Local idoxuridine treatment of herpes simplex and zoster

The clinical manifestations of herpes simplex and zoster have been well described by Juel-Jensen & MacCallum (1972). Most would agree that recurrent herpes simplex, zoster pain, and postherpetic neuralgia can on occasions be most unpleasant, and effective prophylaxis and treatment should be the aim. Many non-specific remedies had been tried before a specific anti-viral agent, 5-ido-2'-deoxyuridine (idoxuridine, IDU) appeared. IDU is a thymidine analogue which is incorporated into the DNA of the virus and stops its multiplication. However, use of topical idoxuridine for herpes simplex and zoster remains controversial. Some consider it useless, others believe it unnecessary, and yet others like myself, are convinced of its effectiveness, but appreciate that it may fail in an individual patient. There are still some who may not deny its effectiveness but state that it is too expensive to use. The current hospital cost of IDU is £4-10/gm or less, provided that it is bought in bulk. In my view expense is exaggerated and in any case is relative, if for instance IDU used in the elderly zoster patient, can prevent severe postherpetic neuralgia. Controversy also exists regarding the concentration of IDU to use and the highest concentration commercially available is 5%. IDU is likely to incorporate into the DNA of rapidly dividing cells so it should be used with caution in pregnancy and probably not at all in early pregnancy (Juel-Jensen & MacCallum, 1972).

One factor that accounts for treatment failure, is that IDU is very insoluble in most solvents and when topically applied in aqueous solution or in an ointment is inactive except in the eye and within the mouth; it does not penetrate the skin (Burnett & Katz, 1963, Juel-Jensen & MacCallum 1964) except perhaps the thin skin of the genitalia (Juel-Jensen & MacCallum, 1972). Systemic use of IDU is without benefit and gives rise to severe side effects. The problem of insolubility of IDU in topical use was overcome by dissolving it in a powerful solvent, dimethyl sulphoxide (DMSO). DMSO is bacteriostatic but is also a primary irritant producing skin maceration with prolonged treatment. It may also produce a transient wealing due to histamine release. It must be used in purified undiluted form and has not been shown to have toxic effects in man (Juel-Jensen & MacCallum, 1972). After applying DMSO to the skin some patients may find that their breath has a garlic smell due to the allcin exhaled. DMSO is such a powerful solvent, dimethyl sulphoxide (DMSO). DMSO is bacteriostatic but is also a primary irritant producing skin maceration with prolonged treatment. It may also produce a transient wealing due to histamine release. It must be used in purified undiluted form and has not been shown to have toxic effects in man (Juel-Jensen & MacCallum, 1972). After applying DMSO to the skin some patients may find that their breath has a garlic smell due to the allcin exhaled. DMSO is such a powerful solvent that it may fail in an individual patient. There are still some who may not deny its effectiveness but state that it is too expensive to use. The current hospital cost of IDU is £4-10/gm or less, provided that it is bought in bulk. In my view expense is exaggerated and in any case is relative, if for instance IDU used in the elderly zoster patient, can prevent severe postherpetic neuralgia. Controversy also exists regarding the concentration of IDU to use and the highest concentration commercially available is 5%. IDU is likely to incorporate into the DNA of rapidly dividing cells so it should be used with caution in pregnancy and probably not at all in early pregnancy (Juel-Jensen & MacCallum, 1972).

Longson (1978) has suggested that by the age of 35 years, 90% of the general population especially in urban communities, will have been infected by herpes virus simplex (HSV) and thereafter 50% of affected subjects will experience recurrent episodes, characterized by repeated recrudescences of circumscribed areas of herpetic vesiculation around the mouth or genitalia, or on the cornea or elsewhere on the skin. The primary disease which usually occurs in childhood is mild or even sub-clinical in the majority of cases and is caused by transmission of virus from an already infected human whilst the source of virus in recurrent herpetic disease is almost certainly endogenous to the patient.

For HSV superficial corneal infections idoxuridine is effective (Ashton et al., 1971). It is applied as a 0.1% aqueous solution (Dendrid, Kerecid, Ophthalmadine) or as a 0.5% ointment (Kerecid, Ophthalmadine).

There is no doubt that many patients with primary herpetic gingivostomatitis require no treatment or just a bland mouth wash. However, if the condition is extensive severe and distressing and topical IDU indicated. Lehner (1978) recommends 0.1% aqueous solution applied to lesions with a brush or cotton wool, hourly if possible on the first day, and then
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application, with rapid reduction of pain and infection responds well to 5% IDU in DMSO sores'. In my experience widespread skin HSV should keep away from individuals with 'cold sores'. Verbov (1971) confirmed this, finding that 5% IDU in DMSO hastened resolution of lesions and in many patients either decreased the likelihood or reduced the severity of a further attack in the skin area treated. Early application to intact blisters only, was essential; application to dried lesions was a waste of time and money. The solution was applied with a small brush 4 to 5 times daily.

