Drug Update

DRUG THERAPY OF CYTOMEGALOVIRUS INFECTIONS

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Introduction

There is a dearth of chemotherapeutic agents for treatment of Cytomegalovirus (CMV) infections. The number of CMV infections is on the rise concurrent with increase in number of HIV infected persons and patients with other immunocompromised states. Ganciclovir was the first drug found effective in this disease [1].

Ganciclovir

Ganciclovir is an analogue of 2'-deoxyguanosine and is a homologue of acyclovir. It terminates chain elongation of viral DNA and inhibits viral DNA polymerase.

Ganciclovir has a low oral bioavailability (3.0-4.6%). Intravenously administered drug has a half-life of 2.9 - 4 h and a peak serum concentration of 8.3 mg/mL. It crosses the blood brain barrier and is excreted by the kidney unchanged. Oral administration of 1000 mg of ganciclovir thrice daily achieves a peak serum concentration of 1.2 mg/mL which is close to the ED50 of most isolates of CMV [3].

Approximately one third of patients experience side effects [2]. Granulocytopenia (13%) occurs usually in the 1st or 2nd week. Other side effects are thrombocytopenia, neurological side effects, nausea, fever and skin rash, vomiting, diarrhoea and anemia. Ganciclovir is not to be administered in presence of low counts of neutrophils and platelets. It is to be avoided in pregnancy, nursing mothers and children.

Foscarnet Sodium

It is a analogue of phosphonoacetic acid with activity against herpes virus. It inhibits the DNA

polymerases of all human herpes virus. It is active against resistant herpesvirus mutants that are deficient in thymidine kinase. Only 12-22 per cent of orally administered drug is absorbed and serum concentrations are too low to inhibit either CMV or HIV [4].

The adverse effects of this drug are fever, nausea, diarrhoea, abnormal renal functions and rarely anemia and granulocytopenia. Safety in pregnancy and in children is not known [5].

Clinical Application

CMV retinitis is a sight threatening infection in 26 per cent of AIDS patients. Treatment with ganciclovir in doses of 5 mg/kg 12 hourly IV for 14 days stabilises retinal lesions with complete response in one month in many patients. Intraocular sustained release implants and intravitreal injections of ganciclovir have also been found effective [6]. Foscarnet is used in treatment of CMV retinitis in dosage of 60 mg/kg 8 hourly for 2-3 weeks followed by 60-120 mg/kg daily as maintenance therapy [4]. Recent studies have shown a combination of ganciclovir and foscarnet to be superior to ganciclovir alone [7].

IV ganciclovir in doses of 5 mg/kg 12 hourly for 3 weeks is the present recommendation for gastrointestinal manifestations of CMV. The treatment of primary CMV pneumonia with ganciclovir is most successful in renal transplant recipients [8]. However in bone marrow transplant recipients it is not as effective.

CMV is implicated in about 25 per cent of AIDS related encephalopathies [9,10]. These patients have a median survival of only 1-2 months. Ganciclovir given in a dose of 5 mg/kg per day for

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7 days is said to prolong survival. Foscarnet can be given in dose of 60 mg/kg thrice a day followed by 90 mg/kg once daily and in severe infections a combination of the two drugs may be tried [9].

In vitro, foscarnet has shown synergistic action with zidovudine against HIV infection. Oral ganciclovir prevents CMV disease and prolongs survival in patients of AIDS with CD4 count <100/cmm [11]. In patients who are recipients of bone marrow, cardiac or liver transplantation, IV ganciclovir has been clearly shown to be effective in prevention of CMV disease [12].

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Drug Toxicity/Accident Bulletin

STOMACH PERFORATION BY A BLISTER-WRAPPED CAPSULE

A recent report describes a 63-year-old woman who developed perforation of stomach following ingestion of a blister-wrapped capsule of acetaminophen (paracetamol) [1]. She was admitted to hospital for treatment of depression and was prescribed oral lorazepam, paroxetine, buspirone, cyamemazine and ranitidine. On the 3rd day she developed vomiting, headache, pain abdomen, tachycardia and hypertension. She was treated with oral nifedipine. Next day she developed profound hypotension, diaphoresis with increasing severity of pain abdomen. Cardiac evaluation and endoscopy revealed no abnormality. CT scan re-

vealed a perihepatic haematoma, a splenic wound and haemoperitoneum. Laparoscopy showed perforation of stomach by the sharp edge of a blister-wrapped capsule of acetaminophen. History taken subsequently confirmed the prescription of acetaminophen "as needed" for toothache. Perforation of the gut in this manner is uncommon and can be avoided or diagnosed if the possibility is kept in mind.

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