Access to highly active antiretroviral therapy for injection drug users: adherence, resistance, and death

Acesso de usuários de drogas injetáveis ao tratamento anti-retroviral altamente potente: aderência, resistência e mortalidade

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Abstract

Injection drug users (IDUs) continue to comprise a major risk group for HIV infection throughout the world and represent the focal population for HIV epidemics in Asia and Eastern Europe/Russia. HIV prevention programs have ranged from HIV testing and counseling, education, behavioral and network interventions, drug abuse treatment, bleach disinfection of needles, needle exchange and expanded syringe access, as well as reducing transition to injection and primary substance abuse prevention. With the advent of highly active antiretroviral therapy (HAART) in 1996, dramatic clinical improvements have been seen. In addition, the treatment's impact on reducing HIV viral load (and therefore transmission by all routes) provides a stronger rationale for an expansion of the focus on prevention to emphasize early identification and treatment of HIV infected individuals. However, treatment of IDUs has many challenges including adherence, resistance and relapse to high risk behaviors, all of which impact issues of access and ultimately effectiveness of potent antiretroviral treatment. A major current challenge in addressing the HIV epidemic revolves around an appropriate approach to HIV treatment for IDUs.

Highly Active Antiretroviral Therapy; Intravenous Substance Abuse; HIV Infections

Introduction

Background of drug user related HIV risks

The association of drug abuse and HIV infection is well appreciated and several mechanisms may underlie this association. Foremost, administration of drugs by injection with multiple reuse of injection equipment, and possibly sharing straws or pipes for inhalation, can transmit fluids that contain HIV [1,2]. Also, the psychoactive effect of drugs can impair judgment and reduce impulse control for sexual as well as injection risks and treatment adherence [3]. Finally, the direct pharmacologic action of drugs on immunological susceptibility or up-regulation of HIV has been reported in vitro and in vivo [4]. While data on the impact of continuing drug use on HIV progression has been inconclusive [5], the role of drugs in HIV acquisition remains an open question and warrants further research [6].

Scope of the problem

In 2004, the World Health Organization (WHO) reported that estimates of injection drug user (IDU) prevalence were available for 130 countries and the number of IDUs worldwide is approximately 13.2 million [7]. Over ten million (78%) live in developing and transitional countries (Eastern Europe and Central Asia, 3.1 mil-

lion; South and Southeast Asia, 3.3 million; East-Asia and Pacific, 2.3 million) [8]. HIV prevalence among IDUs of over 20% was reported for at least one site in 25 (of 78 reporting) countries and territories: Belarus, Estonia, Kazakhstan, Russia, Ukraine, Italy, Netherlands, Portugal, Serbia and Montenegro, Spain, Libya, India, Indonesia, Malaysia, Myanmar, Nepal, Thailand, Vietnam, China, Argentina, Brazil, Uruguay, Puerto Rico, USA and Canada. Twenty-six countries reported injection drug use as the primary mode of HIV transmission [7]. Comparable data on drugs used by other modes of administration are sparse. The UN Office of Drug Control estimates world wide there are over 200 million illicit drug users; 34 million using amphetamines, 15 million using opiates, 14 million using cocaine, 8 million using ecstasy (http://www.unodc.org/unodc/en/global_ilicit_drug_trends.html, accessed on 09/Mar/2005). Alcohol use is considerably higher [9]. Thus, the problem of HIV infection among injection and non-injection drug users is prevalent world-wide.

Approaches to preventing acquisition of HIV infection in drug users

The most widely advocated approach for prevention of HIV transmission among drug users has been drug abuse treatment [10]. Early clinical trials have shown that methadone treatment reduces drug use although relapse is frequent [11]. Limited observational data suggest lower HIV rates in IDUs during drug abuse treatment [12], but it is difficult to determine whether the lower rates reflect selection issues. No trial has been reported to show whether treatment (rather than selection) reduces HIV incidence. To date, only the U.S. National Institutes of Health (NIH) funded HIV Prevention Trial Network (HPTN) protocol (058), testing a newly approved medication, buprenorpine, will address this question for opiate users. While opiate treatments have received considerable attention, HIV infection related to stimulant abuse (cocaine, methamphetamines) whether injected, ingested or inhaled, has received growing attention especially from recent reports relating a link between stimulant use and the resurgence of risky behavior (e.g., barebacking) and HIV infection in gay men in the US, South America and Asia [13,14,15,16,17,19,19,20,21,22,23]. Behavioral and pharmaceutical treatments for stimulant abuse are evolving and early data suggest promise for reducing sexual risk [24,25]; formal evaluation of these treatments for reducing HIV incidence is urgently needed. Marijuana and alcohol abuse are more widespread and of concern globally including Africa [26,27,28], but have received considerably less attention by the HIV prevention community.

