PHYSICIAN ADHERENCE TO PHARMACOLOGICAL ADVICE IN AN ANTIRETROVIRAL THERAPEUTIC DRUG MONITORING PROGRAM

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BACKGROUND

- The level of health benefits derived from antiretroviral (ARV) therapeutic drug monitoring (TDM) programs has varied from one study to another;
- Physician adherence to pharmacological advice may influence the level of such benefits;
- This study evaluated physician adherence to pharmacological advice provided by the Quebec provincial ARV TDM program which became operational in June 2006.

STUDY OBJECTIVE

- To describe the Montréal Chest Institute physician adherence to ARV TDM pharmacological advice.

METHODS

- Retrospective review of the Québec Provincial ARV TDM program database;
- Study approved by the research ethics board;
- Type of pharmacological advice given was characterized : no change in therapy, repeat analysis, discontinue (D/C) or add ritonavir, change ARV, increase or decrease dose of analyzed ARV, change concomitant medication due to interaction, verify and encourage adherence, and other;
- Medical charts reviewed to determine if the treating physician had carried out the recommended intervention before or at the time of the patient's next medical visit for the following types of advice: dose change, respect of recommended dose, medication change, repeat analysis, respect of recommended delay to repeat analysis and no change in therapy;
- Involvement of a clinic pharmacist in the patient's care was noted;
- We determined the overall proportion of pharmacological advice the physicians acted upon (adherence) and the proportion of adherence specific to the different types of advice.

Data collection

- Data collected from the TDM database included: patient demographics, clinical, virologic, immunological and resistance data [ie: history of PI failure, cumulative protease mutation list (Trugene and/or Virco), ARV measured, dose and concentration (mg/L), sample time post-dose, viral load and CD4+].
- Data from patients followed at the Montréal Chest Institute having used the TDM program at least once between June 1st 2006 and December 31st 2007.

Statistical Analysis

- Descriptive statistics; continuous variables are presented with medians while categorical variables are presented with proportions.
- Multivariate logistic regression was used to evaluate the determinants of physician overall adherence (including repeats). For this analysis, to be adherent, the physician had to have followed the pharmacological advice **and** repeated the analysis as directed;

RESULTS

307 interpretations from 136 patients were included.

TABLE 1: BASELINE CHARACTERISTICS OF STUDY POPULATION [median (range) or %]

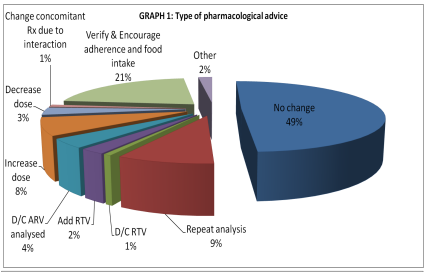
Age (years)	47 (21-74)
Race	
Caucasian	68.6 %
Black	28.0 %
Sex - Male	78.5 %
HIV clade	
Clade A	1.5 %
Clade B	73.2 %
Clade C	7.8 %
Other	4.4 %
Patient ARV status	
ARV Naïve	26.1 %
ARV Experienced	73.9 %
Past Failure to Protease Inhibitors (PIs)	43.7 %
Resistance to NNRTIs	41.6 %
Number of past ARV regimens	3 (1-14)
Number of ARVs in patient's regimen at time of analysis	3 (2-5)
Number of active ARVs in patient's regimen at time of analysis	3 (0-5)
Number of reverse transcriptase mutations	5 (0-29)
Cumulative number of protease mutations	5 (1-18)
Cumulative # of protease mutations conferring resistance to the measured PI	2 (0-12)
Viral load (VL) at time of TDM (log copies/mL)	1.7 (1.7-5.43)
VL undetectable (< 50 copies/mL) at time of TDM	67.9 %
CD4+ count at time of TDM (cell/mm³)	357 (10-4810)
% CD4 at time of TDM	20.5 (2-53)

TABLE 2: INDICATIONS FOR TDM

Indication	n	(%)
Drug Interaction	104	(34,6%)
Control	67	(22,3%)
Toxicity	56	(18,6%)
Virologic Failure	46	(15,3%)
Hepatic Impairment	10	(3,3%)
Pregnancy	8	(2,7%)
Non adherence	6	(2,0%)
Malabsorption	1	(0,3%)
Other	3	(1,0%)

TABLE 3: ANTIRETROVIRAL ANALYZED

ARV	n	(%)
Lopinavir	96	(31,3 %)
Atazanavir	66	(21,5 %)
Efavirenz	56	(18,2 %)
Saquinavir	48	(15,6 %)
Nevirapine	23	(7,5 %)
Fosamprenavir	11	(3,6 %)
Indinavir	2	(0,7 %)
Nelfinavir	2	(0,7 %)
Amprenavir	1	(0,3 %)
Ritonavir	1	(0,3 %)
Tipranavir	1	(0,3 %)



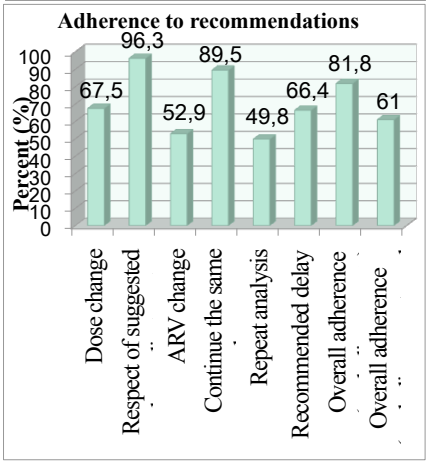


TABLE 4: SIGNIFICANT DETERMINANTS OF PHYSICIAN OVERALL ADHERENCE (including repeats)

Variable in model*	OR	*p*
Advice: continue the same dose	0.081	< 0.001
Physician: specialist	0.163	0.03
Indication: control	7.575	0.011
Clinical pharmacist involved in patient care	7.649	0.04
Viral load at time of TDM (per 1 log increase)	1.948	0.013

*Multivariate logistic regression

- Other variables included in the multivariate logistic regression model were not related to physician overall adherence (including repeats): advice – change dose, advice – repeat analysis, indication – virologic failure, indication – toxicity, patient ARV experienced, number of past ARV regimens, CD4+ at time of TDM;
- A clinical pharmacist participated in the care of 83.8% of the patients.

CONCLUSIONS

- Physician adherence to pharmacological advice obtained via an ARV TDM program was moderate to high in the Montréal Chest Institute cohort and was enhanced by participation of clinical pharmacists in patient care;

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