Antiretroviral Therapy (ART) Use, Human Immunodeficiency Virus (HIV)-1 RNA Suppression, and Medical Causes of Hospitalization Among HIV-Infected Intravenous Drug Users in the Late ART Era

Gabriel Vallecillo,1 Sergio Mojal,3 Marta Torrens,2 and Roberto Muga1

1Departments of Internal Medicine and Drug Addiction Unit of Psychiatry and 2Drug Addiction Unit of Psychiatry, Hospital del Mar, Universitat Autònoma de Barcelona, Barcelona, Spain; and 3Department of Statistics and Operations Research, Parc de Recerca Biomèdica de Barcelona, Barcelona, Spain

Background. Antiretroviral therapy (ART) has reduced the rates and changed the causes of hospital admission. However, human immunodeficiency virus-positive intravenous drug users (HIV-IDU) continue to have increased hospitalizations and discharge diagnosis are less defined in the late ART era. Our aim was to examine ART use, HIV-1 RNA suppression, and hospital discharge diagnoses among HIV-IDU admitted to an urban hospital.

Methods. A retrospective analysis was made of HIV-IDU admitted for medical causes for the first time (2006–2010). Surgical, obstetric, or mental (except HIV-associated neurocognitive disorder) diagnoses were excluded. Clinical characteristics, number of admissions, and primary discharge diagnoses were determined for each patient.

Results. Three hundred and seventy-five admissions were recorded among 197 hospitalized HIV-IDU. Lifetime prevalence of ART use was 83.2% (164 of 197) and the rate of HIV-1 RNA <50 copies/mL was 38.1% (75 of 197). Primary discharge diagnosis groups were as follows: bacterial infections (59.2%), chronic end-organ damage (16.8%), complications derived from injected drug use (16.8%), malignancies (9.1%), and opportunistic infections (6.6%). Chronic end-organ damage was diagnosed more frequently in patients with HIV-1 RNA <50 copies/mL (36% vs 4.9%; P < .000), and complications derived from injected drug use (23.8% vs 5.3%; P < .0008) and acquired immune deficiency syndrome (AIDS) opportunistic infections (19.8% vs 1.3% P < .019) were usually diagnosed in patients with HIV-1 RNA detectable viral load.

Conclusions. Human immunodeficiency virus-positive intravenous drug users are admitted to hospitals mainly for non-AIDS-related illnesses; however, sustained HIV-1 RNA viral load suppression is poor and determines hospital discharge diagnoses. Providers need to be aware of the management of HIV-related comorbidities and reinforce strategies to improve ART retention in this population.

Keywords. antiretroviral therapy; HIV-infected drug users; hospitalization.

Received 10 February 2014; accepted 26 March 2014.
Correspondence: Gabriel Vallecillo Sánchez, MD, Department of Internal Medicine, Hospital del Mar, Passeig Marítim 25-29, 08003 Barcelona, Spain. (91773@parcesalutmar.cat).

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DOI: 10.1093/ofid/ofu010

With the widespread use of antiretroviral therapy (ART), hospitalization rates, length of stay, and morbidity and mortality have dramatically declined among patients infected with human immunodeficiency virus (HIV) [1–10]. The causes of hospitalization and death in regions where ART is available have shifted from predominantly acquired immune deficiency syndrome (AIDS)-defining opportunistic infections to non-AIDS-related comorbidities [1, 2, 4–7, 9, 10].
Despite a recent reduction in the number of HIV infections attributed to injected drug use in developed countries, drug users still represent a large proportion of individuals living with HIV infection in the era of ART [11] and continue to have disproportionately high hospitalization rates compared with other HIV categories [1, 3, 7, 8, 12]. Late HIV diagnosis, low CD4 counts, and not receiving ART drugs and comorbidities are strong predictors of hospitalization among HIV-positive intravenous drug users (HIV-IDU) [2, 3, 5, 8–10, 12].

However, for HIV-IDU, the causes of hospitalization in the late ART era are less well defined, and whether the use of ART has been able to change the causes of hospital admission in the same way as in the non-drug user HIV population remains unclear.

