STICKLER SYNDROME
Prophylactic treatment may do more harm than good
by Roibeard O’Héineachain in Milan

Prophylactic treatment of Stickler syndrome with laser or cryotherapy has yet to demonstrate any benefit in clinical trials and may actually be harmful in the long term, said G W Aylward FRCS, FRCOphth, MD, at a joint WCPOS/EURETINA symposium at the 2nd World Congress of Paediatric Ophthalmology and Strabismus.

“For every case you can show me that has benefited from laser or cryotherapy prophylaxis, I can show you a case that has been harmed by it,” said Dr Aylward, Moorfields Eye Hospital, London, UK.

He noted that there are very good reasons for desiring an effective prophylaxis against retinal detachment in eyes with Stickler syndrome. Patients with the condition are at a high risk of giant retinal tears. In addition, their rate of successful retinal re-attachment tends to be only around 80 per cent, compared to around 90 per cent among patients without Stickler syndrome. (Abeysiri et al, Graefes Arch Clin Exp Ophthalmol 2007; 245: 1633-1666.)

However, there is little evidence from studies conducted to date that prophylactic laser or cryotherapy has any protective effect, he pointed out. Moreover, there are reports in the literature that have implicated prophylactic therapy in the pathogenesis of retinal detachment.

“When you apply cryotherapy or laser, what you are doing is creating a new abnormality in the chorio-vitreo-retinal relationships, and that may not be an apparent problem until much later in life,” he noted.

In eyes that have undergone prophylactic laser or cryotherapy for indications other than Stickler syndrome there is a phenomenon in which a posterior vitreous detachment occurring 40 or so years later can lead to tears along the edge of the treated area, Dr Aylward said.

“It may be that your treatment hasn’t actually prevented the detachment, but has in fact caused it. The trouble is that, because it will be 40 years later, you will have retired by then and so you will never know, he added.

Prophylactic therapy also carries the risk of retinal complications occurring in the shorter term, Dr Aylward said. He described the case of a seven-year-old girl with Stickler syndrome who presented with a giant retinal tear in one eye and who underwent prophylactic laser in the other eye. Ten days postoperatively, she presented with a retinal tear on the edge of the laser treatment, such that the prophylactically treated eye is now the one with worse vision.

Selection bias Some of the early investigators into the prophylaxis of retinal detachment in Stickler syndrome patients went so far as to perform scleral buckling. However, most have abandoned that practice in favour of less extreme treatments like cryotherapy and laser treatment, Dr Aylward continued.

A study investigating the prophylactic use of 360° cryotherapy in the fellow eyes of patients with giant retinal tears – including some Stickler syndrome patients – indicated that the treatment provided a clinically significant and statistically significant benefit compared to no treatment in historical controls (Wollensberger, Ophthalmol 2003; 110: 1175-7).

That is, among the fellow eyes that underwent cryotherapy, two per cent had retinal tears without retinal detachment, six per cent had retinal detachment and two per cent had giant retinal tears. By comparison, among the fellow eyes of historical controls, 60 per cent had retinal tears, 18 per cent had retinal detachments and 17 per cent had giant retinal tears.

However, it is in the nature of such trials that a selection bias for the historical controls can be difficult to rule out, Dr Aylward said.

A more recently published study yielded similar results. The retrospective study involved 204 Stickler syndrome patients who underwent 360 degree cryotherapy. After a follow-up of one to 27 years, the rate of retinal detachment was only eight per cent among the treated eyes, compared to 73 per cent among the eyes that weren’t treated (Ang et al, Ophthalmol 2008; 115: 164-168).

On the basis of these results, the study’s authors concluded that cryotherapy significantly reduces the likelihood of retinal detachment in patients with type 1 Stickler syndrome. However, a closer scrutiny of the details of the study reveals a strong selection bias regarding the controls, Dr Aylward said.

For example, the average age of the patients receiving cryotherapy was 21 years, compared to 49 years among the controls, he pointed out. The longer a Stickler syndrome patient lives, the greater will be their likelihood of having a retinal detachment, he noted. Therefore, the control population was inherently at increased risk of retinal detachment, he said.

Furthermore, the location of the study in a Stickler syndrome clinic that advocates prophylactic therapy in itself creates a selection bias, Dr Aylward argued further.

“This gives the authors an enormous problem, because if you’re treating most Stickler patients, where do you get the control group from? They are the patients who come into the department unexpectedly, most likely because of retinal detachment. So I’m afraid that the reason the incidence of retinal detachment is so high is because of the way the treatment and control groups were selected,” he said.

Dr Aylward noted that he was not alone in his criticism of the study. In fact, all of the retinal consultants at Moorfields Eye Hospital wrote a letter to the journal, Ophthalmology, to express their rejection of the conclusions of the study’s authors.

“We know that Stickler’s syndrome patients have a higher risk for retinal detachment, but that doesn’t equate with the idea that we can modify that risk. It would be great if we could prevent their retinal detachments, but I don’t think that we have enough evidence now that prophylaxis works,” he concluded.