Would drug intracellular concentrations be correct by own patients median cellular volume?

Authors: Antonio D'Avolio and Marco Simiele

HAART can rely on more than 20 drugs to inhibit viral replication and most of them have an intracellular target. In many studies, correlations between NNRTIs and PIs plasma concentrations and efficacy have been found, however PBMCs concentrations could be a more reliable measure of drug exposure. Intracellular quantification of anti-HIV drugs requires sensitive instrumentations, an accurate PBMCs count, and standardized methodology. Medium corpuscular volume (MCV) is commonly estimated to be 400 femtolitres (fL) and cells count is often manually performed by microscope count using Burker/Malassez counting chamber. Therefore, intracellular concentrations measurement could be potentially biased by errors in the PBMCs count and by inter-individual variability of corpuscular volume, as described by Caroline Bazzoli et Al in their review (Bazzoli C. 2010). In our intracellular method PBMCs count and volume (MCV) were calculated by a Coulter Counter instrument (Beckman Coulter Z2) and data used to calculate total PBMCs volume.

Our preliminary results:

20 PBMCs samples were collected from 20 patients. Mean MVC (±SD) was 281.2 fL (±18.9 min 255.6 - max 325.5) with a SD% of 6.7. Mean difference between intracellular concentrations calculated using total PBMCs volume and standard MCV value of 400 femtolitres was 42.2% (22.9% – 56.5%). The observed mean MVC 281.2 fL (±18.9 min 255.6 - max 325.5) was lower than 400 fL. Use of the latter as a presumptive standard value could significantly bias the methods of quantification, and consequently previous reports could have potentially underestimated intracellular drugs exposure. Therefore, we suggest calculation of individual MCV as a more accurate and reliable tool way to quantify intracellular antiretroviral drugs concentrations.

Dr Antonio D'Avolio (BSc, MSc, SM)
Università degli Studi di Torino / ASL TO2
Clinica Universitaria di Malattie Infettive (Direttore Prof. Giovanni Di Perri)
Laboratorio di Farmacologia Clinica e Farmacogenetica, Padiglione Q
Ospedale Amedeo di Savoia, C.so Svizzera 164 - 10149 TORINO (Italy)
Tel. +39.011.4393979, Fax: +39.011.4393882, Tel. Lab. +39.011.4393867
e-mail: antonio.davolio@unito.it

Web Site: www.tdm-torino.org ; e-mail: info@tdm-torino.org
UNI EN ISO 9001:2000 CERTIFIED LABORATORY