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Immunosuppressive Agents May Enhance Corticosteroid Treatments for Uveitis

In 2000, a panel representing ophthalmological, pediatric and rheumatologic specialties published recommendations for the use of immunosuppressive drugs in patients with ocular inflammatory diseases. The panel noted that in many patients, the severity of the disease, corticosteroid-resistant side effects, or the need for high doses of systemic corticosteroids ultimately supported the use of steroid-sparing immunosuppressive drugs in the management of those patients.

Corticosteroids remain a cornerstone in the therapeutic approach to uveitis. The only drugs currently approved by the Food and Drug Administration for use in ocular inflammatory diseases, excluding postoperative inflammation, are corticosteroids and topical cyclosporine. "In patients with uveitis who require long-term corticosteroid therapy, however, it often is prudent to add another immunosuppressive agent to the therapeutic regimen, so lower dosages of corticosteroids can be employed," says Wendy M. Smith, M.D., a uveitis specialist with the Department of Ophthalmology at Mayo Clinic in Rochester, Minn.

Treatment Considerations

Some studies indicate that many physicians are not familiar with or do not adhere to recommended guidelines for management of uveitis. "For example, it is important to taper systemic prednisone to a daily dose of 10 mg or less within three months, because of the potential for side effects," says Dr. Smith. "Treatment should be monitored regularly. Many more drug options are available today, but the choice of therapy should still be guided by clinical

indication and individual patient characteristics, just as the panel recommended."

Most immunosuppressive agents are extremely potent and have significant adverse effects, so consideration of three patient-related factors is critical:

- Degree of vision loss or vision-threatening complications
- Ability to adhere to therapy
- Compliance with follow-up visits

"The immunosuppressed state can have potentially devastating ocular effects and long-term systemic adverse effects. It is important to weigh the risks and benefits and discuss them with the patient in detail," says Dr. Smith. "The provider should be certain that immunosuppressive therapy has a realistic chance of improving or preserving the patient's vision."

Appropriate diagnostic testing also should be considered before initiation of immunosuppressive therapy. Noninfectious inflammation in the eye is usually considered an autoimmune disease and requires anti-inflammatory agents to modulate the immune system responses. Infections may simulate autoimmune diseases and if so, immunosuppression may lead to disastrous consequences. Immunosuppressives may mask malignancies, confounding diagnostic tests. An intraocular foreign body may present as chronic or acute intraocular inflammation.

A complete clinical history may help providers avoid unnecessary diagnostic and therapeutic interventions. The age and sex of the patient, presence of diabetes, and the history of previous therapy, whether successful or failed, should be



Wendy M. Smith, M.D.

included in the decision-making process.

The rationale for therapy in uveitis must be carefully considered before a decision is made. Both the therapy and its goals must be tailored to the patient and the condition. "Therapy should be directed objectively at reducing inflammatory signs such as scleral injection, cells and flare in the anterior chamber; cells and haze in the vitreous; and lesions in the uvea and retina," says Dr. Smith. "If the desired therapeutic effect is not obtained after several months at recommended dosages, the addition of another agent or alternative treatments should be considered." The working diagnosis should also be re-evaluated prior to initiating additional therapy at every stage of treatment.

"It is vital for ophthalmologists and other providers to be aware of the array of immunosuppressive medications available today, and of the intrinsic

risks and benefits of each," says Dr. Smith.

For More Information

Dr. Smith presented "Diagnosis of Uveitis: Something Old, Something New" and "Uveitis Treatment: Going Beyond the Medrol Dose Pack" at the Mayo Clinic Ophthalmology Retina Update & Case Conference in September 2012. View the presentations at www.mayoclinic.org/medicalprofs/lao-videos-posters-ophu0113.html.

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Children With Congenital Esotropia Are at Increased Risk of Developing Mental Illness



Brian G. Mohnhey, M.D.

A retrospective study indicates that children diagnosed with congenital esotropia (CET) over a 30-year period are nearly three times more likely to develop mental illness by their third decade of life than are children without strabismus.

Researchers investigated the prevalence of psychiatric disorders among young adults who had CET as children using data from the Rochester Epidemiology Project. The research team identified all patients younger than 19 years who resided in Olmsted County, Minn., and were diagnosed with CET between Jan. 1, 1965, and Dec. 31, 1994. "We defined CET as a nonaccommodative esotropia that developed by age 6 months in a neurologically intact child. A total of 127 children, 67 males and 60 females, were diagnosed with CET in Olmsted County during the 30-year period," says Brian G. Mohnhey, M.D., with the departments of Ophthalmology and Pediatric and Adolescent Medicine at Mayo Clinic in Rochester, Minn.

