COUNSELING INTERVENTIONS CAN IMPROVE ADHERENCE TO HIGHLY ACTIVE ANTIRETROVIRAL THERAPY : A FRENCH PROSPECTIVE CONTROLLED STUDY

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ABSTRACT

- **OBJECTIVE.** To evaluate the impact of an intervention for improving adherence to Highly Active Antiretroviral Therapies (HAART) in HIV - infected patients.
- **DESIGN.** Prospective, controlled, randomised trial comparing a group who received a counseling intervention in addition to ordinary clinical follow - up versus a control.
- **SETTING.** Nice University Hospital (South - Eastern France).
- **PATIENTS.** All patients receiving HAART since at least 1 month who attended a medical follow - up consultation between September and December 1999.
- **INTERVENTION.** Patients in the Intervention group received three individual counseling sessions about HAART regimens by specially trained nurses.
- **MAIN OUTCOME MEASURES.** Proportions of patients achieving 100 % adherence at 6 months follow - up (M6). Evolution in viral load between inclusion (M0) and M6.
- **RESULTS.** Between M0 and M6, HIV-1 RNA significantly decreased in the 123 patients of the Intervention group (log [mean difference] = – 0.22, [± 0.86], p = 0.013) while it increased (= + 0.12, [± 0.90], p = 0.14) in the 121 patients of the Control. However, proportion of patients with HIV-1 RNA < 40 copies/mL remained similar in both groups. Among the 202 patients with available data on adherence, the proportion of 100 % adherent patients was similar in both groups at M0 (58 % vs 63 %, p = 0.59) but became higher in the Intervention group at M6 (75 % vs 61 %, p = 0.04).
- **CONCLUSIONS.** The study brings evidence of the feasibility and efficacy of a counseling intervention to increase adherence to HAART that could be easily implemented in most clinical settings.

INTRODUCTION

- HIV - infected patients' inadequate adherence can have profound negative implications for the individual and public health effectiveness of Highly Active Antiretroviral Therapies (HAART). Because physicians, even those with the greatest experience of HIV care, may have diverse ways of communicating with patients regarding adherence, formalised educational interventions to improve patients' adherence to HAART have been highly recommended. Attempts to evaluate such interventions have however been limited. In a prospective, controlled, randomised study carried out in a sample of HAART - treated patients from a French hospital, we tried to evaluate the impact of a counseling intervention, provided by specially trained nurses, on both measurement of adherence and virological outcomes.

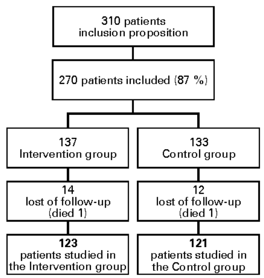
PATIENTS & METHODS

- The study population consisted of all HIV-infected patients who had a medical follow-up consultation at the Nice University Hospital (South-Eastern France) between September and December 1999 and who fulfilled the following eligibility criteria at enrolment : being treated, since at least one month, by a combination of at least one Protease Inhibitor (PI) or one Non Nucleoside Retrovirus Transcriptase Inhibitor (NNRTI) or Abacavir with two Nucleoside Retrovirus Transcriptase Inhibitors (NRTI), being 18 years of age or more, not requiring an hospitalisation and not being included in another protocol.
- Patients were randomised in an intervention and a control group who both received the usual clinical follow-up and were offered similar questionnaires at enrolment (M0) and 6 months later (M6). In addition, the intervention group benefited from an educational program including three counseling sessions, one immediately following enrolment (M0) and every 2 months (M2, M4).
- The sessions were delivered to each patient, on an individual basis, by one of four nurses who attended a five day intensive training by psychologists before the implementation of the intervention. A manual was used to standardise the content of each session into modules targeting cognitive, emotional, social and behavioural determinants known to affect adherence. Each nurse had to record the key features of each individual session and was monthly supervised through a meeting with a psychologist. A clinical supervisor was also assigned to review regularly the content of the counseling sessions.
- The endpoints of the study were : proportion of patients achieving an adherence level of 100 % at M6, evolution in viral load (VL) between M0 and M6 and percentage of patients achieving plasma HIV-1 RNA levels < 40 copies/mL at M6.
- Data collected at M0 and M6 included a medical questionnaire, filled out by the hospital AIDS specialist at the end of consultation, which contained detailed information about the patient's clinical history as well as prescription of anti-retroviral drugs. Viral load was measured by RT - PCR [Amplicor™, ROCHE] assays with lower limits of detection of 40 copies of HIV-1 RNA / mL.
- At M0 and M6, data about patients' characteristics and self - reported adherence to HAART were collected by means of a self - administered questionnaire, which was filled out by the patient apart from any member of medical staff [1, 2, 3].
- The intervention and the control groups were compared at M0 and M6 using a χ^2 test for categorical variables including adherence measurement. A Student t-test or a Mann-Whitney test was used when comparing continuous variables such as VL. Evolutions of adherence and VL between M0 and M6 in each group were assessed by a Wilcoxon rank sum test or a McNemar test. Statistical analyses were performed using SPSS (Carry, Inc. 9.0).