Other approaches for HIV prevention are needed for those who can not or will not stop injection drug use. While results from multiple trials of counseling/testing and individual level cognitive behavioral interventions in IDUs have been disappointing [29,30], interventions using a social learning theory based approach [31] including peer networks and, more broadly, indigenous opinion leaders have shown promise in reducing risk behavior [32,33,34,35]. Currently, The HPTN protocol 037 is in the field and provides a formal test of peer network intervention in two countries, using HIV seroconversion as the primary outcome. While field data on disinfection of injection equipment has been disappointing [36,37,38,39,40], improved access to sterile injection equipment has been studied extensively and shown to reduce HIV incidence [41].

While drug abuse treatment, network and outreach approaches represent the current state of the science, their influence is dependent upon local norms and policies. Researchers have been moving beyond individual and peer network interventions, which are essentially individual or dyadic, toward structural and multi-level interventions [42,43,44,45,46,47,48,49,50,51,52,53,54,55]. Recent data from China for a primary substance abuse prevention effort showed promising results although HIV outcomes were not considered [56]. For IDUs, structural interventions involve policy changes such as increasing availability of substance abuse treatment and access to sterile syringes, e.g., removing requirements that penalize prescription and possession of sterile syringes; nonrandomized designs have shown reductions in high risk behaviors [57,58], although the impact on HIV acquisition remains unknown. Multilevel interventions include education not only of IDUs through street outreach, but also of providers (e.g., pharmacists) and the community to support HIV prevention efforts; nonrandomized designs have shown reductions in high risk behaviors [47,51,54]. A coordinated approach with multiple components of intervention at varying levels are urgently needed as new HIV epidemics among IDUs often are characterized by rapid and even explosive spread in many countries, including China, Russia, Ukraine, Brazil, India and Vietnam, where HIV prevalence has increased from < 10% to > 40% in a one-year time period [1].

Admittedly, evaluation of multi-component programs directed at multiple levels (consumer,

provider, community) is difficult. For example, traditional prospective designs for cohort formation and follow-up have been difficult to field for drug users. However, a convergence of methodological advances in serial cross-sectional design using rapid assessments [59], randomization by geographic units, respondent driven sampling (http://www.respondentdriven-sampling.org, accessed on 09/Mar/2005) and detuned assays for HIV [60] (using cross-sectional surveys with state-of-the-art laboratory assays that can determine the prevalence of recent – past six months – infections among those who are screened HIV positive) have provided a feasible alternative to community trials. With limited data suggesting effectiveness for each prevention component, a non-intervention control group is ethically suspect; a more appropriate design that conforms to the reality of staggered introduction across geographical units is to compare early versus delayed intervention sites. Alternatively, interventions for the control group that focus on other potentially helpful behavior changes are being applied in the field, often in response to suggestions from community advisory boards or other advocacy groups. The underlying approach of multi-component interventions (e.g., drug abuse treatment, needle exchange, outreach, etc.) performed at multiple levels (outreach to drug users, to pharmacists who can dispense syringes, etc.) is not merely to provide wider coverage of as many program parts as possible, but to provide the conditions for changing norms at multiple levels to reinforce the importance of sustained HIV risk reduction.

Risks with modes of transmission other than drug administration

Factors other than multiple reuse of injection equipment are important in controlling HIV among IDUs. As noted above, sexual risks from drug use are vast. A common but faulty image of drug users as a socially marginalized community undermines the fact that drug users can play a critical role in the spread of HIV into the broader population through heterosexual, homosexual and perinatal transmission. Recent reports show that IDUs who reduced injection risk had not similarly reduced their sexual risks [61,62,63]. Stimulant use in gay men, which is reported with increasing frequency, is associated with elevated HIV risk [13,14,15,16,17,18,19,20,21,22,23]. Overlapping drug and sexual risks are reported for especially vulnerable youth around the world, such as children living in the streets [64]. To date, formal evaluation with randomized controlled trials of programs for reducing substance use related HIV risks (direct and indirect, as with effects on sexual risks) has lagged behind trials for other areas of HIV prevention (e.g., STDs control, early HIV treatment, reducing perinatal transmission); conversely, these other interventions have not fully considered or incorporated implications of substance abuse, including alcohol. Sufficient data are now available to develop and scale up trials relating to reducing a broader array of substance use related HIV risks.

