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Poster presentation

Elite controllers or misquantification of virus load by Cobas TaqMan?

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Background

Our outdoor patient clinic in Salzburg (Austria) comprises 170 HIV-infected patients. Since 2004 our laboratory has been using Cobas TaqMan 48 real time PCR analyser (Roche) for detection and quantification of HIV-1 RNA. To date we could identify four patients who remained undetectable (3/4) or who presented with very low viremia (<200 copies per ml) while receiving no antiretroviral therapy at all.

Methods

To evaluate this issue, further analyses of the HIV-1 RNA in plasma were undertaken using Cobas Amplicor version 1.5, and the Abbott m2000 system. For patients 1 and 2, virus was isolated by co-cultivation of patients' PBMCs with uninfected donor PBMCs and the nucleic acid sequences of the gag, pol, and env genes of both virus isolates were determined. For patients 3 and 4, gag and pol genes were sequenced directly from PCR amplicons. All sequences were subsequently subtyped using standard phylogenetic analysis tools. Finally, a positive control amplicon of Cobas TaqMan was compared to the sequences of our patients.

Summary of results

All four patients showed detectable plasma viral loads ranging from 1,700 copies per ml to 22,000 copies per ml using the Abbott m2000 system. With Cobas Amplicor only one patient remained undetectable, while three others had similar virus load results as obtained with the Abbott system. We found three different HIV subtypes: B, F1 and A1 (twice), which according to manufacturer's instructions all should have been recognized by Cobas TaqMan Assay. The analysis of the Cobas TaqMan amplicon revealed numerous mismatches to the patients gag gene sequences in the putative 3'-primer binding region which in combination with the real-time format may be responsible for the observed misquantification. (Table 1.)

Conclusion

In the face of the severe consequences for therapeutic decisions and patient counseling, the observed rate of misquantifications in our patient cohort by Cobas TaqMan HIV-1 is unacceptable. Misquantifications can not be assigned to a rare subtype but occur with different virus strains. There is an urgent need for refinement of the Cobas TaqMan. In addition, these findings shed a different light concerning the definition of so-called elite controllers in clinical practice.

Table 1:

Patient No.	HIV Subtype	Analysis Date	Cobas TaqMan Real Time PCR [cop/ml]	Abbott m2000 PCR [cop/ml]	Cobas Amplicor Version 1.5 PCR [cop/ml]
1	F1	13.09.06	<40	21000	
		25.09.06	<40	2200	<400 (03.01.07)
2	A1	25.01.07	184	13000	11900
		02.06.06	98	22000	18600 (16.02.07)
3	B	17.03.08	<40	12000	7280
		31.03.08	<40	21000	11500
4	A1	05.05.08	<40	1700	2380