Correspondence

Acyclovir and steroids in herpes zoster keratouveitis

SIR, We read McGill and Chapman's article¹ with much interest. While we agree with them regarding steroid dependency of many of the inflammatory ocular complications of zoster with the attendant difficulty of withdrawal, and that there are significant complications of long term topical steroids, we would not agree to withholding these valuable drugs. In the Zoster Clinic carefully controlled topical steroids have been used successfully in the inflammatory complications of ophthalmic zoster for over 10 years.

During the last year acyclovir alone has been tried in a random selection of cases of varying severity. These were new, acute, and had not had ocular steroid or antiviral therapy prior to their first visit. Twenty-three cases in all were treated from a median of one week after the rash onset with the advocated dosage of acyclovir and followed up at regular and frequent intervals to a mean of 6 months. Twelve patients who did not differ significantly from the group as a whole in their age, follow-up period, or interval before treatment continued with inflammatory changes which necessitated introduction of topical steroid. Seven patients had no response at all in the initial 1-3 weeks of treatment, three having hypertensive uveitis, two episcleritis and raised ocular pressure, one sclerokeratitis, and one corneal oedema and uveitis. The five others deteriorated after three months, one with chronic uveitis and the other four with stromal keratitis and vascularisation. All 13 showed a prompt improvement when changed to steroid therapy (dexamethasone soluble 0.1% at the outset reducing to prednisolone 0.3%).

The literature on zoster before topical steroids were available describes much more severe complications than we see nowadays,² and we would urge ophthalmologists not to withhold steroids in the treatment of inflammatory zoster lesions. Clearly during therapy (1) the intraocular pressure must be monitored frequently; (2) when anaesthetic the cornea must be checked for ulceration; and (3) topical steroid should be withdrawn cautiously.

It remains to be seen if a combination of acyclovir and steroids is more effective than steroids alone, and this will require a properly controlled trial of unselected cases.

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References

- 1 McGill J, Chapman C. A comparison of topical acyclovir with steroids in the treatment of herpes zoster keratouveitis. *Br J Ophthalmol* 1983; 67: 746-50.
- 2 Edgerton AE. Herpes zoster ophthalmicus. *Arch Ophthalmol* 1945; 34: 40-8.

SIR, We are all agreed on the problems of steroid dependency and the difficulty of withdrawal of steroids in the treatment of herpes zoster keratouveitis. Our work here in Southampton has suggested that initially the treatment for herpes zoster keratouveitis should be with topical acyclovir, particularly if the lesions have been present for less than three weeks. If the lesions have been present longer than this time, there is usually so much ocular inflammation that steroids should be considered as an initial therapy in combination with acyclovir, although this is a clinical impression rather than any hard and fast rule gained from trials.

In Marsh and Cooper's series 12 patients did not respond favourably to topical acyclovir alone as an initial treatment for their herpes zoster induced keratouveitis, but a high percentage had episcleritis or sclerokeratitis. We have found that these conditions do not respond quickly to topical acyclovir alone¹ (McGill, in press), and I would agree that in these cases the addition of steroids should be considered, particularly if there had been no favourable response within 21 days.

I note that five of their patients deteriorated after three months. We have not seen any patients have a recurrence of their uveitis after this time. Four of their patients with stromal keratitis had a recurrence after three months. They do not specify whether this was a nummular keratitis or a disciform keratitis. We have frequently seen that those small nummular lesions regress on treatment and then develop a few opacities around the nummular lesion over the succeeding months. This response is always mild and is not associated with any stromal swelling or oedema suggestive of an active lesion, though it could represent an antigen-antibody reaction in the stroma. These lesions up to now have not affected vision and they eventually regress. I would agree that if they are in the visual axis and affect the vision, then treatment with topical steroids should be considered, so that there is no permanent visual impairment. It is a clinical impression that if these recurrent lesions off the visual axis are treated just with topical acyclovir they do regress, though this is a clinical impression based on one or two patients.

We have found on an open basis that the addition of acyclovir to topical steroids achieves no beneficial effect and that there is a recurrence rate of over 50% in such patients (McGill, in press).

By using acyclovir as an initial form of therapy in many patients the concomitant problem of the steroid side effects and withdrawal problems are not experienced. Not all patients will respond favourably to just topical acyclovir; in our initial study of 20 patients¹ one patient required the addition of steroids. We have followed these studies up over the last two to three years, and now five patients out of 56 analysed retrospectively required the addition of topical steroids (McGill, in press).

