

Antiviral drug concentrations according to seasonal variation.

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Therapeutic drug monitoring is the clinical practice which measures specific drugs at designated timings to maintain a constant concentration in patient's bloodstream, thereby optimizing individual dosage regimens in various clinical situations. It is known that some drug levels, for example the immunosuppressants tacrolimus and sirolimus, may differ according to seasonal variation; authors justify this variability consistently with changes in vitamin D level, which is able to influence the expression of cytochrome P-450 3A4, main responsible of these drugs metabolism. No data are present in literature concerning antiviral concentration variation according to seasonality.

For these reasons, we decided to evaluate plasma antiviral concentrations and investigated if their levels may vary during the year.

Plasma concentrations of raltegravir, ritonavir, darunavir, elvitegravir, dolutegravir, etravirine, atazanavir, tenofovir, emtricitabine, lamivudine, efavirenz, nevirapine, maraviroc, bacavir, rilpivirine, lopinavir, enfuvirtide, entecavir and ribavirine were measured through liquid chromatography with mass spectrometry or UV detection.

We found a significant trend during the year, with reduced drug concentrations in spring and summer, concerning nevirapine ($p= 0.047$) and etravirine ($p< 0.001$); a statistical significant difference between seasons was suggested for dolutegravir ($p= 0.004$) and between winter and summer for dolutegravir ($p= 0.002$) and etravirine ($p< 0.001$). Finally, we decided to evaluate the difference between patients implemented with vitamin D and not and we reported a difference for dolutegravir ($p< 0.001$) and ribavirin ($p= 0.016$).

This study reports for the first time the variability of antiviral drug concentrations during the year and seasons and between patients who were administered with vitamin D and it highlights the needed of therapy personalization. However, further studies, in bigger and different cohorts, are required to confirm this data and to clarify the role of vitamin D in drug pharmacokinetics.