Integration of Methadone Maintenance Treatment and HIV Care for Injecting Drug Users: a Cohort Study in Bandung, Indonesia

Yanni Melliandari Achmad*, Arifah Nur Istiqomah**, Shelly Iskandar**, Rudi Wisaksana***, Reinout van Crevel****, Teddy Hidayat*

* Health Research Unit, Faculty of Medicine, Padjadjaran University/Hasan Sadikin Hospital. Jl. Pasirkaliki no. 190, Bandung 40151, Indonesia. ** Department of Psychiatric, Faculty of Medicine, Padjadjaran University/Hasan Sadikin Hospital, Bandung, Indonesia. *** Department of Internal Medicine, Faculty of Medicine, Padjadjaran University/Hasan Sadikin Hospital, Bandung, Indonesia. **** Department of Internal Medicine, Radboud University Nijmegen Medical Centre, The Netherlands

Correspondence mail to: melliandari@yahoo.com.

ABSTRACT

Aim: to know the effectiveness of antiretroviral treatment (ART) among methadone clients and patients who started ART outside the methadone program during the same period

Methods: uptake of HIV testing and treatment were evaluated in a cohort of IDUs starting MMT. Effectiveness of anti-retroviral treatment (ART) was compared with matched 175 HIV-patients with a history of IDU outside MMT.

Results: overall, 223 patients were enrolled in MMT between May 2006 and January 2009, of whom 44% were tested for HIV, with an HIV prevalence of 73%. Screening of MMT clients was responsible for diagnosing HIV and starting ART in 31.9%, respectively 45.7%. Two year retention (100% vs 97.1%; p=0.23) and survival (93.9% vs 92.3%; p=0.76) during ART were not significantly different for 35 patients who combined ART with methadone, and the control group (n=175). Virological failure was found in one patient (3.7%) in MMT compared to 10.5% of the control group.

Conclusion: providing HIV testing and treatment is a feasible and effective way to increase detection and treatment of HIV among clients enrolled in MMT. HIV-treatment integrated with methadone maintenance can be very effective. These results support wider application of integrated HIV care and opioid substitution.

Key words: methadone, HIV care, injecting drug user.

INTRODUCTION

Injecting drug use (IDU) is the main risk factor for HIV infection in Indonesia. HIV-prevalence rates above 50% have been found among injecting drug users (IDUs), but unfortunately, many IDUs have not been HIV-tested. For those who are HIV-positive, access to HIV-treatment is usually poor. Health providers often think that IDUs have a poorer adherence to treatment which may compromise its effectiveness and increase circulation of drug-resistant HIV-virus. Indeed, many guidelines suggest only starting HIV-treatment once the opioid dependence has been treated.

Opioid abstinence often shows a higher relapse risk compared with other treatment. Opioid substitution, mostly with methadone, postpones relapse, reduces drug injecting, and is a key to HIV-prevention among IDUs. Methadone maintenance treatment (MMT) may be a good entry point for HIV-testing and effective HIV-treatment. So far, no studies from Indonesia have reported on integration of HIV care and MMT. We evaluated HIV-testing and treatment among clients of a methadone program in Bandung, West-Java, where 70% or more of HIV-infection is due to IDU. The uptake of HIV-testing and treatment was measured, and the effectiveness of antiretroviral treatment (ART) among methadone clients was compared with patients who started ART outside the methadone program during the same period.
METHODS

Study Design and Methods

HIV-status and possible HIV-treatment of methadone clients were evaluated at the time of entry and during their time of enrollment to the methadone maintenance program. In second part of the study, the effectiveness of HIV-treatment among methadone clients was compared with a control group of HIV-patients outside the methadone program, who were matched for the date they started ART.

Setting and Patients

All IDUs enrolled in methadone maintenance treatment (MMT) between May 2006 and January 2009 at Hasan Sadikin hospital as the supervisory hospital for MMT in West Java were included in this cohort study. Following Health Department guidelines, inclusion criteria for patients entering MMT are an age above 18 years, ICD-X criteria for opioid dependence, opioid dependence in the last 12 months and a previous effort to stop using opioids at least once. Since September 2007 methadone clients have been offered voluntary counseling and HIV-testing (VCT), CD4 cell-measurement, and ART in the methadone clinic, on a weekly basis. Measurement of HIV-RNA has only become available since January 2008. A control group was chosen (5:1) of patients taking ART outside MMT. HIV patients with a previous history of IDU, and matched for their date of starting ART, were selected from Teratai clinic, the HIV-policinic in the same hospital as the MMT.

Data Collection and Analysis

Sociodemographic data, history of drug use, history of ART and laboratory results were retrieved from medical records. The proportion of clients diagnosed with HIV-infection, as a result of enrollment to the MMT was calculated as the number diagnosed following screening in MMT divided by the total number of HIV-infected clients. A similar calculation was made for the proportion of patients treated for HIV as a result of enrollment in MMT. To evaluate the effectiveness of ART for MMT-clients, the following endpoints were used: adherence, mortality, retention, virological and immunological response to ART. Adherence (correct intake of medication) was measured by self-report. Death was recorded from medical records. In addition, patients were classified as dead if reported by family or community organizations or confirmed by telephone calls from the clinic. Patients not returning for more than three months without confirmation of death or transfer were considered lost to follow-up. Virological failure was diagnosed when plasma HIV-RNA was above 400 copies/mm³ after at least six months of ART and immunological response was defined as the proportion of patients with a CD4 cell-count > 200 /mm³ after at least six months ART.

