Oral acyclovir in first 72 hours may reduce pain of post herpetic neuralgia

Jackson J L, Gibbons R, Meyer G, Inouyer L. The effect of treating Herpes zoster with oral acyclovir in preventing post herpetic neuralgia. A meta-analysis. Arch Intern Med 1997; 157: 909–912

Objective To test the hypothesis that treatment with oral acyclovir reduces the incidence of Post-herpetic neuralgia.

Data sources A medline search of English language papers from 1966–1996 (MeSH terms 'acyclovir', 'herpes zoster' and 'randomised clinical trials'). Additional references were identified from references retrieved and the National Institute of Heath database of funded studies and Cochrane database of Randomised Controlled trials were searched for published and unpublished data.

Study selection 30 studies were originally identifies and articles were assessed blind by two of the authors using predefined criteria. 25 were excluded because of use of intravenous or topical acyclovir (7), duplicate data (8) lack of placebo group or randomisation (4) sub-optimal oral dosage (5) and late commencement of treatment (1).

Data extraction and synthesis Data from the five studies was pooled and the odds ratios calculated for the incidence of 'any pain' at 6 months.

Results The odds ratio for incidence of any pain at six months was 0.54 (95% CI 0.36–0.81). This translates to a number needed to treat to prevent one case of 6.3.

Conclusions This meta-analysis suggests that patients treated within 72 hours of rash onset may experience a 46% reduction in the incidence of pain in the distribution of the rash at 6 months in immunocompetent adults.

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Commentary

In several randomised clinical trials, the effect of treating Herpes zoster with oral acyclovir in preventing postherpetic neuralgia remains uncertain because of conflicting results. There have been numerous critical reviews of the literature. Schmader and Studeoski[1] found no benefits with acyclovir and Lancaster *et al.*[2] concluded in their review that firm recommendations for clinical practice are not possible because existing evidence neither confirms nor refutes the hypothesis that treatment during the acute phase of Herpes zoster reduces pain later. The authors of this present paper have conducted a meta-analysis of published randomised clinical trials on the use of acyclovir to prevent postherpetic neuralgia using the fixed-effects model. The meta-analysis were used to test the hypothesis that treatment with oral acyclovir reduces the incidence of postherpetic neuralgia. Originally the authors identified 30 scientific articles. Of these only 5 were included for further analysis. The authors concluded based on this meta-analysis, that treatment of herpes zoster with 800 mg/d of oral acyclovir within 72 hours of rash onset may reduce the incidence of residual pain at 6 months by 46% in immunocompetent adults.

However, meta-analysis is only useful when intervention and outcomes are similar across a number of studies. In the present paper only 5 clinical trials could be included for meta-analysis. It thus demonstrates an extensive variation in design for different clinical studies. Performing a meta-analysis on clinical trials involving acyclovir, postherpetic neuralgia and Herpes zoster will demonstrate several difficulties regarding the inclusion of acceptable trials. A universally accepted definition of postherpetic neuralgia is lacking, furthermore it will be observed that individual investigators report the prevalence of pain at different points in the course of the illness and data are not available at comparable time points. The measurement of pain, a subjective concept, is not standardised across different studies.

Further research and more standardised studies are necessary before recommendations for clinical practice can be given. Individual clinicians trying to decide how to treat Herpes zoster must exercise their judgement, weighing factors such as toxicity and cost in their decision. However, it may be reasonable to offer antiviral therapy to patients with severe pain not controlled with analgesics, or to patients considered to be at high risk of postherpetic neuralgia.

1 Schmader K E, Studenski S. Are current therapies useful for the prevention of postherpetic neuralgia? *J Gen Intern Med* 1989; **4**: 83–89.

2 Lancaster T E, Silgay C, Gray S. Primary care management of acute Herpes zoster. A systematic review of evidence from randomised controlled trials. *Br J Gen Pract* 1995; **45**: 39–45.

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