ORAL BROMOVINYLDEOXYURIDINE TREATMENT OF HERPES ZOSTER OPHTHALMICUS

P.C. MAUDGAL¹, M. DIELTIENS¹, E. DE CLERCQ² and L. MISSOTTEN¹

¹Eye Research Laboratory of the Ophthalmology Clinic, and ²Rega Institute for Medical Research, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium.

1. INTRODUCTION

Bromovinyldeoxyuridine [(E)-5-(2-bromovinyl)-2'-deoxyuridine, BVDU] is a highly potent and selective antiviral agent that inhibits the replication of herpes simplex virus type I (HSV-1) (1-3) and varicella-zoster virus (VZV) (4,5) at a very low concentration (0.002 - 0.01 µg/ml), while 5,000 to 10,000-fold higher concentrations are needed to affect normal cell metabolism.

When applied to rabbit eyes as either eye ointment or eyedrops, BVDU is superior to 5-iodo-2'-deoxyuridine (IDU) in suppressing the development of HSV-1 keratitis, and in promoting the healing of established epithelial disease (6,7). BVDU is also superior to 1% TFT eyedrops in the treatment of stromal keratitis produced by intrastromal inoculation of HSV-1 (8), and keratouveitis caused by inoculation of HSV-1 into the anterior chamber (9). Oral administration of BVDU to rabbits at 10 mg/kg/day or 100 mg/kg/day also promotes healing of keratouveitis (9). BVDU eyedrops have been found efficacious in the treatment of corneal dendritic or geographic ulcers and stromal keratitis (10-12).

Efficacy of oral BVDU therapy has been demonstrated in the treatment of severe herpes zoster in cancer patients, and herpes zoster ophthalmicus with or without involvement of the ocular tissue (13-15). In this paper we report on the results obtained in 15 herpes zoster ophthalmicus patients who were treated with oral BVDU combined with topical 0.1% BVDU eyedrops.

2. SUBJECTS AND METHODS

Seven male and eight female patients who presented with typical symptoms of herpes zoster ophthalmicus were admitted to the study. Except for one young patient (age: 31 years), other patients were either elderly (12 patients) or middle-aged (2 patients). Skin eruption consisted of papules,
vesicles, bullae with or without hemorrhage, necrotic lesions, and sometimes crusts on the scalp, forehead, temporal region, nose, cheek and periorbital skin. One patient had disseminated skin lesions. All subjects had experienced prodromal symptoms in the involved dermatome before skin lesions appeared. The lesions themselves had been present for an average time of 5.6 days when the patients presented to us. All patients complained of severe neuralgic pain in the involved dermatome. Various associated systemic disorders were present in 11 patients, i.e. hyperthyroidism, hypothyroidism after partial thyroidectomy, angina pectoris, old myocardial infarction, liver cirrhosis, gallstones, rheumatism, Reiters disease, diabetes mellitus, asthma and recurrent epididymitis.

Lesions of periorbital skin or ulcerative blepharitis were noted in 13 patients. Ptosis of the upper eyelid was present in 2 patients, one of them having total ophthalmoplegia. Two patients had mild conjunctivitis whereas all others had marked conjunctivitis and chemosis. Two patients had corneal ulcers. Dendritic keratitis was observed in 2 other cases, and 5 patients had diffuse punctate keratitis. Stromal edema or infiltrates were noted in 3 patients. Aqueous flare was present in 7 eyes, two of these also having keratic precipitates. Associated ocular diseases were lid lag of the other eye (hyperthyroidism), absent eye movements and pupillary reaction (total ophthalmoplegia), limited elevation (superior rectus palsy), vitreous hemorrhage in the fellow eye, diabetic cataract and retinitis pigmentosa.

All patients were hospitalized and informed consent was obtained for BVDU treatment. BVDU 125 mg capsules were administered orally at 8 hour intervals (375 mg/day) for 5 days. Hospitalized patients were examined daily and at regular intervals thereafter. Routine blood and urine tests as well as urea, creatinine, platelets, electrolytes and liver enzymes (SGPT, SGOT, γGT) measurements were done before, during and after BVDU therapy. Drug levels in blood and urine were determined by a bio-assay based on the inhibition of HSV-1 cytopathogenicity in cell cultures. All patients also received topical 0.1 % BVDU eyedrops administered hourly during the day only. Patients who developed corneal edema due to endothelium damage were also given topical corticosteroids.