It should be noted that hospitalizations have become a major outcome measure and constitute a considerable component of excess healthcare costs in this special population [3, 13, 14]. Thus, analyzing the clinical characteristics of admitted patients is a useful strategy to assess the effectiveness of health programs and provide areas of interest to improve healthcare to HIV-IDU.

Therefore, the aim of this study was to examine ART use, HIV-1 RNA suppression, and hospital discharge diagnoses among HIV-IDU admitted to an urban hospital in the late ART era.

**MATERIAL AND METHODS**

A retrospective analysis was undertaken in HIV-IDU admitted for the first time to the Infectious Diseases Unit of The Hospital del Mar from January 2006 to December 2010. The Hospital del Mar is a large tertiary teaching hospital, located in the old part of the city of Barcelona (Spain). The catchment area consists mainly of old buildings, the unemployment rate is high, and there is an overrepresentation of immigrants, people with legal problems, drug trafficking, and commercial sex. The Infectious Diseases unit has 20 beds.

Human immunodeficiency virus-positive IDU aged 18 years or older residing in the hospital area of influence and who had injected an illegal drug in the previous 6 months were included in the study. Human immunodeficiency virus-positive IDU admitted to other hospital services for surgical, obstetric, or mental causes (except HIV-associated neurocognitive disorder) were excluded.

Specialized HIV care, including ART, treatment of substance use disorders, and hospitalization are guaranteed free of cost through Spanish Health System for HIV-IDU.

Demographics and clinical characteristics (CD4 cell count, presence or absence of an AIDS diagnosis, usage of ART, date of hospital admission, discharge diagnosis, and outcomes) were obtained directly from the HIV-infected patient database of the Medical Documentation Service of the Hospital for each patient infected with HIV.

Antiretroviral therapy was defined as a combination of at least 3 drugs from 2 or more classes of antiretroviral agents. On admission, patients were classified as either ART-naive, current ART users, or dropouts (patients who had been on ART but had discontinued the medication more than 1 month before admission).

The International Classification of Diseases (ICD-9 and ICD-10) was used to determine hospital discharge diagnosis. For more than 1 diagnosis, the primary diagnosis leading to hospitalization was used. To characterize causes associated with hospitalizations over the 5-year period, the diagnoses were grouped for analysis as follows: AIDS opportunistic infections, malignancies, chronic end-organ damage (vascular, liver, kidney, lung), nonopportunistic infections, and complications derived from injected drug use (overdose, soft tissue infections, and bacteremia).

Descriptive statistics were expressed as mean, standard deviation, median and range for quantitative variables, and absolute frequencies and percentages for qualitative variables. The χ² or nonparametric tests were applied. Values from \( P < .05 \) were considered statistically significant. Statistical analysis was made with SPSS version 15.0 (SPSS, Chicago, IL).

**RESULTS**

Over the 5-year period, 197 HIV-IDU were hospitalized and 78 (39.6%) patients were readmitted, yielding a total of 375 admissions; this figure represents 14.9% (375 of 2518) of the total admissions to the Infectious Disease Unit.

The clinical characteristics of HIV-IDU admitted to the unit are shown in Table 1.

Substance use disorders were treated in 80% of HIV-IDU at an outpatient center. Lifetime prevalence of ART use was 83.2% (164 of 197) and prevalence of ART use at admission was 50% (99 of 197). Antiretroviral therapy at admission was currently used in 61.3% (97 of 158) of patients receiving treatment of substance use disorders versus 5.1% (2 of 39) who were not (\( P < .000)\). Reasons for not using ART at admission were dropouts from ART in 66.3% (65 of 98) and naive to ART in 33.7% (33 of 98).

Complete viral suppression was observed in 38.1% (75 of 197) of patients. These patients had a higher median CD4 cell count (442 vs 209 cells/μL; \( P < .01 \)) and CD4 cell count > 350 cells/μL (62 of 75 [82.6%] vs 12 of 122 [9.8%]; \( P < .000 \)) than patients who had HIV-1 RNA detectable viral load.

