Highly active antiretroviral treatment does not increase sexual risk behaviour among French HIV infected injecting drug users

A-D Bouhnik, J P Moatti, D Vlahov, H Gallais, P Dellamonica, Y Obadia and the MANIF 2000 Study Group

**Study objective:** This study examined the impact of highly active antiretroviral therapies (HAART) on sexual risk behaviours of HIV infected injecting drug users (IDUs) included in the French MANIF 2000 cohort study.

**Design:** Longitudinal analysis including baseline and last follow up characteristics using generalised estimating equations (GEE).

**Setting:** Hospital departments for specialist AIDS care in south eastern France and inner suburbs of Paris.

**Patients:** All patients antiretroviral treatment naive, who reported being sexually active at enrolment, and who had at least one follow up visit in the cohort between October 1996 and May 1998 (n=188).

**Main results:** Of the 188 HIV infected IDUs who were antiretroviral treatment naive at enrolment, 34 were prescribed HAART during follow up. Proportion of patients who reported at least one episode of unprotected sexual intercourse in the previous six months only significantly decreased in the HAART treated group (from 47.1% to 23.5%, \(p=0.008\), compared with 43.5% to 35.7% in the rest of the sample, \(p=0.10\)). GEE multivariate model confirmed that prescription of HAART was associated with reduced sexual risk.

**Conclusions:** The concern that HAART might result in clinical improvement leading to resumption of high risk activities that could inadvertently result in HIV transmission was not supported by these data. Reasons for further reductions in HIV risk with taking HAART remain to be clarified.

Highly active antiretroviral therapies (HAART) including protease inhibitors (PIs) have been proved to be effective for decreasing HIV viral loads to undetectable levels, for significantly reducing the incidence of HIV related opportunistic infections, and for restoring a decent quality of life for a high number of HIV infected patients. However, concerns have been raised that these improvements may increase the opportunities for continued or relapse to risk behaviours against actual treatments. Such concerns may even be more pronounced for specific groups, like HIV infected injecting drug users (IDUs), who are often confined to unsupportive social environments and squalid physical living conditions that create additional barriers for HIV secondary transmission.

The MANIF 2000 study provided the opportunity to examine the evolution of sexual risk behaviours in a cohort of French patients HIV infected through injecting drug use whether or not they were prescribed HAART after enrolment.

**METHODS**

**Study population**

MANIF 2000 is a prospective cohort study, which enrolls patients HIV infected through injection drug use, aged 18 years or more, with CD4+ cell counts \(\geq 300/\text{mm}^3\), no opportunistic infections, and CDC stage A or B at last visit before entry, in 12 hospital departments of south eastern France (Marseilles, Avignon, Nice) and the inner suburbs of Paris. For each patient, data collected at enrolment and at each six months follow up visit included a medical questionnaire completed by the hospital AIDS specialist at the end of consultation, which contains clinical and biological information as well as prescriptions of antiretroviral treatment. In parallel, in depth data about patient’s sociological and psychological characteristics as well as their personal experience with HIV infection and care are obtained by means of two questionnaires: a face to face questionnaire administered by a nurse, and a self administered questionnaire that deals with HIV related risk behaviours. This questionnaire includes 21 questions about type of drug use, frequency of injection, needle sharing and borrowing, and access to drug maintenance treatment during the six months before the visit. It also includes 22 questions about sexual behaviour including occurrence of vaginal, anal, and oral intercourse, number of sexual partners, HIV serological status of main partner, as well as condom use with main and occasional partners during the same period.

All patients who were antiretroviral treatment naive, who reported being sexually active at enrolment, and who had at least one follow up visit in the cohort between October 1996 and May 1998, were included in this analysis. Risky sexual behaviour was defined as a dichotomous variable (yes/no) on the basis of patient’s reports that he/she has been engaged in unprotected (that is, without a condom) intercourse at least once during the six months before the visit. Evolution of risky sexual behaviour was compared between enrolment and last follow up visit in the cohort in two groups of patients: those for who prescribing physician started HAART during the follow up period and those who were not prescribed HAART.

Abbreviations: HAART, highly active antiretroviral therapies; IDU, injecting drug user; GEE, generalised estimating equations.
**Statistical analysis**

The χ² test, Fisher’s exact test, or Mann-Whitney test were used to compare sociodemographic, clinical, and behavioural characteristics of the two groups of patients at enrolment and at last follow up visit. MacNemar χ² test was used to compare the proportions of patients who declared injecting drug use and unprotected sexual intercourse between enrolment and follow up within the two groups as well as in the whole sample. To analyse factors associated with HIV related sexual risk behaviour, and in particular to analyse if HAART prescription had an impact on this behaviour, we performed a logistic regression with repeated measures including baseline data at enrolment, for the entire sample (from 48.4% to 52.8%), and follow up data, using the generalised estimating equations method (GEE). GEE is a statistical method that permits the marginal expectation of an outcome discrete variable to be described as a function of the covariates while accounting for the correlation among the repeated observations for each given subject. The equations used are extensions of those used in quasi-likelihood. The dependent dichotomous variable used a model for binomial distribution with a logit link function. All variables significantly associated to sexual risk behaviour in an univariate GEE model including baseline and follow up data (p<0.05) were included in the multivariate GEE model. As visits took place at different moments in time, this analysis allowed us to account for the year of the visit.