Mental illness was defined as a disease meeting the *Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR*, Fourth Edition, criteria diagnosed by a psychiatrist, family physician or emergency physician. A history of mental illness diagnosed elsewhere was included when confirmed by a mental health care provider within Olmsted County.

The team then identified one age- and sex-matched control who did not have a diagnosis of strabismus for each case of CET. Cases were followed to an average age of 20 years (ranging from 6 months to 42 years old), compared with 19

years (ranging from 1 month to 58 years old) for the controls.

CET Outcomes

A mental health disorder was diagnosed in 42 (33 percent) of the children with CET, compared with 20 (16 percent) of the controls. A mental health disorder was diagnosed in 22 (33 percent) of the 66 males and 20 (30 percent) of the 61 females with CET. A diagnosis of CET increased the odds of being diagnosed with a mental illness by early adulthood 2.6 times.

"Cases with CET were more likely than their controls to have a greater number of mental illness diagnoses and use psychotropic medications. Individuals with CET were also more likely to have been born prematurely or have had some difficulty with pregnancy, although premature birth did not seem to significantly alter mental health outcomes," says Dr. Mohnhey.

The most commonly diagnosed forms of mental illness disorders among males were major depression, attention-deficit/hyperactivity disorder, substance abuse and alcohol dependence. Among females, the most prevalent forms of mental illness disorders were major depression, depression not otherwise specified, adjustment disorder and eating disorders.

"Although the sample size of individual mental health disorders was too small to demonstrate statistical significance, these findings do expand further the forms of childhood strabismus associated with the subsequent development of mental illness," says Dr. Mohnhey. "Previously, intermit-

tent exotropia and convergence insufficiency were associated with an increased risk of developing mental illness. Until we extended the cohort to 30 years, cases with CET were found to have no greater risk than controls.”

The increased risk of developing mental illness by early adulthood among children with CET may be explained by environmental factors. Hereditary factors may also play a part in the development of mental illness among children with CET. “Future studies may explore those factors. The findings from this study may also raise questions regarding the prevalence of mental illness among young adults,” says Dr. Mohney. A rate of 16 percent among controls in this study is consistent with reports that indicate mental illness occurs in 15 to 30 percent of young adults. Strabismus affects 3 to 5 percent of children worldwide.

For More Information

Olson JH, et al. Congenital esotropia and the risk of mental illness by early adulthood. *Ophthalmology*. 2012; 119:145.

Rochester Epidemiology Project

In 1966, Leonard T. Kurland, M.D., an epidemiologist with the Department of Neurology, expanded the Mayo Clinic medical records system to generate studies based on the population of Olmsted County, Minn. Dr. Kurland obtained National Institutes of Health funding to link records of all of the county’s health care providers.

The Rochester Epidemiology Project (REP) is a system for accessing medical records of 96 percent of the population of Olmsted County, accrued since the records were kept. It encompasses all ages, races, income levels and degrees of illness. Health care institutions in the REP provide virtually all medical care for the relatively isolated, semiurban county.

Mayo studies resulting from the use of this system are considered among the best medical research in the world. More than 1,500 studies determining the incidence, long-term trends and outcomes of virtually every major disease have been published and extrapolated to portray the U.S. population.

Incidence of Cataract Surgery Continues to Increase Steadily

A population-based study conducted in Olmsted County, Minn., confirms that the incidence of cataract surgery has steadily increased over 32 years, reaching record levels in 2011 (Figure 1). Additionally, second-eye surgery is performed sooner and more frequently. Between 2005 and 2011, 60 percent of residents had second-eye cataract surgery within three months of first-eye surgery, more than double the 28 percent rate recorded between 1998 and 2004 (Figure 2).



Jay C. Erie, M.D.

A research team led by Jay C. Erie, M.D., used Rochester Epidemiology Project (REP) databases to identify all incident cataract surgeries — 8,012 procedures in 5,725 persons — in Olmsted County, Minn., residents between Jan. 1, 2005, and Dec. 31, 2011. “We intended to estimate incidence rates of cataract surgery in a defined population and determine longitudinal cataract surgery patterns,” says Dr. Erie. The team calculated age- and sex-specific incidence rates and merged that information with previous REP incidence data from 1980 to 2004 to assess long-term temporal trends.

