cytotoxic drugs, just when the risk of emesis is highest.[5] Conversely, in the placebo group antiemetic drug concentrations would have been lower during the period of maximum risk of emesis and approaching a steady state only the next day. Other drugs likely to accumulate during pretreatment may also be suitable, and their pharmacokinetics should be studied.

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Lack of effect of acyclovir on postherpetic neuralgia

M W McKendrick, J I McGill, M J Wood

Department of Medicine and Communicable Diseases, Lodge Moor Hospital, Sheffield S10 4LH
M W McKendrick, MRCP, *consultant physician*

Southampton Eye Hospital, Southampton SO9 4SW
J I McGill, FRCS, *consultant ophthalmologist*

Department of Communicable and Tropical Diseases, East Birmingham Hospital, Birmingham B9 5ST
M J Wood, FRCP, *consultant physician*

Correspondence to: Dr McKendrick.

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In 1986 we reported that in 209 elderly immunocompetent patients with herpes zoster oral acyclovir (800 mg five times daily for seven days) significantly accelerated the rate of resolution of the rash and reduced the acute pain.[1] The reduction in pain did not, however, seem to continue for more than a few days after the treatment was stopped. Altogether 376 patients were ultimately enrolled in that trial, and we report here the effect of acyclovir on postherpetic neuralgia.

Patients, methods, and results

This randomised, double blind, placebo controlled domiciliary based study was conducted in Sheffield, Birmingham, and Southampton. All 376 patients were aged 60 or over and were entered into the trial within 72 hours after the onset of the rash. They were given placebo or oral acyclovir 800 mg five times daily for seven days. Patients were seen 28 days after entry and at monthly intervals thereafter until six months or they were pain free, whichever occurred sooner. At each visit the patient was asked about pain in the previous four weeks. The severity of pain was recorded on a visual analogue scale of 0-100 ranging from "none" to "very severe." For the purposes of analysis this was converted to nil=0, 1-24=1, 25-75=2, and 76-100=3.

Data on 364 patients (181 taking acyclovir and 183 taking placebo) were suitable for analysis (177 from Sheffield, 113 from Birmingham, 74 from Southampton). The groups were comparable for demographic variables.

There was no evidence of any effect of acyclovir on the incidence or severity of postherpetic neuralgia during the six months of follow up (table). Further analysis of the data according to severity of pain at onset, the interval between the onset of the rash and the start of treatment (<48 hours or 48-72 hours), and age (60-69 and ≥70) failed to identify any subgroup in which acyclovir had an effect. In the placebo group the incidence and severity of postherpetic neuralgia decreased steadily during follow up. One month after the onset of the rash 110 out of 180 (61%) patients still had some pain, but this proportion had fallen to 38 out of 156 (24%) by three months and to 20 out of 155 (13%) at six months.

Comment

In the first 209 patients studied oral acyclovir given as treatment for herpes zoster significantly reduced pain and analysis of the data on the total population recruited confirmed these findings.[2] There was, however, no evidence of a reduction in the incidence or severity of postherpetic neuralgia. This was not altogether unexpected as analysis of data from the acute phase did not show any difference in mean pain scores of patients taking acyclovir and placebo beyond 21 days,[1] and five days of treatment with intravenous acyclovir did not affect the incidence of postherpetic neuralgia. Would a longer duration of antiviral treatment have a more protracted effect on the pain? An American study of oral acyclovir in acute herpes zoster showed that a 10 day course at a daily dose similar to the one we used significantly reduced postherpetic neuralgia, particularly the chronic type of pain.[3] Further studies of longer courses of acyclovir are needed.

In this study the incidence of postherpetic neuralgia in the placebo group was surprisingly low (13% at six months), given that only people aged 60 or over were enrolled into the trial. The risk of this complication rises greatly with increasing age, and reports have quoted rates as high as 30-40% for patients over 60.[4,5] Our study was, probably, the largest prospective study of elderly patients with herpes zoster, and we believe that it more accurately reflects the true incidence of postherpetic neuralgia.

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Distribution of pain scores over six months for patients with postherpetic neuralgia treated with acyclovir or placebo. Figures are numbers (percentages) of patients

	Month 1		Month 2		Month 3		Month 4		Month 5		Month 6	
Pain score	Acyclovir (n=178)	Placebo (n=180)	Acyclovir (n=166)	Placebo (n=169)	Acyclovir (n=161)	Placebo (n=156)	Acyclovir (n=157)	Placebo (n=149)	Acyclovir (n=160)	Placebo (n=156)	Acyclovir (n=162)	Placebo (n=155)
0	67 (38)	70 (39)	102 (61)	99 (59)	122 (76)	118 (76)	131 (83)	123 (83)	134 (84)	130 (83)	140 (86)	135 (87)
1	60 (34)	63 (35)	33 (20)	35 (21)	19 (12)	23 (15)	12 (8)	16 (11)	17 (11)	17 (11)	13 (8)	13 (8)
2	44 (25)	35 (19)	25 (15)	30 (18)	16 (10)	12 (8)	12 (8)	8 (5)	7 (4)	7 (4)	6 (4)	6 (4)
3	7 (4)	12 (7)	6 (4)	5 (3)	4 (2)	3 (2)	2 (1)	2 (1)	2 (1)	2 (1)	3 (2)	1 (1)
p Value	0·78		0·60		0·91		0·91		0·92		0·83	