OHTAC Recommendation

Intrastromal Corneal Ring Implants for Corneal Thinning Disorders

January 2009

OHTAC Ontario Health Technology Advisory Committee

Background

The Ontario Health Technology Committee (OHTAC) met on November 21, 2008 and January 23, 2009, to evaluate the effectiveness and safety of intrastromal corneal ring implants (ICRS) for the treatment of corneal thinning disorders following an evidence review produced by the Medical Advisory Secretariat (MAS).

The primary treatment objectives for ICRS are to normalize corneal surface topography, restore contact lens tolerability, and rehabilitate vision in order to delay or defer the need for corneal transplant. The purported advantages of corneal implants are that they are minimally invasive, safe, and effective. The procedure is also claimed to be adjustable, reversible, and both eyes can be treated at the same time. Further, ICRS do not limit the performance of subsequent surgical approaches or interfere with corneal transplant.

Corneal Thinning Disorders

Corneal ectasia (thinning) comprises a range of disorders involving either primary disease conditions such as keratoconus and pellucid marginal corneal degeneration, or secondary iatrogenic conditions such as corneal thinning occurring after refractive surgery. It is a condition in which the normally dome-shaped cornea progressively thins, causing a cone-like bulge or forward protrusion in response to the normal pressure of the eye. This bulging can lead to irregular astigmatism of the cornea resulting in a loss of visual acuity that can seriously impair an individual's ability to work or perform routine daily activities such as driving, television viewing, or reading.

The most common naturally occurring corneal thinning disorder is known as keratoconus (KC). Although the specific causes of the biomechanical alterations in the corneal stroma that occur with KC are unknown, there is a growing body of evidence to suggest that genetic factors may play an important role. KC is a rare disease (< 0.05% of the population) and is unique among major chronic eye diseases in that it has an early age of onset (median age of 25). Patients with KC are referred for corneal transplant as a last option when they can no longer tolerate contact lenses or when lenses no longer provide adequate visual correction.

Keratoconus is one of the leading indications for corneal transplants and has been so for the last three decades. Yet, despite high graft survival rates up to 20 years of corneal transplants, there are reasons to defer receiving transplants for as long as possible. Patients with KC are generally young and life-long transplant survival duration would be necessary. Recovery also involves lengthy time off work and there are potential complications from long term steroid use following the surgery, as well as the risk of developing secondary cataracts, glaucoma etc. After transplant, recurrent KC is possible creating the need for subsequent interventions. Residual refractive errors and astigmatism can remain challenging after transplantation and high refractive surgery rates and re-graft rates in KC patients have been reported. Finally, visual rehabilitation after transplant may be slow and/or unsatisfactory for some patients.

Corneal Implants

In Canada, INTACS® (Addition Technology Inc. Sunnyvale, CA) are the only currently licensed corneal implants. These implants are micro-thin poly methyl methacrylate crescent-shaped ring segments that act as passive spacers. When implanted, they cause a flattening of the central cornea that corrects for the effects of corneal thinning. The procedure can be performed on an outpatient basis either by corneal specialists or refractive surgeons and is generally carried out with topical anesthesia.

Not all KC patients are eligible candidates for corneal implants. Treatment with corneal implants is considered for patients who are contact lens intolerant, have adequate corneal thickness (particularly

around the area of the implant incision site), and with no central corneal scarring. Patients desiring to have visual rehabilitation that does not include glasses or contact lenses would not be suitable candidates for corneal ring implants.

Evidence Review

The literature search strategy employed keywords and subject headings to capture the concepts of 1) intrastromal corneal rings and 2) corneal diseases, with a focus on keratoconus, astigmatism, and corneal ectasia. The initial search was run on April 17, 2008, and a final search was run on March 6, 2009 in the following databases: Ovid MEDLINE (1996 to February Week 4 2009), OVID MEDLINE In-Process and Other Non-Indexed Citations, EMBASE (1980 to 2009 Week 10), OVID Cochrane Library, and the Centre for Reviews and Dissemination/International Agency for Health Technology Assessment. Search results were limited to human and English-language published between January 2000 and April 17, 2008. The Web sites of several other health technology agencies were also reviewed including the Canadian Agency for Drugs and Technologies in Health (CADTH), ECRI, and the United Kingdom National Institute for Clinical Excellence (NICE).