The main point to be made is that those patients treated with acyclovir alone do not have the same recurrence rate as those with steroids. In a recent analysis of the 56 patients treated with topical acyclovir only two patients had a recurrence of their keratouveitis, and this was after 18 months, and one of those patients had had a topical steroid preparation to the lids. In the same period 74 patients were treated with topical steroids for their keratouveitis and 50% (i.e., 37) had had a recurrence within the first year, and four

(5.4%) after 18 months. It is the initial recurrence rate that is prevented by using topical acyclovir. If the use of topical acyclovir does not lead to the suppression of ocular signs within 21 days, then steroids should be added, because prolonged keratouveitis can lead to endothelial damage, which if it persisted could lead in the long term to corneal decompensation and the development of a bullous keratopathy. Also, intraocular damage in the form of adhesions or secondary cataracts can result if steroids are withheld and if the disease process is still active after 21 days.

The main problem with all our trials is that we have not yet *actually* shown an active role for antivirals in the treatment of herpes zoster keratouveitis. This is because it is ethically not possible to carry out placebo controlled trials in acute herpes zoster keratouveitis when the patient has a painful red eye. Our trials have compared the use of topical steroids with topical acyclovir, and may be showing only the deleterious effect of steroids. There are ways round this problem. Firstly, a retrospective analysis with all its attendant problems can be carried out on patients with keratouveitis. If enough patients are analysed, a clear pattern should emerge. In our retrospective analysis of 144 patients treated over the last four years such a pattern did emerge, and topical acyclovir was superior to topical steroids. The alternative is to carry out a prophylactic trial

on all those patients either with an acute herpes zoster skin rash or with minimal ocular involvement, such as a slight conjunctivitis or punctate epithelial keratopathy, comparing placebo with acyclovir. The comparison in such patients might give an answer in that, if it could be shown that one group progressed into more serious forms of ocular involvement and the other did not, then this would give an indication of whether the antiviral drugs have an active part to play in the disease treatment. Such trials are under way. Currently, though, I advise that all forms of herpes zoster keratouveitis are treated initially with topical acyclovir, and if there is no initial favourable response, or if the disease process does not regress within 21 days, then steroids should be added. Once steroids have been added, they should be slowly withdrawn over up to 18 months in order to prevent the problems of rebound.

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Reference

- McGill J, Chapman C. A comparison of topical acyclovir with steroids in the treatment of herpes zoster keratouveitis. *Br J Ophthalmol* 1983; 67: 746–50.

Notes

Cataract surgery

The Seventh Annual International Cataract Surgery Symposium will be held on 18–20 February 1985 at Loews Paradise Valley Resort, Scottsdale, Arizona. Details from the Eye Foundation, 525 N 18th Street, Suite 504, Phoenix, Arizona 85006, USA.

Death of Professor Jules François

It is with great regret that we report the death of Professor Jules François on 13 August. An obituary notice will appear in a later issue of the *BJO*.

List of future meetings

At the request of the International Agency for the Prevention of Blindness the International Center for Epidemiologic and Preventive Ophthalmology will maintain a computerised list of the dates of major future ophthalmic meetings. It is hoped this will facilitate scheduling and reduce the risk of conflicting dates. Relevant organisations are encouraged to write for a free print-out of meetings already scheduled, and to inform the center as soon as dates for their own meetings have been finalised. Correspondence should be addressed to Meeting Coordinator, ICEPO, Dana Center for Preventive Ophthalmology, Wilmer Institute Room 120, 600 N Wolfe Street, Baltimore, Maryland 21205, USA.

Glaucoma, laser, cataract

The Eye Foundation of America will hold a symposium on 'Glaucoma, laser, cataract' on 1–2 February 1985 at the Meridien Hotel, New Orleans, Louisiana, USA. Details from Kenneth G. Haik, MD, Eye Foundation of America, 823 Maison Blanche Building, New Orleans, Louisiana 70112, USA.

Eye banks

The 1st International Cornea and Eye Banking Symposium will be held at the Hotel Inter-Continental, San Diego, California, on 6–8 June 1985 under the aegis of the Eye Bank Association of America. Details from Lila Lerner, Symposium Coordinator, Office of Continuing Education, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030, USA.

OSUK Annual Congress

The Annual Congress of the Ophthalmological Society of the United Kingdom will be held on 17–19 April 1985 at the Harrogate Conference Centre, Harrogate, North Yorkshire. Details from Miss M. Hallendorff, Royal College of Surgeons, Lincolns Inn Fields, London WC2A 3PN.