Primary and secondary prevention of HIV with antiretroviral treatment for drug users

Highly active antiretroviral therapy (HAART) significantly improves the prognosis of HIV-infected persons, by reducing HIV viral load, increasing CD4+ cell levels, delaying progression to AIDS and reducing mortality [65,66,67,68,69,70,71]. A secondary consideration is that the reduced HIV viral load may be important for reducing transmission, and as such, the availability of HAART may be an important addition to the arsenal of HIV prevention tools described thus far. However, there are a number of considerations about the use of HAART in populations of drug users. The unresolved issues include questions about whether the degree of effectiveness of HAART is affected by potential differences between the natural history of HIV infection in drug users and other populations (due to the effects of the illicit drugs themselves on natural history) and concerns about access to HIV treatment and adherence to HAART regimens. In addition, questions of treatment effectiveness for IDUs lead to concerns about whether clinical improvement may lead to behavioral relapse, which in turn may lead to reduced regime adherence, the development of antiretroviral therapy resistance, and, ultimately, its transmission to others through risky sexual and/or drug use behaviors.

Natural history of HIV in drug users

Providing HIV treatment to drug users first must acknowledge that guidelines for treatment have been developed primarily from cohort studies that have not included drug users or considered drug use within the population being studied. An early question therefore is whether the natural history of HIV infection is influenced by use of illicit drugs. An analysis comparing HIV seroconverters in the ALIVE

Study (IDUs) to seroconverters in the SHARE study (men who have sex with men or MSM) in Baltimore, USA, found that there were larger changes in CD4+ and CD8+ among MSM following seroconversion compared to IDU [72]. However, these modest and non-significant differences were limited to the first two years after seroconversion, after which point CD4+ decline rates converged. While this report was limited to observations up to four years post seroconversion, a study by Pezzotti et al. [73] examined CD4+ cell decline among seroconverters with longer follow-up and found a continued pattern of no difference by active or former drug use or between exposure risk groups (including IDUs, MSM and persons infected by heterosexual contact). While the ALIVE study was complicated by the fact that over two-thirds of drug users were poly-substances users, the Italian cohort was limited predominantly to heroin only users, thus reducing the concern that differences observed in laboratory studies compared to those observed in cohort studies were a function polydrug use, which may have offset the effects of individual drug use on CD4+ decline. In an early analysis (before the advent of HAART) that compared rate of progression to AIDS between injection drug users from Baltimore (mostly African-American) and Italy (mostly white) as well as comparison to Italian MSM and those infected through heterosexual contact, no differences were noted after accounting for age [74], suggesting that natural history of HIV was unlikely to be affected in a major way by use of illicit drugs. The implications were that concerns over a possible difference in HIV progression due to illicit drug use would not be a major consideration when developing clinical guidelines for HIV treatment. Data on effectiveness of HAART should not therefore differ between risk groups, and treatment should not be withheld from IDUs seeking care because of concerns with the effect of continuing opioid or other drug use on HAART.

Effectiveness of HAART in HIV infected injection drug users

Epidemiologic studies of the effects of drug use on the course of HIV progression among those who have initiated HAART have shown mixed results [75,76,77,78,79,80]. Findings from the Swiss HIV Cohort Study [75] and the EuroSIDA study [76] provide evidence indicating no significant difference in HIV progression among injection drug users compared to MSM and heterosexual HIV seropositive individuals receiving HAART. Two reports were published from the ALIVE study, showing high effectiveness of HAART among IDUs with late stage HIV infection with no differences by type, frequency or route of administration [77,78]. However, Lucas et al. [79] reported reduced HAART induced viral load suppression among active IDUs compared to former and non-users (0.8 $\log_{10}$ copies/ml versus1.6 $\log_{10}$ copies/ml in former users and 1.7 $\log_{10}$ copies/ml in non-users). The authors found these findings were significantly associated with lack of utilization and adherence to HAART among active injection drug users compared to former and non-users (34% vs. 17% in former users and 24% in nonusers) [77]. In addition, while Johns Hopkins HIV Clinic investigators Poundstone et al. [80] noted substantial reductions in time to AIDS and death during the HAART era, they found that these gains did not apply equally to IDU. In fact, there was reduced disease-free survival time among IDU compared to non-IDU in the HAART era compared to the period before the advent of HAART [80]. These findings raise the question of whether higher mortality in drug users is due to access [81] and adherence [82] rather than effects of the drug use per se.