RESULTS

- 123 patients in the Intervention group and 121 in the Control group were compared below.

(n = 244, South-Eastern France)



- Table 1 shows that no significant difference was found between both groups at M0 for socio - demographic, biological and clinical as well as treatment characteristics.
- In the Intervention group, 67 (54 %) patients had followed all three counseling sessions, while 56 (46 %) had only partly followed the program.
- Two hundred and two (83 %) of the 244 patients answered the self - administered questionnaires on adherence, and the proportion of non respondents was similar in both groups (19 % vs 16 %, p = 0.62). As seen in Table 2, among these 202 patients, the proportion of those who were adherent was similar in both groups at M0 (58 % vs 63 %, p = 0.59), while it became significantly higher in the intervention group at M6 (75 % vs 61 %, p = 0.04), the increase in the proportion of adherent patients being significant in the intervention group (McNemar test, p = 0.04). It must be noted that among the 122 patients who were initially adherent at M0, the proportion who remained adherent at M6 was higher in the intervention group (88 % vs 69 %, p = 0.02), while among the 80 initially non-adherent patients, the proportion of those who became adherent at M6 was not significantly different (57 % vs 47 %, p = 0.52). It must also be noted that in the intervention group, the proportion of adherent patients at M6 was significantly higher among the 59 patients who had received all three counseling sessions (83 % vs 63 %, p = 0.05).
- Table 2 also presents the results of an "intent-to-treat analysis" (all patients whether or not assessment of adherence was available and whether or not they followed the whole three sessions in the intervention group) comparing virological outcomes.

TABLE 1 : BASELINE CHARACTERISTICS OF HAART - TREATED PATIENTS INCLUDED IN A PROSPECTIVE, CONTROLLED STUDY FOR EVALUATION OF A COUNSELING INTERVENTION TO INCREASE ADHERENCE (n = 244, South-Eastern France)

N (%)		INTERVENTION GROUP (n = 123)	CONTROL GROUP (n = 121)	p
Median age [IQR]		39.8 [35 - 49]	38 [36 - 45]	0.26(1)
Gender	Male	87 (71 %)	91 (75 %)	0.52(2)
	Female	36 (29 %)	30 (25 %)	
HIV-infected by injecting drug use	Yes	40 (33 %)	35 (30 %)	0.64(2)
	No	83 (67 %)	86 (70 %)	
High school certificate	Yes	41 (32 %)	36 (30 %)	0.61(2)
	No	81 (68 %)	85 (70 %)	
Mean plasma HIV RNA { log [copies/mL] } ± SD		2.70 ± 1.23	2.63 ± 1.13	0.60(3)
Median CD4 cell count/mm^3 [IQR]		340 [170 - 576]	361 [214 - 502]	0.59(1)
CDC clinical stage	A	65 (53 %)	54 (44 %)	0.14(2)
	B	19 (15 %)	31 (26 %)	
	C	39 (32 %)	36 (30 %)	
HAART regimen	Protease inhibitor(s) + 2 NRTI	102 (83 %)	97 (80 %)	0.84(2)
	NNRTI + 2 NRTI	17 (14 %)	20 (17 %)	
	3 NRTI	4 (3 %)	4 (3 %)	
Antiretroviral naive before HAART initiation	Yes	34 (28 %)	35 (29 %)	0.94(2)
	No	89 (72 %)	86 (71 %)	
Median duration of HAART (months), [IQR]		28.6 [18.7 - 35.7]	26.1 [15.6 - 33.7]	0.20(1)

(1) Mann-Whitney test, (2) χ^2 test, (3) Student t-test.

