Viral load undetectability after HAART holds when changed from <400 copies/ml to <75 copies/ml assay

[1] Wong KH, [1] Chan WK, [1]Chan KCW, [1]Tse ICT, [1]Bognar FA, [2]WL Lim.

[1]Integrated Treatment Centre, Special Preventive Programme, Centre for Health Protection, Department of Health, [2]Public Health Laboratory Centre, Centre for Health Protection, Department of Health (khwong@dh.gov.hk) (Virtual AIDS Office www.aids.gov.hk)

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Background

The advent of highly active antiretroviral therapy (HAART) since mid-1990s has revolutionalized medical management of HIV/AIDS, turning a previously fatal disease into chronic illness. Significant reduction in AIDS morbidity and mortality as a consequence of HAART has been demonstrated in many parts of the World. Locally, there was some 90% reduction in AIDS complications and death among advanced disease patients followed up at the Department of Health HIV clinic in the HAART era, as compared to pre-HAART era.

Achieving maximal HIV suppression is the foremost target of HAART, through which the natural course of immune and clinical deterioration in infected patient could be halted and, not uncommonly, reversed. It is thus important to gauge virus load response after HAART initiation and regularly monitor thereafter, more so than in untreated subjects.

HIV-1 viral load can be readily measured using commercial assays. For over a decade, we have been using a polymerase-based test (Amplicor, Roche) with a lower detection limit of 400 copies/ml (cpm) to monitor disease progression and treatment effect of our patients. In June 2008, the government Public Health Laboratory Centre switched to a more sensitive HIV-1 viral load assay, with detection limit lowered to 75 cpm (Real-time, Abbott). We are interested to know the impact of assay change on the detectability of viral load and thus set to study a group of patients stable on HAART.

Methods

All treated patients who were on HAART (3 or more drugs with at least one protease inhibitor or non-nucleoside reverse transcriptase inhibitor) for at least one year and had his/her viral load being <400 cpm prior to switch to the new viral assay were recruited under the study. We looked at their first viral load after switch of assay, and classified the patients into two groups - now still undetectable at <75 cpm or became detectable. We examined factors which may be associated with viral detectability, including patient demographics, HIV transmission route, HIV disease status, HAART regimen, drug adherence and history of prior virologic failiure.

Results

Seven hundred and three patients stable on HAART with <400 cpm had at least one viral load done after change to the more sensitive assay. Six hundred and eight 683 (97.1%) had viral load <75 cpm after switch to the new assay. Nine of the 20 now detectable patients had VL <400 cpm (median 120, range 87-160) while 11 had median VL 1400 cpm (range, 430-140000). (Table 1) Factors associated with a >75 cpm VL were history of virologic failure (>400cpm), and lower CD4 both before and after new assay whereas demographics, HIV risk factor, AIDS status, last self-reported adherence and duration of treatment and regimen were not factors. (Table 2)

Table 1. Viral load level of 20 patients who became detectable after change to the more sensitive assay with detection limit <75 copies/ml.

	>400 cpm		>75-400 cpm
1	140000	12	160
2	110000	13	150
3	20000	14	120
4	4700	15	120
5	2500	16	120
6	1400	17	110
7	1300	18	96
8	770	19	87
9	670	20	87
10	630		
11	430		

Table 2. Factors on viral detectability (n=703)

		Undetectable (<75 cpm) (n=683)	%	Detectable >75 cpm (n=20)	%	P value # (95% CI)
Sex	Female	121	17.7%	4	20.0%	0.793 (0.38-3.53)
	Male	562	82.3%	16	80.0%	
Ethnicity	Non-Chinese	107	15.7%	6	30.0%	0.094 (0.16-1.15)
	Chinese	576	84.3%	14	70.0%	
HIV risk	Sex between men	227	33.2%	7	35.0%	0.749
	Blood	11	1.6%	0	0.0%	
	Heterosexual	436	63.8%	12	60.0%	
	Injecting drug use	6	0.9%	1	5.0%	
	Undetermined	3	0.4%	0	0.0%	
Subtype	02_AG	3	0.4%	0	0.0%	0.057
	03_AB	1	0.1%	1	5.0%	
	07_BC	6	0.9%	0	0.0%	
	08_BC	5	0.7%	1	5.0%	
	11_CPX	1	0.1%	0	0.0%	
	A	1	0.1%	0	0.0%	
	AE	191	28.0%	6	30.0%	
	B	167	24.5%	5	25.0%	
	C	7	1.0%	2	10.0%	
	D	1	0.1%	0	0.0%	
AIDS	No	439	64.3%	9	45.0%	0.084 (0.19-1.11)
	Yes	244	35.7%	11	55.0%	
Ever Viral load >400 cpm	No	391	57.2%	4	20.0%	0.003 (1.77-16.18)
	Yes	292	42.8%	16	80.0%	
Latest adherence, %	Mean	99.48		99.47		0.988 (0.87-1.15)
CD4 before HAART, /uL	Mean	439.40		343.50		0.05 (0.995-1)
	Median	404.00		321.50		
CD4 after HAART, /uL	Mean	447.30		294.20		0.001 (0.992-0.998)
	Median	407.00		300.50		
Present regimen base	PI	447	65.4%	16	80.0%	0.665
	NNRTI	223	32.7%	4	20.0%	
	PI/NNRTI	11	1.6%	0	0.0%	
	Other	2	0.3%	0	0.0%	
Treatment months	Mean	73.62		58.01		0.142 (0.98-1)
	Median	62.79		48.39		

Logistic regression at 95% CI

Discussion

Albeit the goal of HAART is full or maximal viral suppression, the extent of which achieved in specific patient populations depends on the viral load detection limit and is somewhat arbitrary. The present study found that only a minority (<3%) of our patients who had been on HAART for >= one year and with a viral load <400 cpm just prior to switch to the more sensitive assay became virologically detectable with level >75 cpm at first new test. That means a vast majority still had undetectable viral load despite a lowering of the detection threshold of the assay. Moreover, only 9 of the 20 now detectable had a viral load 75-400, signifying detectability with the new but not old assay. The rest 11 patients had viral load >400 cpm, which likely represented viral rebound and coincidental failure unrelated to change of assay. We did not have paired testing of new and old assays in this study. We assumed the correlation of the two assays of previous testing held as well as relied on the accuracy of the new assay to determine who were now virologically detectable after switch of assay.

The presence of detectable but low level viral load has been shown to predict greater virologic failure subsequently. This is why detection limit of viral load in clinic practice is preferred to be lower (at 50-75 cpm) if possible. Our findings suggested that many of the patients stably controlled after one year of HAART can be presumed to have <75 cpm viral load even if the assay only detects down to 400cpm. Although HAART is being much scaled up globally, the availability of viral load testing does not correspond. It is conceivable that the more sensitive viral load assay is not available in some resource-constrained countries. Our results, if extrapolable, can serve as reference for these countries. We have to caution, however, that this cannot be taken for granted, given the difference in clinic set-up, patient population, treatment practice and other factors.

Previous treatment failure and a lower CD4 before and after HAART were found to be associated with higher chance of viral detectability after switch to the new assay in our patients. If without a more sensitive assays, the presence of such factors may point to the need of higher alertness for viral breakthrough. Despite these, the clinical significance of low level viraemia detectable after change to a more sensitive viral assay is unclear for the moment and remains to be determined.