In the MAS evidence review, 66 reports were identified on the use of implants for management of corneal thinning disorders. These varied according to their primary clinical indication, type of corneal implant, and whether or not secondary procedures were used in conjunction with the implants. In addition to KC, implants were reported to manage post-LASIK thinning and/or uncorrected refractive errors and as an adjunctive intervention both during and after corneal transplant to manage recurrent thinning and/or uncorrected refractive error

Findings

Ten pre-post cohort longitudinal follow-up studies were identified examining the safety and effectiveness of INTAC corneal implants in patients with KC. Five additional cohort studies were identified using the Ferrara corneal implant for KC management, but because this implant isn't licensed for use in Canada, these studies were omitted from the review. The cohorts implanted with INTACS comprised 608 KC patients (754 eyes) followed for 1, 2 or 3 years. The overall quality of evidence determined using the GRADE hierarchy of evidence was moderate.

The outcomes reported across the studies involved statistically significant and clinically relevant improvements in corneal topography, refraction and visual acuity. Patients' vision was usually restored to within normal functioning levels and, for patients not achieving satisfactory vision, insertion of intraocular lenses were reported in case studies to result in additional vision improvement. Vision loss, which was only infrequently reported, was usually reversed by implant exchange or removal. Improvements in visual acuity and refractive error reported 6 months after surgery were maintained at 1 and 2-year follow-up. High levels of technical success and/or ability to place INTAC segments were reported. Technical difficulties (when reported) were delayed and generally reported as segment migration and generally attributed to early experience. Overall, complications were infrequently reported and largely involved minor reversible events without clinical sequelae.

Despite the limited evidence base for corneal implants (which consisted solely of longitudinal follow-up studies), these devices appear to be a valuable clinical tool for improving vision in patients with corneal thinning. Implants may also have a rescue function, treating corneal thinning occurring after LASIK refractive surgery in normal eyes, and for the management of recurrent or residual refractive errors following corneal transplant. The treatment offers several advantages in that it is an outpatient based procedure, is associated with minimal risk, and has high technical success rates. Both eyes can also be

treated at once and the procedure is adjustable, reversible, and implants can be removed or exchanged to improve vision without limiting the possibility of subsequent interventions, particularly corneal transplants.

Ontario Health System

At present, there are approximately 70 ophthalmologists that have had training with corneal implants in Canada, of which 30 practice in Ontario. Industry currently sponsors the training, proctoring and support for the procedure. The cost of the implants ranges from $950 to $1200 CAD$ and costs for instrumentation range from $20,000 to $30,000 CAD$ (a one time capital expenditure). There is no physician service fee code for corneal implants in Ontario and there have been no out of province treatment requests for corneal implants. In Ontario, the treatment is currently offered in private clinics and increasing numbers of ophthalmologists are being certified in the technique by the manufacturer.

Based on published population rates of KC occurrence, it can be projected that there is a prevalent population of approximately 6,545 patients in Ontario and an incident population of 240 newly diagnosed cases per year. The estimated average cost per patient for treatment, based on device costs and surgical fees, was $1,964 CAD$ (range $1,814 to $ 2,114) per eye. The estimated budget impact for managing the incident population, assuming the most conservative scenario (i.e., all are eligible and all receive bilateral implants) ranges from 923 thousand to 1.1 million CAD$. The actual impact to the provincial budget would vary based on a variety of criteria including eligibility, unilateral or bilateral intervention, re-interventions, capacity and uptake.

OHTAC noted that since corneal thinning is a complication of refractive eye surgery, an increasingly popular alternative to eye glasses for the correction of refractive errors in normal eyes, the use of ICRS to treat this subgroup of patients may increase in the future.

OHTAC Recommendations

Based on the above findings, OHTAC recommends the following with regard to ICRS:

1. Based on moderate quality evidence, OHTAC recommends improved access to intrastromal corneal rings for the treatment of corneal thinning diseases such as KC for patients who are unable to achieve functional vision and have a clear central cornea and adequate corneal stroma.
2. OHTAC recommends close monitoring of this technology, perhaps through refinement of a fee code, to track ICR removal rates after 6 months and subsequent corneal transplantation, given the short follow-up observation periods used in studies that examined safety.