Data are presented as mean (SD) if normally distributed, median (interquartile range) if not normally distributed, or as proportion. A 95% confidence interval (95% CI) was calculated around HIV-prevalence. Comparisons between groups were done using chi-square and Mann-Whitney U test. Retention to ART and survival were plotted using Kaplan-Meier survival methods. Differences in retention and mortality were calculated by Cox’s regression and expressed as hazard ratio’s (HR) with 95% CI. All statistical analyses were done using SPSS version 13.00.

RESULTS

Baseline Characteristics

A total of 223 IDUs started MMT between May 2006 and January 2009. MMT-clients had a median age of 27 years (IQR 25 – 30), 93.7% were male, 52.5% were single and 57.4% were employed. They had started injecting drugs at median age of 19 years and used heroin for a median of 10 years before entering the methadone program. A large majority (90.3%) of IDUs were co-infected with hepatitis C.

Utilization of HIV –testing and –treatment

Less than one third (29%) of IDUs knew their HIV status upon entry in the methadone program (Figure 1). Through repeated counseling provided in the MMT clinic, 34 patients (four patients who previously had been tested negative and 30 patients who never had been tested) were tested in MMT clinic. The remaining 128 clients whose HIV-status was unknown were not tested due to refusal (10.9%), death (11.7%), referral (38.3%) and drop-out (39.1%). A total of 72 out of 95 MMT clients tested (75.8%, 95% CI 67.2 - 84.4%) were HIV positive, and 31.9% of HIV-diagnosis was due to counseling and testing in MMT. CD4 cell-count measurements were performed in all HIV-infected clients. From those who had an indication for ART (as CD4 count less than 200 cell/mm³), 72.7% started ART in the MMT clinic (Figure 1). Almost half (44%) of those who were HIV-positive upon entry to MMT, but who had yet to start ART had a CD4 cell-count below 200 cells/mm³. Sixteen patients initiated ART following counseling and CD4-cell measurement in the MMT-clinic, out of a total of 35 on ART (45.7%).

Some drugs, including nevirapine and efavirenz for HIV and rifampicin for tuberculosis induce hepatic
metabolism of methadone.\textsuperscript{10,11} To prevent opioid withdrawal symptoms after starting ART, the methadone dose needs adjustment. The average methadone dose in the last month for 35 MMT clients taking these-drugs was 95.1 mg (IQR 47.9 - 110), compared with 45 mg (IQR 28.7 – 75.5) among MMT-clients not taking ART.

**Response to ART**

Response to ART of all 35 MMT-patients who were started on ART, was compared with 175 HIV patients with a history of IDU who started ART during the same period outside MMT, in the HIV-polclinic of the same hospital. Baseline characteristics of these two groups were mostly similar, except for slight differences in marital status, level of education and initial CD4 cell-count (Table 1). The median follow up of MMT patients was 447 days (IQR 209 – 949) compared with 406 days (IQR 183 – 953) in the control group. Mortality, non-adherence (missed doses of medication) and loss of follow-up did not occur more frequently in the MMT group. For adherence, the number of missed doses in the last month was not statistically different from MMT group (15.8%) compared with the control group (17.6%). These applied also in the number of missed doses in the last week (15.8% versus 12%). Using Kaplan-Meier estimates, mortality during two years of follow-up was slightly lower among MMT clients than among control patients, although this difference was not statistically significant (HR 0.8; 95% CI 0.2-3.2). Similarly, loss to follow-up was not different between groups. HIV-RNA measurements were available for 140 patients. After a median duration of ART of 418 days (IQR 190 - 955), HIV-RNA was below 400 copies/mL in 96.3% of patients enrolled in MMT compared to 89.5% of control patients (p=0.27). CD4 cell-counts were available for 26 MMT clients (median duration 819 days, IQR 336-1007) and 94 control patients (median duration 758 days, IQR 313-1039). No statistically significant difference was noted in the immunological response. Among patients in MMT group, 69.2% had a CD4 cell-count > 200 cells/mm\textsuperscript{3}, compared with 57.4% of patients in the control group (p=0.93).
DISCUSSION

Our data confirm the very high prevalence of HIV among IDUs in Indonesia. HIV is often undiagnosed and untreated, but our study shows that MMT offers a good opportunity to test IDUs for HIV-infection and to initiate HIV-treatment. The longitudinal data show that retention, mortality, and virological response are very good in MMT patients taking ART, and not different from HIV patients in a regular HIV-policlinic.