Age-related cataract affects more than 22 million Americans. That number may rise to 30 million by 2020. “The resulting cataract treatment burden will likely influence the distribution of U.S. health care funding,” says Dr. Erie. “Understanding temporal cataract surgery incidence rates and the factors that influence them will help us develop effective policies and procedures to manage costs and to ensure access to care.”

Inclusion and Impact

With approval from the Mayo Clinic and Olmsted Medical Center institutional review boards, all incident primary cataract surgeries performed on all Olmsted County residents during the study period were retrospectively identified. Thirteen ophthalmologists were available to provide

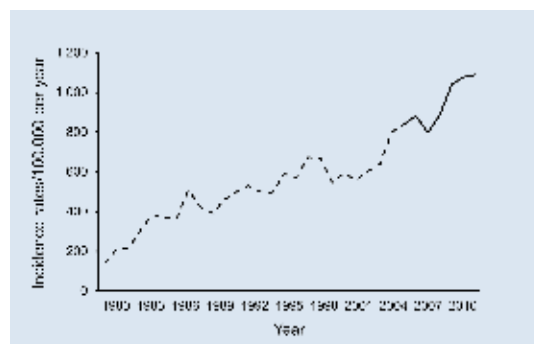


Figure 1. Age- and sex-adjusted rates of cataract surgery among residents of Olmsted County, Minn., 1980 to 2011, by year. The solid line represents 2005 to 2011 and the dashed line represents 1980 to 2004.

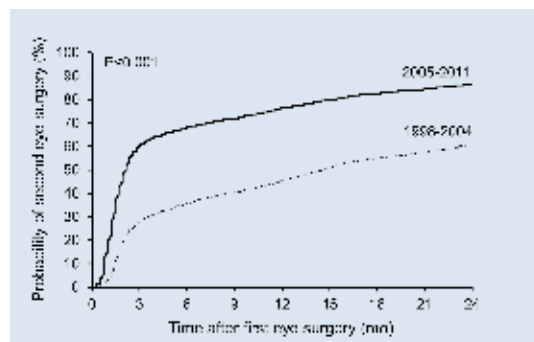


Figure 2. Cumulative probability of second-eye cataract surgery in Olmsted County, Minn., residents between 2005 and 2011 (solid line) versus 1998 to 2004 ($P < 0.001$), Kaplan-Meier analysis).

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cataract surgery to county residents during the study period.

Current data were merged with previous REP data for 1980 to 2004 to create a 32-year, population-based, longitudinal cataract surgery registry. In the extended study period, cataract surgery was higher among women and increased with age. Overall incident cataract surgery rates continued to steadily increase with no indication of leveling off.

Reasons for the rising cataract surgery incidence rates include:

- Improved access to surgery for patients with new cataract or previously unmet needs. The number of cataract surgeons increased 27 percent since 2002, and Mayo Clinic shifted from hospital-based surgery to an outpatient surgery center in 2003.
- Adoption of widening indications for surgery, which creates a larger surgical population and an increase in second-eye surgery. Second-eye surgery is associated with higher patient satisfaction

and improved quality of life, but earlier second-eye surgery is also associated with increased surgery rates.

“Although the characteristics of Olmsted County residents are similar to the state of Minnesota and the Upper Midwest, residents are less ethnically diverse, more highly educated and wealthier than the overall U.S. population,” says Dr. Erie. “Results from numerous previous REP studies, however, have generally been consistent with national data.”

The updated cataract surgery registry will be used to estimate changes in annual demand for cataract surgery, plan future health care spending and ensure adequate access to appropriate cataract treatment.

For More Information

Dr. Erie will present his results at the annual American Society of Cataract and Refractive Surgery and American Society of Ophthalmic Administrators symposium and congress in April 2013.

Meet Thomas Liesegang, M.D., Editor-in-Chief

Thomas J. Liesegang, M.D., has been in practice at Mayo Clinic for more than 33 years, first in Rochester, Minn., and then in Jacksonville, Fla. Since 2002, Dr. Liesegang has also served as editor-in-chief of the *American Journal of Ophthalmology*. Dr. Liesegang enjoys reviewing and judging new research to enhance patient care. Selecting among many submissions is always a challenge, but Dr. Liesegang says, “A strong editorial board helps reinforce the decisions. A major function of a peer-reviewed journal is to provide a filter to readers among all possible forms of communication.”



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