HTW GUIDANCE

Technoleg Iechyd Cymru
Health Technology Wales

Clinical and cost effectiveness of epithelium-off corneal crosslinking (CXL) to treat adults with keratoconus

Guidance Number:	FIELD: Ophthalmology
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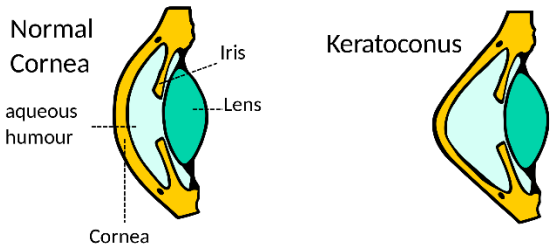
HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 002 (February 2018)

Clinical and cost effectiveness of epithelium-off corneal crosslinking (CXL) to treat adults with keratoconus



Why did Health Technology Wales (HTW) appraise this topic?

This topic was proposed by Dr Kelechi Nnoaham, Director of Public Health, Cwm Taf University Health Board, and submitted to HTW by the Welsh Health Specialised Services Committee (WHSSC) to support evidence-informed decision making over provision of epithelium-off corneal crosslinking within NHS Wales.

The evidence about epithelium-off corneal cross-linking (CXL) to treat adults with keratoconus is inconclusive. There is insufficient evidence to show that CXL is effective in the long term. HTW guidance is that routine provision is not currently supported. Research is recommended into the long term effectiveness and cost-effectiveness of epithelium-off CXL in adults, compared with no treatment

Evidence:

- A recent systematic review compared outcomes of epithelium-off CXL with no treatment, based on changes from baseline after one year. Their meta-analysis of Best Spectacle-Corrected Visual Acuity (BSCVA) showed a significant difference between groups at one year. However, the long term clinical significance of the result beyond one year was uncertain.
- No significant differences between groups were found for changes in corneal thickness or cylindrical refraction, and it was not possible to evaluate maximum keratometry (Kmax), or other outcomes due to study heterogeneity.
- A UK health economic model suggested a high likelihood of cost effectiveness of CXL. However, cost effectiveness was contingent upon a long effect duration of CXL treatment, which has not been verified. If treatment benefit was not sustained beyond 5 years CXL was not cost effective, exceeding conventionally accepted UK thresholds.

The status of HTW guidance is that NHS Wales should adopt this guidance or justify why it has not been followed. HTW will evaluate the impact of its guidance.

Image credit: http://3.bp.blogspot.com/-bruMg4e7n_c/ThF1eESviJI/AAAAAAAABhw/ifID4s92_1w/s1600/Keratoconus-Image.jpg

SUMMARY OF EVIDENCE APPRAISAL REPORT[1]

Context

Keratoconus is a non-inflammatory, bilateral eye condition. It is estimated that there are approximately 3,000 affected people in Wales; it is not clear how many would be eligible for treatment. Keratoconus is characterised by a progressive thinning and distortion of the cornea, causing a cone-shaped bulge to develop. This results in vision problems such as short-sightedness, blurred vision, astigmatism or light sensitivity. The condition typically develops in children and young adults and can deteriorate over time.

Corneal crosslinking (CXL) procedures aim to slow or stop the progression of keratoconus. Criteria for treatment include proven progression of keratoconus, patient aged under 30, and corneal thickness > 400-450 µm. Riboflavin (vitamin B2) drops are administered in conjunction with ultraviolet light (UVA). The photochemical reaction leads to stiffening and strengthening of the cornea. This is expected to prevent disease progression, but the duration of benefit is uncertain.

The standard CXL procedure follows the Dresden protocol – an "epithelium-off" procedure in which the epithelium of the cornea is removed to allow penetration of riboflavin into the corneal tissue. Variations on this protocol may be used at the surgeon's discretion, including Accelerated CXL, or differences in composition or timing of application of riboflavin drops. Current practice in Wales is based on a variation of the Dresden protocol.