The prevalence of HIV among IDUs in Indonesia is among the highest in the world.\textsuperscript{12} National reports put the figure at 42.5%. Our figure of 75.8% HIV-prevalence is higher, but of course IDUS in MMT are a selected group. Unfortunately, and in line with official statistics\textsuperscript{13} only a minority of IDUs in MMT were tested for HIV. Through screening in MMT, many patients got tested for HIV and started ART, confirming that MMT may be an entry point for HIV care. As such, MMT can take away some of the psychological or logistic barriers to HIV-testing. Most likely, ‘one stop service’, the long-term relationship with clients, and the chance of repeated counseling facilitate uptake of HIV-services.

Addiction treatments, including methadone maintenance, can improve utilization and effectiveness of ART.\textsuperscript{2-3,7,9} We found that MMT significantly contributed to start of ART, and that retention and treatment outcome were at least as good as in a control group. Through the integration of HIV care with addiction care, many more eligible HIV-infected persons may be engaged to consider HIV therapy and monitoring.\textsuperscript{14,15} Another advantage is that counseling practices that have been tailored to MMT setting can be offered for HIV treatment.\textsuperscript{16} Previous studies have shown a correlation between consistent participation in a methadone program and uptake of, and adherence to ART.\textsuperscript{17} Having one provider control both HIV therapy and other prescribed medications may also reduce the likelihood of drug interactions between medications prescribed by multiple providers, and it may be more cost-effective.\textsuperscript{16}

But integrating HIV-care into MMT also poses particular challenges since this population commonly exhibits several co-morbidities and social issues that complicate the delivery of ART, such as ongoing illegal drug use, non-compliance\textsuperscript{18-19}, psychiatric conditions\textsuperscript{19}, concurrent infections like hepatitis C and late presentation\textsuperscript{20}. Worse clinical outcomes among IDUs have been attributed to a range of problems related to ART access and adherence that fall broadly into the categories of socio-structural, individual-level, and provider-based barriers. Despite these problems, efforts should be made to deliver effective HIV-treatment, both from a patient- and public health perspective. For the individual patient, ART will improve survival, health and quality of life. For the Indonesian setting (like elsewhere)

\begin{table}[h]
\centering
\caption{Baseline characteristics}
\begin{tabular}{|l|c|c|c|c|}
\hline
 & MMT Clients & Control group & \( p \) value &&
\hline
Male gender, % & 97.1 & 93.7 & 0.425 &&
\hline
Mean age, years (SD) & 29.9 (3.8) & 29.1 (3.4) & 0.165 &&
\hline
Methadone dose, mg (median, IQR) & 95.1 (47.9-110) & - & &&
\hline
Marital Status & & & &&
\hline
Married, % & 28.6 & 43.4 & 0.103 &&
\hline
Education & & & &&
\hline
\begin{itemize}
  \item Less than senior high school, % & 2.9 & 6.8 & 0.370 &&
  \item Senior high school, % & 45.7 & 54.9 & 0.322 &&
  \item Academy or university, % & 51.4 & 38.3 & 0.148 &&
\end{itemize}
\hline
BMI at presentation & & & &&
\hline
\begin{itemize}
  \item \(< 18.5 \text{ kg/m}^2, \% & 39.4 & 34.7 & 0.608 &&
  \item median, kg/m\(^2\) (IQR) & 19.4 (17.8-20.6) & 19.7 (17.9-21.7) & 0.299 &&
  \item HBsAg-positive, \% & 2.9 & 8.2 & 0.266 &&
  \item Anti HCV-positive, \% & 90.3 & 92.5 & 0.673 &&
\end{itemize}
\hline
CD4 at time of first presentation & & & &&
\hline
\begin{itemize}
  \item \(< 200 \text{ cells/mm}^3, \% & 100 & 87.3 & 0.138 &&
  \item median, cells/mm\(^3\) (IQR) & 59.1 & 40.7 & 0.078 &&
\end{itemize}
\hline
For MMT-clients, data were missing for BMI (n=2), HCV (n=4); for control patients for age (n=2), marital status (n=1), BMI (n=25), HbsAg (n=5), HCV (n=14), CD4 (n=4).}
\end{tabular}
\end{table}
treatment of IDUs will help reduce HIV-transmission to others, both through sexual contacts and needle sharing.

CONCLUSION

Our study suffers from the limitations of a small study, and from the fact that we could not compare uptake of HIV-services with a group of active IDUs outside MMT. Still we can conclude that MMT may be a good entry point for HIV care, and that HIV treatment can be delivered effectively to IDUs in MMT. Therefore, the results support wider application of integrating HIV care into MMT.

ACKNOWLEDGEMENT

We would like to thank Prof.Dr.dr. Cissy R.S. Prawira, Sp.A(K), MSc, Director of Hasan Sadikin General Hospital, and Dr. Eri Surahman, Sp.An (K), Dean of the Medical Faculty Padjadjaran University for encouraging and accommodating research in their institutions. Dini Norviatin, Agus Darwin Firdaus, Tria Sutrisna, Novianti Yudistianingsih and Kiki helped data collection and entry.

This study was financially supported by ‘IMPACT’ (Integrated Management of Prevention And Control and Treatment of HIV/AIDS), a 5-year program funded by the European Commission.

REFERENCES