TABLE 2 : EVOLUTION OF ADHERENCE AND VIROLOGICAL OUTCOMES AT 6 MONTH FOLLOW - UP IN HAART - TREATED PATIENTS INCLUDED IN A PROSPECTIVE, CONTROLLED STUDY FOR EVALUATION OF A COUNSELING INTERVENTION TO INCREASE ADHERENCE (n = 244, South-Eastern France)

Total sample (n = 244)	INTERVENTION GROUP (n = 123)	CONTROL GROUP (n = 121)	p
EVOLUTION OF ADHERENCE :			
Adherent M0 & M6	51 (41 %)	44 (36 %)	-
Adherent M0 / Non adherent M6	7 (6 %)	20 (17 %)	
Non adherent M0 & M6	18 (15 %)	20 (17 %)	
Non adherent M0 / Adherent M6	24 (19 %)	18 (15 %)	
Missing data	23 (19 %)	19 (15 %)	
VIROLOGICAL OUTCOMES :			
Mean difference of VL between M6 & M0 (log [copies/mL]) ± SD	-0.22 ± 0.86^a	$+0.12 \pm 0.90^b$	0.002(3)
Mean VL at M6 (log [copies/mL]) ± SD	2.48 ± 1.16	2.75 ± 1.34	0.10(3)
Patients with VL < 40 copies/mL at M6	58 (47 %)	58 (48 %)	1.00(2)
Patients with VL < 400 copies/mL at M6	79 (64 %)	65 (54 %)	0.12(2)

Sub-sample of patients with HIV-RNA > 40 copies/mL at M0 (n = 146)	INTERVENTION GROUP (n = 73)	CONTROL GROUP (n = 73)	p
Mean difference of VL between M6 & M0 (log [copies/mL]) ± SD	-0.48 ± 0.96^c	$+0.15 \pm 1.13^d$	0.001(3)
Mean VL at M6 (log [copies/mL]) ± SD	2.99 ± 1.22	3.49 ± 1.27	0.016(3)
Patients with VL < 40 copies/mL at M6	19 (26 %)	11 (16 %)	0.15(2)
Patients with VL < 400 copies/mL at M6	31 (42 %)	18 (25 %)	0.036(2)

^{a} p = 0.013, ^{b} p = 0.14, ^{c} p < 0.001, ^{d} p = 0.25 (Wilcoxon Rank Sum test)
(2) χ^2 test, (3) Student t-test.

CONCLUSIONS

- **To our knowledge, only one controlled study from Tuldra et al [1], carried out at initiation of first or second-line prescription of HAART, had previously demonstrated that significant improvements in adherence and HIV-RNA VL could be obtained among HIV-infected patients receiving a psycho-educative intervention. Our study is the first to show similar positive results of an adherence counseling intervention in a sample of patients who were HAART - treated, regardless of the timing and type of their antiretroviral therapy. Our results correspond to the "real life" situation that most clinical settings delivering HIV care would encounter if they introduce formalised educational interventions about adherence.**
- **A significant reduction of HIV - RNA VL was obtained in patients who benefited from the intervention, particularly in patients with detectable VL (> 40 copies/mL) at baseline. However, the proportion of patients who reached an undetectable VL was not significantly different between groups. Because data suggest that it is necessary to always take a high proportion (95 % or more) of drug doses to reach and maintain undetectable VL, it might be possible that the improvement in adherence facilitated by the intervention was not sufficient to obtain such complete inhibition of viral replication.**
- **The intervention was more effective in the subgroup of patients who completed the three planned counseling sessions and in helping initially adherent patients to maintain this behaviour during follow-up rather than in modifying non adherent behaviours. This may be partly due to the specific design of our intervention. Psycho-social research had already pointed out the dynamic character of HAART - treated patients' adherence behaviors which are influenced by multiple factors varying overtime. Because the follow-up period of our study was limited to six-months, the impact of educational interventions on adherence needs further longer term investigation.**
- **In spite of its limitations, our study brings clear evidence in favour of the feasibility and efficacy of counseling interventions to increase adherence to HAART that could be easily implemented, with limited additional resources, in most clinical settings.**

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