Poster

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

Chair: Birgit C. P. Koch, The Netherlands

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[P27-3-3] Methadone reduced nevirapine pharmacokinetic parameters in patients with HIV

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Background

In Malaysia, since the first detected HIV case in 1986, HIV infection has become one of the most serious health problems and development challenges facing the country. The epidemic in this country is predominantly affects males because they constitute 90% of cumulative HIV cases of whom the majority are intravenous drug users (IDUs). Combinations of nevirapine based HAART that permit once- or twice-daily dosing is chosen to increase the accessibility and efficacy of antiretroviral therapy for HIV-infected IDUs with methadone replacement therapy. Initial study was to identify nevirapine pharmacokinetic parameters in Malaysian HIV patients. Fifteen-percent of the patients recruited were treated with methadone replacement therapy. Therefore, the possible interaction of nevirapine-methadone was explored.

Methods

In total, 112 patients treated with 200 mg twice daily nevirapine-based antiretroviral therapy were included in the study. Blood samples were drawn at pre-dose, 0.5, 1.0, 1.5, 2.0, 3.0, 4.0 and 8.0 hours after nevirapine morning dose. Plasma nevirapine concentrations were determined by high performance liquid chromatography with UV detector. The pharmacokinetic parameters of nevirapine were modeled using non-parametric pharmacokinetics analysis with Pmetrics software. The minimum (Cmin) and the maximum (Cmax) plasma concentration of nevirapine were obtained from visual inspection of the concentration-time curves. Three single nucleotide polymorphisms (SNPs) within CYP2B6 and ABCC10 were genotyped.

Results

Methadone therapy was independently associated with reduced nevirapine concentrations (Cmin: 15.2%; p =0.011, Cmax: 19.5%; p=0.003). The Cmin and Cmax of nevirapine are predicted to be 1.47 mg/L and 2.65 mg/L lower respectively in patients with methadone therapy. The nevirapine area-under-curve was significantly lowered by 16.2% with concurrent methadone administration was consistent with the lowering in nevirapine concentrations observed. In the univariate analysis, concomitant methadone administration significantly increased the nevirapine clearance by 25.3% (p=0.046). This correlated with the previous decrease in nevirapine exposure with methadone.

Conclusions

This study provides evidence on decrement of nevirapine exposure when co-administered with methadone. It is important to note that 40% of people living with HIV in Malaysia were injection drug users and majority of them were under methadone replacement therapy, suggesting the need for regular monitoring of nevirapine levels.