Hospital discharge diagnoses are shown in Table 2. Bacterial infections were the leading cause of hospitalization, mainly bacterial pneumonia, followed by chronic end-organ damage and complications of injected drug use. Acquired immune deficiency syndrome-defining illnesses were diagnosed in 27 of 197 (13.6%) HIV-IDU (6.6% AIDS opportunistic infections, 5.5% recurrent pneumonia, and 1.5% AIDS malignancies).

Causes of inpatient hospitalization according to HIV-1 RNA suppression are shown in Table 3. Patients with HIV-1 RNA suppression are shown in Table 3.
The results of this study show that HIV-1 RNA <50 copies/mL were admitted for chronic end-organ damage, particularly for complications of hepatitis C (20.0% vs 2.5%; P < .0001). In contrast, patients who had a detectable viral load HIV-1 RNA viral load were admitted for complications derived from injected drug use and opportunistic infections.

Hospital readmissions were observed in 39.6% (78 of 197) of patients. Risk factors for readmission were as follows: HIV-1 RNA >50 copies/mL (odds ratio [OR], 4.8; 95% confidence interval [CI], 2.4–9.4; P > .0001), CD4 cell count >350 cells/μL (OR, 3.6; 95% CI, 1.9–6.8; P > .0001), and women (OR, 2.1; 95% CI, 1.1–4.0; P > .03). Causes of readmissions were as follows: bacterial infections, 95 of 178 (53.3%); injected drug use-related complications, 49 of 178 (27.5%); chronic end-organ damage, 26 of 178 (14.6%); and AIDS opportunistic infections, 8 of 178 (4.5%). No patient died in the study period.

DISCUSSION

The rate of successful ART was low at admission in the present study but similar to cohort studies that included active injected drug use [19, 22–24]. This observation implies that adherence interventions should be applied for active drug injectors at the time of ART initiation. In this regard, clinical guidelines and policy recommendations support integrating substance use disorder treatment into ART [25–26] to facilitate the use of directly observed therapy that sustains treatment adherence and leads to clinically significant improvements in health outcomes [27–34].

Other factors associated with a reduction in hospitalization rates in HIV patients are a higher nadir and proximal CD4 counts >350 cells/μL [2, 4–9]. This study revealed that two thirds of patients had CD4 counts <350 cells/μL. Historically, HIV-IDU started ART with significantly lower CD4+ T cell counts, had more advanced HIV disease, and worse immune recovery compared with other HIV groups [35]. These data emphasize the need for including in specific health programs to achieve immune recovery and successful therapy in HIV-IDU.

The majority of hospitalizations observed were not related to HIV in this study, and it highlights the importance of providers being aware of the management of HIV-related comorbidities and of patients being included in preventive health programs to reduce the probability of hospitalization.

Bacterial pneumonia and other bacterial infections were the most common causes of admission, as described in other HIV-transmission categories [36]. Pneumococcal vaccination is a reasonable prevention strategy for patients infected with HIV at all stages of immunodeficiency, and efforts should be directed towards improving vaccination levels among HIV-IDU [36].

Liver disease was the main cause of chronic end-organ damage observed in this study, particularly among patients on ART.
However, treatment of hepatitis C virus (HCV) is restricted in drug users owing to their continued use of injected drugs. An alternative is the provision of assessment and treatment via opioid substitution treatment clinics, which has proven to be an effective means of engaging populations with a high HCV prevalence [37, 38].

