Role of TDM in anti-retroviral therapy

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Scope of the lecture:
To summarize the actual knowledge in the field of clinical pharmacology of antiretroviral therapy, focusing on the lights and shadows of therapeutic drug monitoring (TDM) as a tool to optimize drug dosing in HIV-infected patients

Learning objectives:
1. Which are the clinical applications of TDM in the management of HIV-infected patients
2. Which are the therapeutic ranges/targets of drug concentrations for each antiretroviral
3. How to adjust antiretroviral drug doses based on TDM results

Extended abstract:
The management of pharmacological therapy in HIV-positive patients is a complex procedure: there is a latency between the onset of therapy and the onset of therapeutic or toxic responses, an incomplete knowledge of the pharmacokinetics of antiretroviral drugs in the atypical patients, and a high risk of drug-to-drug interactions. These conditions may limit the optimal response of HIV-infected patients to therapies, both in terms of effectiveness and toxicity. However, new diagnostic tools have been available in recent years to control individual variability in drug response, including therapeutic drug monitoring (TDM).
In our center, TDM of antiretroviral agents has been carried out as day-by-day clinical practice for the optimization of drug dosing in HIV-infected patients for nearly 10 years. As first finding, we observed that a significant proportion of patients treated with conventional drug dose had trough concentrations exceeding the upper therapeutic threshold. These patients may benefit from TDM-driven adjustments in antiretrovirals doses. A second main role of TDM is in the field of drug-to-drug interactions (DDIs). Indeed, patients with HIV who are receiving antiretroviral (ARV) therapy are at high risk for DDIs, which can significantly impact patient care and represent a substantial opportunity cost for healthcare systems. DDIs are prevalent in the developed world and in resource-poor settings, with the cost being potentially greater in the latter. Although practically unavoidable in HIV care, many DDIs can be better managed, reducing the risks to patients and the burden on resources. The scope for DDI management is likely to be greater in the developed world, due to the availability of new agents and second-line drugs, which allow greater flexibility of ARV regimens and co-administered drug choice. The advent of electronic prescribing and patient medication records represents an opportunity to aid the identification and management of DDIs. Searchable electronic databases of HIV drug interactions are available, which are a useful tool for HIV healthcare professionals and non-specialists for managing DDIs involving ARVs. Although general active systems that alert prescribers to DDIs currently exist, there is

an indication for the development of specialist active databases to be incorporated into electronic prescribing or dispensing systems, with the aim of improving the quality of prescribing and the safe dispensing of the therapeutically risky drugs and complicated regimens used in HIV management.

A third clinical application of TDM relates to antiretroviral safety/tolerability. In fact, significant associations have been reported between the plasma concentrations of some drugs (such as tenofovir, efavirenz, atazanavir and lopinavir) and their toxicity (renal, neurological and metabolic toxicity, respectively), while therapeutic windows for other antiretroviral drugs have not be firmly established yet.

Finally, we have also provided evidence that inclusion of TDM as part of routine clinical optimization of drug dosing in HIV-infected patients is associated with higher adherence to therapy, reduced length of hospitalization stay, and reduced cost of illness

It is advisable that TDM would be even more applied in the clinical practice for the routine management of HIV-patients to limit the onset of multi-resistant viral strains while at the same time improving tolerability to antiretroviral therapy.