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Acyclovir in recurrent herpes labialis

Justified as oral prophylaxis only in severely affected people

Recurrent herpes labialis is one of the most common skin complaints general practitioners see; in his meticulous record of all patients seen in his NHS practice Hodgkin estimated the incidence to be about 10 cases per 1000 patients seen per year.[1]

After the initial attack of herpes labialis, herpes simplex virus type 1 is thought to remain latent in the trigeminal ganglion and to be reactivated by various types of stress.[2] Although things such as fever, upper respiratory tract infections, ultraviolet light, and psychological stress are thought to trigger recurrence, the condition is variable and unpredictable in most patients, as is the extent and duration of each attack.[3] Recurrent attacks are usually shorter and less painful than the original attack.

The discovery of acyclovir seemed to offer great promise in the treatment of herpes labialis. Acyclovir acts as a substrate for the thymidine kinase enzyme of the herpes virus and thus selectively inhibits viral replication. It was found to be effective in suppressing recurrent herpes labialis in immunocompromised patients[4]; however, in non-immunocompromised people it was more effective against herpes genitalis (due to herpes simplex virus type 2)[5] than herpes labialis, which is typically caused by herpes simplex virus type 1.[6]

General practitioners rarely see patients during a first attack of herpes labialis. They are usually faced with patients who have had several previous attacks, most of whom will visit them only after an attack has started. The question confronting general practitioners is whether to prescribe topical acyclovir cream.

A systematic review of the evidence in 1991 showed that topical treatment was not efficacious in the acute phase of recurrent herpes labialis, [7] and a randomised controlled trial in the same year found that it was hardly any better when used prophylactically.[8] In this trial, oral acyclovir used in the acute phase was also of marginal benefit; it had no effect if treatment was started after the skin lesions had appeared.[8] A randomised double blind, placebo controlled trial showed that if patients started taking oral acyclovir during the prodromal period it reduced the duration of pain by a mean of 1.4 days and the time to crusting of the lesion by 2·1 days.[9]

A review of seven trials (five of them randomised controlled trials) of prophylactic oral acyclovir in recurrent herpes labialis showed that the drug reduced the occurrence of new lesions by 50% to 78%.[10] Several of these trials can be criticised on methodological grounds: they were not blind; their applicability to community acquired infection may be doubted because some trials studied lesions that were experimentally induced by surgery or by artificial ultraviolet light; some of them had a high drop out rate; and they were mostly done in academic centres, where patients are likely to differ from patients in family practice both in the frequency and the severity of their attacks. None the less, oral acyclovir, if taken in the correct dose of between 600-1000 mg per day in two doses, does seem to reduce the frequency and severity of attacks. In one crossover trial, the mean time to recurrence rose from 46 to 118 days and the mean number of recurrences in the four months during which acyclovir was taken dropped from 1·80 to 0·85 attacks.[11]

Evidence is accumulating that herpes labialis lesions may be of two types. When attacks of recurrent herpes labialis are induced by ultraviolet light "immediate" lesions develop within 48 hours, while "delayed" lesions occur after three to seven days. The immediate lesions may arise through activation of herpes viruses that are latent in the skin around the mouth and in the ganglion of the trigeminal nerve.[12] The immediate lesions comprise up to one third of all lesions, and they do not seem to be responsive to acyclovir. On the other hand, the delayed lesions seem to be prevented by prophylactic oral acyclovir.[10]

The cost of oral acyclovir and its low efficacy in recurrent herpes labialis make it inappropriate for most non-immunocompromised patients in the community. However, there is moderately good evidence that prophylactic oral acyclovir is of some benefit in preventing recurrence. This should therefore be considered in patients whose attacks are sufficiently frequent, prolonged, severe, and psychologically distressing. Short term prophylaxis may also be offered to the few patients whose attacks of herpes labialis have been clearly linked to a recurrent and unavoidable precipitating factor.

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