SHORT REPORTS

Oral (E)-5-(2-bromovinyl)-2'-deoxyuridine in severe herpes zoster

(*E*)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU) is a nucleoside analogue that inhibits the replication of herpes simplex virus type 1 (HSV-1) in cell culture (primary rabbit kidney) at a concentration of 0·01 mg/l, but does not affect normal cell metabolism at concentrations up to 100 mg/l.[1] BVDU has also been found effective in the local and systemic treatment of HSV-1 skin lesions, and its associated mortality, in athymic nude mice[1] and in the local treatment of HSV-1 keratitis in rabbits.[2] The compound is readily absorbed when given orally to mice[3] or rabbits. BVDU doses of 500-1000 mg/kg body weight/day are well tolerated by mice, even if administered over 20 days.[4]

Recently we have found that BVDU is also highly active against varicella zoster virus, inhibiting the cytopathogenicity of this virus in human skin fibroblast cultures at a minimum concentration of 0·004 to 0·04 mg/l. We now report on a clinical study with oral BVDU in the treatment of four patients with severe localised or disseminated herpes zoster.

Clinical details of four patients with herpes zoster given oral BVDU

Case No	Age (years)	Sex	Location of lesions	Duration of lesions before treatment (days)	Underlying disorder	Other antiviral treatment
1	47	F	Thoracic	2	Metastatic breast carcinoma	None
2	54	M	Thoracic	6	Non-Hodgkin's lymphoma	Zoster immune globulin
			Disseminated	2		
3	60	F	Cervical	2	Metastatic breast carcinoma	None
4	68	F	Ophthalmic	5	Hyperthyroidism	BVDU eye drops (0·1%)
			Disseminated	0·5		

Case reports

All four patients that were treated with BVDU (table) had severe localised or disseminated herpes zoster lesions, and three out of the four had a malignant disorder for which they had been given intensive chemotherapy.

BVDU was administered by mouth at 7·5 mg/kg body weight/day (three or four capsules of 125 mg BVDU daily, eight or six hourly) for five days. Informed consent was obtained from all patients. The patients were examined daily during treatment and at regular intervals afterwards. Complete blood count; urea, creatinine, and electrolyte concentrations; and activities of liver enzymes (aspartate transaminase, alanine transaminase, and γ-glutamic transpeptidase) were measured at the first, third, and fifth day of treatment. Drug concentrations in serum and urine were measured by bioassay, based on the inhibition of HSV-1 cytopathogenicity in cell culture.[3]

In all four patients progression of vesicle formation was completely arrested within 24 hours of starting treatment with BVDU: no new lesions developed during treatment, and the lesions which had developed before treatment healed briskly. For those patients (cases two and four) who presented with dissemination of the herpes zoster lesions, the prompt response to treatment was also reflected by a dramatic improvement in their general condition: fever resolved within 24 hours of starting treatment with BVDU. In case 4, where dissemination had occurred just before treatment, the newly formed lesions disappeared completely within two days of treatment. None of the patients who were treated with BVDU experienced any discomfort or showed any signs of drug toxicity. The biochemical and haematological blood values remained unchanged during the observation period. Plasma and urine concentrations of BVDU were measured in cases 1 and 3; the serum drug concentrations varied from 1 to 1·5 mg/l from one to three hours after BVDU administration. This concentration is about 100 times higher than the minimum effective dose required to inhibit VZV replication in cell culture. The urine drug concentrations were 10-15 mg/l throughout, 10 times higher than the serum drug concentrations, which suggests that BVDU is actively excreted by the kidney.

Comment

Oral treatment with BVDU caused prompt recovery of patients with severe herpes zoster. Existing lesions regressed within the first few days after the start of BVDU treatment, and no new lesions developed while the patients were taking BVDU. There was no evidence of drug toxicity in bone marrow, liver, kidney, or any other organ. The beneficial effects obtained with BVDU in the systemic treatment of herpes zoster are reminiscent of those reported with acyclovir.[5]

A practical advantage of BVDU is that it can be administered orally apparently with high efficacy. The clinical value of BVDU as a systemic anti-herpes agent has to be confirmed by carefully controlled studies. Our preliminary results should provide the necessary impetus for such studies.

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Voluntary chlorine inhalation: A new form of self-abuse?

In many forms of self-abuse noxious substances are inhaled. Although accidental exposure to chlorine gas from mixing household cleaning agents has been reported,[1] this patient inhaled chlorine for pleasure.

Case report

In November 1978 a 41-year-old electrician began mixing Vim and Ajax cleaning powders with water and sniffing the fumes released. He would occasionally heat the mixture to produce more fumes and would also smear the mixture over his arms. He was referred to the outpatient department in March 1979 with a six-week history of headache, sore eyes, swollen legs, and lethargy. He had no history of psychiatric illness or other forms of self-abuse, though he did smoke 20 cigarettes a day.

He had severe conjunctival injection, central cyanosis, a raised jugular venous pressure, gross oedema, and ascites. The heart was enlarged, the pulmonary second sound accentuated, and a third heart sound was audible.