Reprinted from transplantation
Volume 46, Number 4, October 1988

EFFECT OF 9-(2-HYDROXY-1-[HYDROXYMETHYL] ETHOXYMETHYL) GUANINE (DHPG) ON CYTOMEGALOVIRUS PNEUMONITIS AFTER RENAL TRANSPLANTATION

Cytomegalovirus pneumonitis remains a common cause of death in renal transplant patients with a reported case fatality of 48% (rising to over 90% if assisted ventilation is required) (*1*). Up to now, no antiviral agent (*2, 3*) has been shown to be effective against overt CMV infections, but 9-(2-hydroxy-1] hydroxymethyl] ethoxymethyl) guanine (DHPG)* (Ganciclovir, Wellcome, Belgium), a new analogue of acyclovir, has been demonstrated to be 100–fold more active in vitro against CMV than acyclovir. However, DHPG seemed to be poorly effective in the treatment of CMV pneumonitis in bone marrow transplant recipients (*4*). In renal transplantation, one case of CMV pneumonitis successfully treated by DHPG has been recently reported (*5*).

We report here 7 recipients of a renal transplant (combined with a pancreatic transplant in one of them) in whom CMV pneumonitis was treated with DHPG. CMV pneumonitis was defined by the existence of a bilateral interstitial pneumonitis associated with CMV isolation in the bronchoalveolar fluid (in 6/6 tested cases) and/or a 4-fold rise in both CMV complement fixation and ELISA test titers (in 6/7 cases). DHPG was given i.v. at a dosage of 2.5 mg/kg 8-hourly (1.5 mg/kg 8-hourly if the creatinine clearance was below 50 ml/min) for 10 (patients 4, 5, and 5 [twice]) or 20 days. DHPG was started in 4 patients (patients 3, 4, 5, and 7) before virologic confirmation of the diagnosis. CMV pneumonia appeared 25 to 74 (mean 55) days after transplantation; 4 infections were primary and 3 were reactivated forms.

In patient 1, DHPG was started 5 days after the appearance of interstitial infiltrate on chest roentgenogram. Despite DHPG, ventilation was required 2 days later. The patient died of respiratory failure 8 days after starting DHPG without having experienced defervescence.

By contrast, a favorable course was observed in the 6 other patients. Patient 2 was already being ventilated before DHPG, whereas patients 3 and 6 required transient pulmonary assistance after the start of DHPG, but their respiratory condition subsequently improved, allowing respirator withdrawal after 5–10 days. Immunosuppressive therapy (combining cyclosporine-azathioprine and prednisone) was continued in the 6 patients, and graft function remained stable in all of them. DHPG therapy was not associated with detectable side-effects. Chest roentgenogram normalization was observed in all but one patient at discharge. In one case (patient 5) CMV pneumonitis recurred 25 days after a 10-day course of DHPG and responded to a second course of the drug. Currently, the 6 patients are well 5–10 weeks after DHPG treatment.

This preliminary experience shows that DHPG is an effective treatment of CMV pneumonitis after renal transplantation. Moreover, our results suggest that DHPG therapy should be initiated very early to be successful. Indeed, the only death occurred in the patient with the longest time between the first signs of intertitial pneumonitis and DHPG initiation. The other patient in whom DHPG was started more than 2 days after the pneumonitis (patient 2) has not completely recovered, as chest roentgenograms and CO-diffusing capacity are consistent with a secondary pulmonary fibrosis. We thus recommend starting DHPG at the first clinical suspicion of intertitial pneumonitis without waiting for virologic confirmation. The development of new diagnostic methods (such as detection of early antigen fluorescent foci [*6*]) should allow appreciable progress toward early diagnosis. Finally, our results suggest that a 20-day course should be preferred to a 10-day course, as our single case of recurrence occurred in one of the two patients treated for 10 days.

Acknowledgments. We thank Mrs. M. Sels (Wellcome Belgium), Dr. C. Van Hoecke (Wellcome Belgium), and Mrs. P. Segers.

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TABLE 1. Patient characteristics and outcome

Patient	Sex/age	Days of CMV pneumonitis before DHPG	Outcome
1.	M/52	5	Died, day 8
2.	M/38	4	Alive, 19 weeks
3.	M/38	1	Alive, 12 weeks
4.	M/46	2	Alive, 13 weeks
5.	M/12	<1	Recurrence, day 25
5. (second course)		<1	Alive, 5 weeks
6.	F/37	<1	Alive, 7 weeks
7.	F/18	<1	Alive, 5 weeks

* Abbreviation: DHPG, 9-(2-hydroxy-1-[hydroxymethyl] ethoxymethyl) guanine.

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Received 1 March 1988.
Accepted 23 March 1988.