Access to HIV therapy has been an issue for injection drug users

One of the observations from surveillance and cohort data that compares pre- and HAART era HIV care without discriminating who receives treatment is that outcomes are generally worse for IDUs. A principal inference drawn from these observations is that IDUs appear to benefit less because they have less access to HAART. Several studies have examined this issue. Within a year after the introduction of HAART, two cross-sectional studies of HAART use among IDUs were reported. In Vancouver, Canada, where antiretroviral therapy (ART) is offered free to all HIV-infected persons who meet International AIDS Society-USA panel (IAS-USA) guidelines [83], only 40% of eligible IDUs received any ART, and 27% received HAART [84]. Younger individuals, females, those not currently enrolled in drug treatment, and those with inexperienced physicians were less likely to be receiving HAART. In Baltimore, during the same interval, the ALIVE study showed that 14% of treatment-eligible IDUs reported HAART use between July 1996 and June 1997; 49% reported no treatment [85]. Factors associated with reporting no ART use included active drug use, sub-optimal HIV health care, not receiving drug treatment and recent incarcera-

tion. In a subsequent analysis [81], by June 30, 1999, 58.5% of participants initiated HAART, most of whom switched from mono- or dual combination therapy (which were no longer recommended) to a HAART regimen. However, nearly one-third of treatment-eligible IDUs never received antiretroviral therapy. Cox proportional hazards regression showed that initiating HAART was independently associated with not injecting drugs, methadone treatment among men, having health insurance and a regular source of care, lower CD4+ cell count and a history of antiretroviral therapy.

In contrast, use of HAART was quickly adopted in several other populations. For example, in a random sample of HIV-infected individuals in the HIV Cost and Services Utilization Study (HCSUS), 85% of participants eligible for therapy (CD4+ cell count less than 0.50 x 10^9/L) reported receiving a PI or non-nucleoside reverse transcriptase inhibitor (NNRTI) treatment by January 31, 1998 [86]. In this national study, inadequate HIV care was more common among Blacks and Latinos, the uninsured and Medicaid-insured, women and risk groups other than men who had sex with men, even after adjusting for CD4+ cell counts. These data indicate that use of HAART may be less common in those with poor access to health care. Data from the HCSUS represents individuals receiving ongoing care; the sampling strategy used thus under-represents those with access barriers to care [87]. While 20% of all HCSUS participants were uninsured and 48% covered by Medicaid, among IDUs these percentages were 15% and 71%, respectively [87]. In the ALIVE cohort [81], a larger percentage (33%) of IDUs are uninsured, and fewer (54%) are covered by Medicaid (which generally does not cover medical care for indigent men), underscoring the strong association between health care access and the initiation of effective HIV treatment. Unlike the national data, however, our participants who reported Medicaid insurance were as likely to receive HAART as those who were privately insured. The level of HAART use was substantially lower among our cohort of drug users than the HCSUS drug users.

What is likely to account for lower utilization of HAART among IDUs? Poor utilization of health care among IDUs can be partially explained by the fact that HIV-infected IDUs seek medical attention significantly later in the course of disease, often first presenting to medical care at the time of an AIDS-defining opportunistic infection [88,89,90,91,92]. Once access to care has been addressed, non-HAART use may reflect provider caution in prescribing HAART. Physician experience with HIV care has also been shown to be associated with IDUs receiving optimal therapy [84]. Studies have shown improved outcomes among HIV-infected patients treated by experienced physicians [93,94,95]. Likewise, less experienced providers may continue patients on non-HAART regimens until the patient demonstrates adherence with their medications and clinic visits and substance abuse is under control. Some providers may believe that if IDUs are less likely to attain undetectable viral loads than non-IDUs because of poorer adherence [96], there could be potential transmission of multi-drug resistant HIV [97,98]. To ensure long-term success of antiretroviral treatment in patients who can wait to initiate HAART, experienced providers often recommend delaying therapy, until adherence-related issues are addressed [12,25,99,100]. Such issues, which include drug and alcohol use, active mental illness, including depression, and homelessness, require referrals to substance abuse treatment, psychiatrists, and social workers. Other factors that may impact adherence to antiretroviral therapy include poor knowledge about HIV infection and treatment and the lack of belief in the efficacy of antiretroviral therapy, which require continual counseling by providers.

