INAHTA Brief

Title Corneal collagen cross-linking and intrastromal corneal ring segments in the treatment of corneal ectasia

Agency HAS, French National Authority for Health (Haute Autorité de Santé)
2 avenue du Stade de France – F 93218 La Plaine Cedex, France
Tel.: +33 (0)1 55 93 70 00 – Fax: +33 (0)1 55 93 74 35, contact.seap@has-santé.fr, www.has-sante.fr

Reference ISBN number: 978-2-11-139091-1, link to full report: http://www.has-sante.fr/portail/jcms/c_1781741/fr/crosslinking-du-collagene-corneen-et-anneaux-intra-corneens-dans-le-traitement-des-ectasies-corneennes.

Aim

These two procedures are presented as an alternative to corneal transplant. The expected effects are stabilisation of the disease from corneal collagen cross-linking (CXL), and visual rehabilitation from placement of intrastromal corneal ring segments (ICRS).

Conclusions and results

The clinical efficacy and safety data for CXL and ICRS are primarily from studies with a low level of evidence. These are prospective, mostly single-centre studies with no comparator or with an inadequate comparator.

For both procedures, most efficacy data are from non-comparative studies. Given the disease's progression profile, this limits the relevance of the results. Conversely, complications and adverse events have probably been under-reported. In addition, for CXL, some studies have a very high lost to-follow-up rate.

The efficacy results for CXL, which come from one randomised controlled trial, seven observational studies and two meta-analyses, all point towards a significant or non-significant reduction in maximum keratometry values. The failure rate for this technique, from the results of four original studies, is between 0% and 11.5% but may have been underestimated. The incidence of the main adverse events and/or complications reported is below 10%, except for corneal oedema and haze, which are very frequently reported but mostly transient.

The efficacy results for ICRS, which come from two clinical trials and eight prospective observational studies, all point towards an improvement in corrected visual acuity. This was significant in nine out of ten studies. The proportion of patients whose visual acuity improved by 1 line or more or 2 lines or more following the procedure was heterogeneous (52.2% to 89%). The failure rates for the technique, estimated from data from seven studies, are below 50%. Adverse events and/or complications were reported with a frequency of less than 10%, except for the appearance of intrastromal deposits and corneal haze, which were reported with an undisclosed or much higher frequency.

For both procedures, all the HTAs analysed (CXL (n=4); ICRS (n=3)) point out the low level of evidence. It should be noted that none of these HTAs rule out CXL and ICRS as therapeutic options. As regards the guidelines (CXL (n=2); ICRS (n=2)), these recommend using the two techniques or consider them applicable but subject to close monitoring.

The stakeholders did not make any comment on the methodological quality of this report or the selection of literature. At the scoping meeting, the stakeholders stated they felt CXL should be indicated as soon as keratoconus is discovered in children and in the case of post-LASIK ectasia, due to the high probability of rapid disease progression in these patients. The stakeholders consider ICRS to be an effective technique in this indication.

This assessment also highlights the lack of studies in children with keratoconus and patients with post-LASIK ectasia, the lack of prospective comparative data, and the lack of efficacy and safety results with long follow-up durations for CXL and ICRS in these patients.

Recommendations

On the basis of literature with a low level of evidence and the favourable opinion of stakeholders, and taking into account the potential disability associated with some progressive forms with no other treatment options, HAS considers that:

- CXL is a possible treatment option in patients with evidence of progressive keratoconus without corneal opacities and with adequate pachymetry (≥ 400 µm);
- ICRS are a possible treatment option in patients with keratoconus without corneal opacities and with adequate pachymetry (≥ 400 µm) who have unsatisfactory visual acuity after correction with lenses or who cannot tolerate contact lenses.

HAS emphasises that these indications should be determined by a specialist centre (reference centres and expert centres).

HAS also notes that in children with keratoconus and patients with post-LASIK ectasia, the practice of CXL without waiting for evidence of disease progression could not be assessed due to a lack of data in the literature.

However, the stakeholders AFO [French Academy of Ophthalmology – CNP [National Professional Board] considered the use of CXL in this indication to be important, due to the high probability of rapid disease progression in these patients.

Consequently, HAS considers that CXL is a possible treatment option in these patients, as long as they are managed in a specialist centre and the decision is made through consultation with the patient, family and a highly specialised team. HAS also recommends that a follow-up registry should be set up for children and cases of post-LASIK ectasia.

HAS reminds professionals and the public that CXL is a curative treatment. Use of this technique as a preventative measure, including before any ectasia appears and in particular before LASIK surgery, is poor practice and is contraindicated.

These techniques should be performed in an operating theatre under surgical conditions.

Finally, HAS notes that the long-term efficacy of these two techniques has not been sufficiently documented, due to the lack of prospective comparative studies with long-term follow-up published in the literature. HAS therefore recommends that such studies should be set up to provide this information.

Methods

The assessment method used in this report is based on:

- a critical analysis of data identified in the scientific literature;
- gathering the viewpoints of stakeholders (French Academy of Ophthalmology – National Professional Board for Ophthalmology and a keratoconus patients association) through a written questionnaire.

Thus, the conclusions of the assessment are based on the data collected. These conclusions are reviewed by the National Commission for the Assessment of Medical Devices and Health Technologies and then validated by the HAS Board.

Written by

Alicia Amigou, HAS, France.