identification of children with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections by a marker associated with rheumatic fever. *Am J Psychiatry* 1997;154:110-2.
2. Swedo S. Sydenham's chorea — a model for childhood autoimmune neuropsychiatric disorders. *JAMA* 1994;272:1788-91.
3. Singer H. PANDAS and immunomodulatory therapy. *Lancet* 1999;354:1137-8.
4. Goodman WK. Obsessive–compulsive disorder: diagnosis and treatment. *J Clin Psychiatry* 1999; 60(S18):27-32.