

Uveitis may be more prevalent than previously thought

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THE incidence of uveitis in the United States may be three times greater than previously thought, a new large-scale population study suggests.

The authors believe that more than 280,000 people every year develop some form of the disease. It is responsible for 30,000 new cases, or 10%, of blindness a year, in the US.

This cross-sectional, retrospective study reviewed databases and medical records to determine the incidence and prevalence of

uveitis in a large, well-defined population in Northern California.

The authors drew the population from the membership of Kaiser Permanente Northern California health care system. They searched the entire database (2,805,443 people) for patients who had the potential diagnoses of uveitis during a 12-month period.

This study population was further divided into six communities (731,898 people), represented by six medical centres and chosen to provide a variety of patient demographics with varying medical centre and population sizes. The sample conformed to the epidemiological definition of a community.

Two uveitis specialists reviewed the medical records of potential candidates to confirm diagnoses and establish time of disease onset. This yielded a sample of 2070 people who had potential diagnoses of uveitis.

The review uncovered 382 new cases of uveitis during the target period, while 462 cases of uveitis were diagnosed before the target period. These data yielded an incidence of 52.4/100,000 person-years and with a period prevalence of 115.3/100,000 people.

In the current study, the incidence and prevalence of disease were lowest in paediatric age groups 6.9/100,000 person years and were very high in patients 65 years or older, 102.7/100,000, 234.6/100,000.

Comparison between the group

of patients who had onset of uveitis before the target period (ongoing uveitis) and the entire cohort of uveitis patients showed that women had a higher prevalence of ongoing uveitis than men and that this difference was largest in the older age groups.

Idiopathic uveitis was the most common type encountered by the authors in complete medical records, both in onset (48% of new cases) and prevalence (33.9%). It was also the most common among incomplete medical records, which lacked a fundus examination.

The authors concluded that the incidence of uveitis was approximately three times that of previous US estimates and increased with the increasing age of patients. Women had a higher prevalence of uveitis than men, and the largest differences were in older age groups.

"I was surprised by the results. I was expecting similar results to those reported previously by Darrell, (Darrell et al., Arch. Ophthalmol. 1962;68:502-14), perhaps tending to be higher because the ethnic diversity is much greater in our study," said lead author David Gritz MD, Associate Clinical Professor, University of California San Francisco.

He said he believed the newly discovered prevalence went unsuspected in part because most cases were relatively simple iritis.

"So you don't realise how common it actually is. It's not as if there's an epidemic of corneal ulcers," he said.

In their discussion, the authors cite several possible reasons for the disparity of their results with earlier studies. There may be selection bias given the sample was drawn from the membership of the Kaiser Permanent health care system, though this encompasses a large cross section of Northern California's population.

People from the sample may report symptoms more readily, because they have easy access to health care, whereas uninsured cases that resolve without treatment may not be reported. This

would affect the reported incidence, but not prevalence. Moreover, different types of uveitis affect various racial groups in different ways.

In a discussion accompanying the paper William G. Hodge MD, Associate Professor of Ophthalmology at the Ottawa Eye Institute, noted that the high incidence of uveitis uncovered by the study gives cause for concern. However, he noted that the findings require careful scrutiny.

"In this study, the overall increase in rates relative to other studies is likely true. However, the highest rate among the elderly is perplexing, as it defies published reports and the common experience of uveitis specialists," Dr Hodge comments.

He believes the denominator (the population) for the elderly group may have been artificially reduced, making the numerator (the cases) artificially high. He also cautions that the overall results probably apply to California only, possibly the US and almost certainly not to other countries.

According to Dr. Gritz, these statements reflect Dr. Hodge's misunderstanding of the Kaiser system and the methodology of the study. The denominator is very accurate and if anything, the rates of disease may be even higher than found in this study, for instance if some Kaiser patients sought care outside of the Kaiser system.

Dr. Gritz said he believed the surge in cases among elderly people might be a result of a change in the epidemiology of the disease.

"It certainly has a very worrisome implication because of the ageing of our population. I wouldn't call it an epidemic, but I think it is of concern how many people may likely be affected."

Dr. Gritz added that ophthalmologists may need to be very meticulous in follow-up after patients finish medication to ensure that apparently resolved cases have in fact resolved. Also, it's important to impress on uveitis patients that they must

report any recurrence.

"My impression is that the longer a patient has problems, the fewer symptoms they experience. I have seen patients who were told to taper their steroids and didn't have a follow-up. When they were finally examined, they were having on-going inflammation all that time. That's my anecdotal experience, but the findings of the study make me concerned, especially if you had incorrectly assumed that the inflammation would resolve."

The research appears in the journal *Ophthalmology*, Gritz, David C., and Wong, Ira G., Incidence and prevalence of uveitis in Northern California, March 2004, (111;3: 491-500).

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PROMISING UVEITIS TREATMENT TO GO TO TRIAL

Daclizumab, a novel treatment for uveitis is poised to enter the Phase III clinical trial stage. Initial results indicate that the daclizumab is effective with far fewer side effects than current treatments, such as systemic corticosteroids and cytotoxic agents.

Researchers at the US National Eye Institute conducted a long-term (more than four years) phase I/II single armed interventional study using intravenous anti-interleukin-2 (anti-IL-2) receptor alpha treatments (daclizumab) and a short-term (26 weeks) phase II study evaluating the use of a subcutaneous daclizumab formulation. The data appeared in the *Journal of Immunology* (21 (2004) 283-293).

Patients were tapered off systemic immunosuppressive therapy and received daclizumab infusions or subcutaneous injections at intervals varying from two to six weeks. In the long-term study, patients were treated exclusively with daclizumab.

The researchers found that six-week injection intervals led to a recurrence of uveitis, while two-to four-week intervals did not. One patient developed resistance, but this disappeared once subcutaneous treatment was begun.

In the short-term study, four of the five patients met study success points within the first 12 weeks, and all five were successful by 26 weeks.

The studies offered preliminary evidence that regularly administered long-term daclizumab therapy can be given in lieu of standard immunosuppression for years to treat severe uveitis. It also appears that subcutaneously administered daclizumab may be a clinically viable treatment option.

The results are promising given the apparent rise in cases of uveitis (see main story) and the side effects associated with current treatments. Further, the subcutaneous treatment may open the way for self-administered medication.

"The initial results sound very promising. I'm anxious to see the full analysis. I am encouraged by the original research that is going into uveitis treatment," said David Gritz MD.