Poster

[P27-3] P27-3: Anti-infective drugs (8): Antiviral

Chair: Birgit C. P. Koch, The Netherlands

Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall)

[P27-3-7] Single-dose pharmacokinetics of acyclovir and its principal metabolite 9-carboxymethoxymethylguanine (CMMG) in subjects with normal or impaired renal function and in hemodialysis patients

Anders Hellden[1], Lars Stahle[2] (1.Karolinska Institutet, 2.Intervention, and Technology)

Keywords: acyclovir, 9-carboxymethoxymethylguanine, neuropsychiatric symptoms, kidney function metabolism

Background

The nucleoside antiviral drug acyclovir (ACV), 9-(2-hydroxyethoxymethyl)guanine, and its prodrug valacyclovir (VACV), is a potent and selective inhibitor of herpes virus, particularly herpes simplex (HSV) and to a lesser extent varicella zoster virus (VZV). Intravenous ACV has decreased the mortality in herpes encephalitis and has substantially improved the quality of life for people who have survived. ACV is regarded as a drug with few and minor side-effects but acyclovir-induced neuropsychiatric symptoms (ANS) have been reported, mainly in patients with renal impairment. ACV is excreted in the urine to about 90-95 % in patients with normal renal function. The rest is metabolized by alcohol dehydrogenase and aldehyde dehydrogenase mainly to its main metabolite 9-carboxymethoxymethylguanine (CMMG). We have earlier shown that CMMG is inconsistently increased in patients with ANS, indicating that CMMG may the cause of or a marker for ANS.

Methods

We performed a study to obtain estimates of the pharmacokinetic parameters of ACV and CMMG in subjects with a renal function ranging from normal to impaired requiring HD.

Results

Total CL for ACV after i.v. infusion decreased with renal function and the relation to CG-CrCL was CL = 3.0*CrCL + 104 mL/min. The total ACV-CL had an intercept with the ACV-CL axis giving an estimate of non-renal CL in the order of 100 mL/min. CMMG concentrations after both oral and intravenous administration exceeded those of ACV in hemodialysis patients.

Conclusions

Our findings may explain the high CMMG concentrations found in ANS patients.