**RESULTS**

Among the 467 patients who provided informed consent to participate in the MANIF 2000 cohort between October 1996 and May 1998, a total of 188 were antiretroviral treatment naive and reported being sexually active at enrolment, and had at least one follow up visit during this period. Among these 188 patients, a total of 34 were ultimately prescribed HAART during follow up. As table 1 shows, these 34 patients had lower CD4+ cell counts and higher plasma viral loads at enrolment than the rest of the sample. Table 1 shows, however, that they did not differ at enrolment for other characteristics including sociodemographic characteristics, active injecting drug use, participation in maintenance treatment for drug misuse, or sexual behaviours. Frequency of HIV related risk behaviours during the six months before enrolment was rather high: 21.3% of the whole sample reported at least one episode of sharing injection equipment (syringe, cooker or cotton), and 44.1% at least one episode of unprotected sexual intercourse.

For those who had been prescribed HAART, mean duration of treatment at the last follow up visit in the cohort was 4.0 months (SD=1.7). Not surprisingly, patients treated with HAART were more likely than untreated patients to have undetectable viral loads at follow up (table 1). Self reports of drug injecting behaviours during the prior six months were significantly reduced at last follow up, when compared with baseline data at enrolment, for the entire sample (from 48.4% to 35.7%).
to 19.7%, p=0.0001) as well as within each group of patients (from 44.1% to 14.7% among those who were prescribed HAART, p=0.002, and from 49.4% to 20.8% among those who were not, p=0.0001). Self report of at least one episode of sharing injection equipment (syringe, cooker or cotton) also decreased over time (from 29.5% to 5.9% among those who were prescribed HAART, p=0.008, and from 19.5% to 5.8% among those who were not, p=0.0001). Among HAART treated patients 17.6% reported no sexual activity at follow up while the proportion was 13.6% among those not treated (p=0.55). There was no significant change over time with respect to the numbers of main or occasional partners, or both. The frequency of patients reporting at least one episode of oral sex significantly decreased for both groups of patients (from 79.4% to 55.9%, p=0.021 among those who were prescribed HAART, p=0.008, and from 61.9% to 58.3%, p=0.104 among the others). Concerning anal sex, the observed declines did not reach a conventional significance level (from 47.1% to 29.4% among HAART treated patients, p=0.109 and from 31.2% to 24.0%, p=0.054 among the others patients). Frequency of HIV related risky sexual behaviour reported during the prior six months declined, but this decline reached statistical significance only in the group of patients who were prescribed HAART (from 47.1% to 23.5%, p = 0.008), and not in the untreated group (from 43.5% to 37.7%, p = 0.10).

Table 2 shows the estimated odds ratios for the univariate and multivariate GEE models for HIV related sexual risk behaviour. After multivariate adjustment, female gender, dec-
Of course, generalisation of our findings to other populations of HIV infected persons remains to be determined. Firstly, our study was not a randomised clinical trial but an observational cohort study in which physicians remained free to make a clinical decision about initiation of HAART and to select patients who had access to these treatments. It had already been shown that in routine clinical practice, physicians’ perceptions of IDU patients’ non-adherent behaviours may explain why these patients had less and delayed access to HIV infection antiretroviral therapies. Because of the relatively low proportion of patients in our cohort who had access to HAART, and although extramedical characteristics at enrolment, including gender, age, and risky behaviours, were similar between those who were ultimately prescribed HAART and those who were not, we cannot totally exclude that some selection bias might have occurred. Prescribing physicians may have been more eager to recommend HAART in patients whose personal characteristics seemed to them as facilitating adherence to both treatment and recommendations for secondary prevention. Secondly, our assessment of behaviours was based on self-reports, in which socially desirable responding cannot be excluded. Evidence supporting the accuracy of self reports about drug use and sexual practices by IDUs has however been provided by various studies, including our own MANIF 2000 cohort study. Finally, our period of observation after initiation of HAART remained confined to a short period. It is sometimes argued that a three month follow up is long enough for observing behaviour change to occur and stabilise. We cannot exclude that long term impact of HAART on sexual and social life of patients may create new opportunities for risk behaviours. Therefore long term follow up is therefore needed, including a more detailed assessment, on the extent to which HAART may be associated with an increase in frequency of episodes of sexual intercourse among treated patients. It remains to be confirmed by additional follow up that patients with continued successful treatment are not more likely than untreated patients to “relapse” to high risk behaviours.

In any case, about one third of our sample of HIV infected IDUs, who benefit from free medical care in French health care system, reported at least one episode of unprotected sexual intercourse during the six months before the last follow up visit. Factors that have previously been shown to be associated with sexual risky behaviours in other studies among people living with HIV/AIDS were also present in our cohort. Some of these factors, like depressive symptoms or heavy alcohol consumption can be targeted for counseling and interventions aimed at facilitating secondary prevention. Of particular concern, in the context of HAART, is the confirmation, in our analysis as in many others, that unprotected sexual intercourse was more likely when both partners were known to be HIV infected. Unsafe sex between HIV positive seroconcordant people has sometimes been interpreted in terms of “negotiated safety.” With the advent of HAART, it has become an important issue to the extent that potential reinfections with viral strains that had already become resistant to antiretroviral drugs may jeopardise the effectiveness of the newly available therapeutic regimens.

The availability of HAART certainly calls more attention about the necessity to increase efforts for both primary and secondary prevention among patients who are already HIV infected. But, our study counters the a priori fears that HAART may facilitate risk behaviours among HIV infected IDUs. Continuing to delay or withhold access to HAART for all IDUs as a class of patients cannot be supported by these data.

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Conflicts of interest: none.

REFERENCES