Evidence on clinical effectiveness, safety, economic analysis and patient issues

A systematic review including five studies (289 eyes) reported a small but highly statistically significant difference in best spectacle-corrected visual acuity in favour of CXL when compared with no treatment one year after follow-up (-0.09 logMAR; 95% CI -0.14, -0.04, p = 0.0005). However, the clinical significance of this finding was uncertain. No significant differences between groups were found for corneal thickness or cylindrical refraction. It was not possible to reach a conclusion for three other outcome measures due to heterogeneity of the effect size (I2 > 50%).

An existing robust UK health economic model suggested a high likelihood of cost-effectiveness. However, the results depended on a long effect duration of CXL treatment. Observational studies with longer-term follow-up (minimum 3 years) were of insufficient quality to verify sustained effect duration. The service currently being established in Wales is estimated to be marginally more costly than the service provided in Bristol by referral.

The evidence base is limited for this rare condition. Studies are heterogeneous (mainly due to effect size rather than direction of effect), and sample sizes are relatively small. Results of other systematic reviews (including a Cochrane review), were broadly consistent with these findings.

Safety issues were not searched specifically. NICE guidance indicates that there is sufficient evidence of safety of epithelium-off CXL for the procedure to be carried out provided that normal arrangements are in place for clinical governance, consent and audit. Delivery of riboflavin as eye drops is outside their usual indication for use in Europe. The US Food and Drug Administration (FDA) approved the ophthalmic solution, after finding a low incidence of adverse events such as corneal opacity (haze), punctate keratitis, corneal striae, eye pain, and reduced visual acuity.

No evidence of patient experiences was identified within the evidence reviewed.

[1]Summary of Evidence Appraisal Report intended for use by decision-makers in NHS Wales.

Organisational issues

The procedure is considered to be relatively straightforward, and could be carried out by a competent practitioner in an outpatient or primary care setting.

There is currently inequity of access in NHS Wales, with the service being readily available to patients of Abertawe Bro Morgannwg University Health Board. Patients from other health boards are only able to access treatment by referral on a case-by-case basis.

Further research

Robust research is recommended into the long term effectiveness and cost-effectiveness of epithelium-off CXL to treat adults with keratoconus, compared with no treatment.

Responsibilities for consideration of this Guidance

Health Technology Wales (HTW) was established by Ministerial recommendation[1,2] to support a strategic, national approach to the identification, appraisal and adoption of non-medicine health technologies into health and care settings. The HTW Appraisal Panel comprises senior representation from all Welsh boards with delegated authority to produce guidance 'from NHS Wales, for NHS Wales'. The status of HTW guidance is 'adopt or justify'. There is an expectation from Welsh Government that HTW guidance is implemented with adoption regularly audited by HTW.[3]

The guidance in this document is intended to assist Welsh care system decision makers to make evidence-informed decisions when determining the place of health technologies and thereby improve the quality of care services.

The content of this HTW guidance was based upon the evidence and factors available at the time of publication. An international evidence base was reviewed and external topic experts and HTW committee members consulted to contextualise available evidence to Wales. Readers are asked to consider the generalisability of the evidence reviewed to NHS Wales and that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. It is acknowledged that evidence constitutes only one of the sources needed for decision making and planning.

This guidance does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

No part of this guidance may be used without the whole of the guidance being quoted in full. This guidance represents the view of HTW at the date noted. HTW guidance is not routinely updated. It may, however, be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the guidance given.

Standard operating procedures outlining HTWs evidence review methods and framework for producing its guidance are available from the HTW website.

Acknowledgements. HTW would like to thank the individuals and organisations who provided comments on the draft Evidence Appraisal Report or HTW guidance.

Declarations of interest were sought from all reviewers. All contributions from reviewers were considered by HTWs Assessment Group. However, reviewers had no role in authorship or editorial control and the views expressed are those of Health Technology Wales.

Chair, Health Technology Wales Appraisal Panel

1. National Assembly for Wales, Health and Social Care Committee. Access to medical technologies in Wales. December 2014.
2. Response to Recommendations from the Health & Social Care Committee: Inquiry into Access to Medical Technologies in Wales. February 2015.
3. Gethin, V. Letter to all Health Board Chairs re Funding for Sacral Nerve Stimulation in Wales. VG_01655_17. September 2017.