LETTER TO THE EDITOR

Ganciclovir prophylasis and β-herpesvirus in renal transplant recipients

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The use of ganciclovir prophylaxis to avoid cytomegalovirus (CMV) disease (CMVD) is extended, but little is known about its effect to inhibit the replication of the new β-herpesviruses (HHV-6 and HHV-7), associated with development of allograft rejection, marrow suppression and predisposition to CMVD[1].

The purpose of this study was to analyze the effects of oral ganciclovir (GCV) prophylaxis on CMV, HHV-6 and HHV-7 viremia in renal transplant recipients (RT), in the first 3 months after transplantation.

The study included 134 patients (50 ± 13 years old) undergoing cadaveric kidney transplantation (according the local ethics committee), which received triple immunosuppressive therapy, including cyclosporine A, steroids and mycophenolate–mofetil (114 RT), or azathioprine (11 RT), or rapamicin (nine RT). According GCV prophylaxis (1 g/8 h adjusted to renal function), three groups were established: 54 without GCV (G1), 29 with <30 days of GCV prophylaxis [short-term prophylaxis (STP)] and 51 with more than 60 days of GCV [long-term prophylaxis (LTP)].

From the 134 RT, 2178 peripheral blood leukocytes samples (PBL) collected weekly after transplant to detect CMV viremia by nested-PCR and antigenemia, and 1242 of them collected every 2 weeks to detect HHV-6 and HHV-7 DNAemia by nested-PCR, were analyzed. Protocols were developed in our laboratory, according standards recommendations.

The results of incidence, apparition and duration of CMV, HHV-6 and HHV-7 viremia are shown in Table 1.

In our study, the use of GCV prophylaxis decreased significantly CMV replication as other authors had previously described [2]. Nevertheless, CMV viremia was present in 14 patients during the course of GCV prophylaxis (two STP and 12 LTP). In STP, maximum CMV-Ag was higher than in the other two groups: 59.3 ± 83.8 (1–290) positive cells per 10^5 PBL versus 27.2 ± 41.9 (1–200) and 22.8 ± 54.2 (1–200) for G1 and LTP respectively. CMVD occurred in eight RT (15%) from G1, in three (10.4%) from STP, and in two (3.9%) from LTP ($P = 0.1$). All these facts may imply a potential emergence of GCV resistance as it has been described [3–5], and suggest increasing vigilance for antiviral resistance.

No influence has been reported from GCV on HHV-6 incidence. But, HHV-6 replication suffered a delay with prophylaxis, and the duration of viremia was shorter significantly in patients with antiviral prophylaxis (Table 1), according with Yoshida *et al.* [6].

No relationship has been observed between GCV prophylaxis and incidence, apparition or duration of HHV-7 viremia, as it has been described [7].

Table 1. Incidence, apparition and duration of CMV, HHV-6 and HHV-7 viremia in the three different groups of GCV prophylaxis after transplantation.

	G1	STP	LTP	*P*-value
CMV				
Incidence	40 (74%)	16 (55%)	15 (29%)	0.05
Apparation (days post-TR)	52 ± 33	73 ± 40	66 ± 43	NS
Duration (days)	37 ± 30	38 ± 58	36 ± 34	NS
HHV-6				
Incidence	41 (76%)	18 (62%)	31 (61%)	NS
Apparation (days post-TR)	21 ± 25	38 ± 29	42 ± 31	0.01
Duration (days)	62 ± 34	41 ± 33	29 ± 30	0.01
HHV-7				
Incidence	39 (72%)	21 (72%)	42 (82%)	NS
Apparation (days post-TR)	22 ± 18	23 ± 18	19 ± 14	NS
Duration (days)	58 ± 30	57 ± 26	63 ± 21	NS

G1, patients without prophylaxis; STP, short-term prophylaxis; LTP, long-term prophylaxis; NS, not significant; TR, transplantation.

The controversy about the influence between HHV-6 and HHV-7 replication and CMV infection is not resolved [8, 9]. In this study, we could observed that CMV replication was longer in the presence of HHV-6 viremia: 40 ± 25 days versus 18 ± 16 days ($P = 0.0001$). However, HHV-7 was always present in the 13 patients with CMVD, in opposite to 37 of 52 with just CMV infection ($P = 0.05$).

In summary, GCV prophylaxis influenced on CMV and HHV-6 viremia, but did not in HHV-7 replication. CMV replication was longer when HHV-6 was present and there was no CMVD without HHV-7 replication. These facts suggest a possible interaction between these viruses.

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References

1. Dockrell DH, Paya CV. Human herpesvirus-6 and-7 in transplantation. *Rev Med Virol* 2001; **11**: 23.
2. Ahsan N, Holman MJ, Yang HC. Efficacy of oral ganciclovir in prevention of cytomegalovirus infection in post-kidney transplant patients. *Clin Transplant* 1997; **11**: 633.
3. Baldanti F, Simoncini L, Sarasini A, *et al.* Ganciclovir resistance as a result of oral ganciclovir in a heart transplant recipient with multiple human cytomegalovirus strains in the blood. *Transplantation* 1998; **66**: 324.
4. Limaye AP, Corey L, Koelle DM, Davis CL, Boeckh M. Emergence of ganciclovir-resistant cytomegalovirus disease among recipients of solid-organ transplants. *Lancet* 2000; **356**: 645.
5. Turgeon N, Fishman JA, Doran M, *et al.* Prevention of recurrent cytomegalovirus disease in renal and liver transplant recipients: effect of oral ganciclovir. *Transplant Infect Dis* 2000; **2**: 2.
6. Yoshida M, Yamada M, Tsukazaki T, *et al.* Comparison of antiviral compounds against human herpesvirus 6 and 7. *Antiviral Res* 1998; **40**: 73.
7. Brennan DC, Storch GA, Singer GG, Lee L, Rueda J, Schnitzler MA. The prevalence of human herpesvirus-7 in renal transplant recipients is unaffected by oral or intravenous ganciclovir. *J Infect Dis* 2000; **181**: 1557.
8. Osman HK, Peiris JS, Taylor CE, Warwicker P, Jarret RF, Madeley CR. ''Cytomegalovirus disease'' in renal allograft recipients: is human herpesvirus 7 a co-factor for disease progression? *J Med Virol* 1996; **48**: 295.
9. Moschettini D, De Milito A, Catucci M, *et al.* Detection of human herpesvirus 6 and 7 in heart transplant recipients by a multiplex polymerase chain reaction method. *Eur J Clin Microbiol Infect Dis* 1998; **17**: 117.