Some patients with erythema multiforme provoked by recurrent HSV lesions benefit from 40% IDU in DMSO according to Juel-Jensen & MacCallum (1972) but I have not found the 5% preparation applied to HSV lesions to be effective in preventing erythema multiforme appearing.

For herpetic whitlow, a primary form of HSV infection, Juel-Jensen & MacCallum (1972) recommend continuous application of 40% IDU in DMSO. Lint wetted with the solution should cover the finger and the lint is rewetted twice daily. Treatment is continued until HSV can no longer be recovered from the lesion. There is rapid disappearance of pain with early treatment and there is a good chance that cure can be achieved without relapse. Fortunately eczema herpeticum is uncommon but it is important to emphasize that those with active or latent atopic eczema and some other skin diseases (Verbov et al., 1972) should keep away from individuals with 'cold sores'. In my experience widespread skin HSV infection responds well to 5% IDU in DMSO application, with rapid reduction of pain and early drying of lesions. Eczema herpeticum is usually a manifestation of primary herpes infection and it is the young who are particularly affected.

A recent answer to a question in the British Medical Journal (1977) regarding treatment of genital herpes mentioned IDU as being dis-

six times daily for the next four days. I usually prescribe the 0.1% solution as a mouth wash three times daily, held in the mouth for about ten minutes and then spat out. 0.1% IDU in Orabase ointment (sod. carboxymethylcellu-

lose, pectin and gelatin, in Plastibase) will adhere to ulcers, and also reduces discomfort. MacCallum & Juel-Jensen (1966) showed in a double blind trial that a 5% solution of IDU in DMSO [now prescribable as Herpid solution (5 ml)] was effective in recurrent herpes simplex of the face when given early in the eruption. Verbov (1971) confirmed this, finding that 5% IDU in DMSO hastened resolution of lesions and in many patients either decreased the likelihood or reduced the severity of a further attack in the skin area treated. Early application to intact blisters only, was essential; application to dried lesions was a waste of time and money. The solution was applied with a small brush 4 to 5 times daily.

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without any specific treatment there is a good prognosis in many cases with attacks becoming progressively less frequent and less severe and often ceasing after a few years. That perhaps is a reasonable argument for no treatment in some cases. Thin (1978) moreover, mentioned the practical point that if genital lesions are not complicated by secondary infection, healing will occur in about 10 days if lesions are simply kept clean. He mentioned IDU both as a 0.5% ointment and as 5% IDU in DMSO but quotes the latter as being too painful to apply and expensive. He considered that there is no convincing evidence of therapeu-

tic benefit with higher concentrations of IDU in genital herpes. However, McKenzie & Wilkinson (1977) found IDU in DMSO valuable in genital herpes and Juel-Jensen (1976) advocated treatment of recurrent genital HSV with a 35% solution of IDU in DMSO applied about five times a day for not more than three days; he mentioned that he had been unable to grow virus from lesions after 48 h. With this therapy the duration of the lesion was cut significantly and the interval between recurrences becomes longer and recurrences may cease. I have not exceeded a concentration of 5% IDU in DMSO for penile and vulval herpes and although painful application has not been a problem I have not been impressed with results. This may be explained by the fact that Type 2 HSV is more resistant to IDU that is Type 1 (Juel-Jensen, 1973).

Dawber (1977) believes that all cases of zoster merit treatment not only to relieve pain but also to minimize or prevent scarring and post-herpetic neuralgia. He found in a double blind trial (Dawber, 1974) that intermittent application of 5% IDU in DMSO (using a brush) had as great an effect as 25% IDU in DMSO and was in turn more effective than a 5% solution of IDU in DMSO according to Juel-Jensen, 1973. Simpson (1975) showed that both 5% and 40% IDU in DMSO produced equal benefit. Juel-Jensen & MacCallum (1974) however, found continuous application of 35% IDU in DMSO to be more effective than 20% which was in turn more effective than a 5% solution. If continuous topical application of IDU in DMSO is employed lint is wetted with the antiviral solution, covered with layers of dry lint and then held in place with tubular gauze. The lint is not allowed to dry but is rewetted daily or twice daily and treatment continued for 3 days, or less if the blisters dry earlier; pain usually subsides within 48 hours of commencing treatment. Apart from relieving pain it often prevents post-herpetic

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neuralgia which can be very severe and very difficult to treat in the over-60 age group. One cannot predict which patient will get severe post-herpetic neuralgia therefore early use of 5% IDU in DMSO is indicated in the elderly patient. It has to be applied with care so that a relative or a district nurse is often essential for correct application. In many attacks of zoster only few groups of blisters are present so that large amounts of IDU in DMSO are often in practice unnecessary. 35% IDU in DMSO should probably be reserved for the older hospitalized patient in much pain with extensive zoster.

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References