Furthermore, unlike non-intravenous drug user HIV patients, skin and soft tissue infections are also common, injection-related complications that lead intravenous drug user to hospitalization. By providing environments in which these patients can receive supervised injection, overdose management, and education, supervised injecting facilities can reduce...

| Groups of Causes | Diagnoses | No. (%) | Etiologies | No. |
|------------------|-----------|---------|------------|-----|
| Bacterial infections | Pneumonia | 70 (35.5%) | *Streptococcus pneumoniae* | 47 |
| | Haemophilus influenzae | 6 |
| | Nonfiliated | 17 |
| | Salmonella sp | 7 |
| | *Escherichia coli* | 5 |
| | Campylobacter jejuni | 3 |
| Enteric infections | 15 (7.7%) | *E coli* | 6 |
| Urinary tract infections | 8 (4.0%) | *S pneumoniae* | 3 |
| | *Neisseria meningitidis* | 1 |
| Meningitis | 4 (2.0%) | | |

| Chronic end-organ damage | Hepatitis C | 21 (10.7%) | Decompensated cirrhosis | 21 |
| Cardiovascular disease | 9 (4.6%) | Chronic heart failure | 9 |
| Kidney disease | 3 (1.5%) | Acute nephritis | 3 |
| Complications of IDU | Soft tissue infections/bacteriemia | 21 (10.7%) | Cellulitis | 17 |
| | | | Endocarditis | 3 |
| | | | Osteomyelitis | 1 |
| | Overdose | 12 (6.1%) | Overdose | 12 |
| Malignancies | Non-AIDS malignancies | 15 (7.5%) | Lung | 9 |
| | | | Colorectal | 3 |
| | | | Breast | 2 |
| | | | Hodgkin’s lymphoma | 1 |
| | AIDS-malignancies | 3 (1.5%) | Non-Hodgkin’s lymphoma | 3 |
| AIDS opportunistic infections | AIDS opportunistic infections | 13 (6.6%) | *Pulmonary tuberculosis* | 6 |
| | | | *Pneumocystis* | 4 |
| | | | jiurovecii Cerebral toxoplasmosis | 2 |
| | | | Esophageal candidiasis | 1 |
| ART secondary effects | ART secondary effects | 3 (1.5%) | Anemia zidovudine | 2 |
| | | | Acute renal failure tenofovir | 1 |

Abbreviations: AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy; HIV, human immunodeficiency virus; IDU, intravenous drug use.

| Groups of Causes | Total Group No. (%) | HIV-1 RNA 50 < Copies/mL No. (%) | HIV-1 RNA 50 > Copies/mL No. (%) | P |
|------------------|---------------------|-----------------------------------|-----------------------------------|---|
| Bacterial infections | 97 (69.2%) | 31 (41.3%) | 66 (54.1%) | .081 |
| Chronic end-organ damage | 33 (16.8%) | 27 (36.0%) | 6 (4.9%) | .0000 |
| Complications derivatives of IDU | 33 (16.%) | 4 (5.3%) | 29 (23.8%) | .0008 |
| Malignancies | 18 (9.1%) | 12 (12.0 %) | 6 (7.4%) | .277 |
| AIDS opportunistic infections | 13 (6.6%) | 2 (1.3%) | 12 (9.8%) | .019 |
| HAART secondary effects | 3 (1.5%) | 3 (4.0%) | 0 (0.0%) | .026 |

Abbreviations: AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy; HAART, highly active ART; HIV, human immunodeficiency virus; IDU, intravenous drug use.
hospitalization rates for complications of intravenous drug use and support the importance of implementing needle and syringe programs for drug users [39].

Apart from the limitation of being a cross-sectional study, including the lack of a non-intravenous drug user HIV-positive control group, the study was conducted at a single center, and thus the sample might not be representative of the whole population since the impact of external factors may have significantly affected the admission patterns and demographics of this study population. However, the hospital where the study was conducted is located in one of the areas of the city with a high prevalence of intravenous drug use and immigration, and these findings may be consistent with those of other centers. Furthermore, the study was conducted over an extended period of time.

In summary, HIV-IDU are admitted mainly for non-AIDS-related illnesses in the late ART era; however, current ART use is low and the discontinuation of ART is frequent. To reduce the probability of hospitalization, providers need to be aware of the management of HIV-related comorbidities, especially hepatitis C coinfection, and include patients in preventive health programs. Integrated and multidisciplinary care of the patients infected with HIV-1 should be implemented to achieve successful HIV-1-RNA suppression among HIV-IDU.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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