In terms of addressing the use of HAART for drug users, integrating ART regimens and drug abuse treatment may offer one avenue for the effective management of these two related medical problems. Current treatment guidelines call for addressing issues of substance abuse as an integral component of HIV management. Participants who reported being on methadone maintenance may be viewed by their providers as being stable and more likely to be adherent to HAART regimens, although some data suggest that this may not be the case for women [81]. It is also possible that methadone treatment may encourage health-seeking behaviors, including ART utilization, among drug users who had previously not sought care. As providers become more experienced in the HIV treatment of drug users, there appears to be increased willingness to prescribe more complex and aggressive therapies for this population. Although several factors are shown to be associated with initiating HAART, ultimately, the decision to start therapy needs to be individualized for each patient.

Adherence

Adherence to antiretroviral regimens is critical for HIV treatment success [101,102] with adher-

ence levels of 90% or more commonly cited as essential for maximal virologic suppression and immunologic protection [103] and in preventing the development of drug resistant viruses [104]. This level of adherence is higher than that required for acceptable treatment of other chronic diseases [105]. This level of adherence is also difficult to attain given that average adherence rates of 70-75% are found in primary care settings [103,106].

As noted above, studies have shown that IDUs are less likely to receive HAART compared to non-drug users [84,85,86]. This underutilization of HAART has been attributed to provider concern about injection drug users' potential for non-adherence due to their unstable lifestyle and other psychosocial problems. Most studies have found injection drug users to be less adherent to combination therapies [107,108,109], but some reports involving small numbers of injection drug users have found the opposite [103,110].

In a recent study from the ALIVE Study [111], 76% of 366 participants reported 90% or more adherence to their ART in the prior 3 days. Almost half were on a HAART regimen, of which 64% were adherent compared to just 36% among those on non-HAART regimens. This study uses multivariate analyses to show that better adherence was significantly and independently associated with the lack of daily injection drug use, absence of medication-related side effects, use of a medication reminder, and recent participation in a methadone maintenance program.

A major factor in lack of adherence to HIV regimens among substance users is active drug use. Two studies reported a strong relationship between non-adherence and suboptimal virologic and immunologic responses to HIV therapy when the treated individual was an active drug user [109,112]. While the association of active injection drug use and non-adherence is consistent across most studies [106,109,112], the finding of no similar significant association among those who occasionally injected suggests that in this case some were adherent and others were not.

The role of drug abuse treatment in adherence has been well established. Early studies that found significantly more adherence among those who attended a methadone program than those who did not attend [113,114]. Earlier reports also showed that individuals who attend methadone maintenance treatment programs exhibit a desire for drug addiction recovery and that those who attend such programs are more likely to practice positive health behaviors [115,116,117,118]. Getting injection drug users into drug treatment programs and consistent participation in these programs is essential to reduce their risk behaviors.

With respect to factors associated with ART adherence, important considerations are positive attitude about treatment [119] and medication reminders [106,108,120,121]. Forgetfulness is a common reason for missing or skipping a dose, and is a frequently cited reason for lack of adherence across HIV infected populations [106, 107,108,121,122,123]. Assistance with adherence and addressing ongoing illicit drug use may enable occasional users to be more adherent to their antiretrovirals.

Impact of HAART on sexual risk relapse

Before starting HAART, risk behavior among HIV seropositive people might have been dampened due to concerns about not transmitting to others or due to lack of energy to engage in sexual (including risky) behaviors. With the advent of HAART, there is a concern that persons receiving HAART could relapse to high risk behaviors because learning that they have "undetectable viral load" may lead them to believe they are no longer infectious or simply because feeling better and more invigorated may stimulate interest in sex. However, undetectable viral load does not mean absence of virus, and a relapse could result in possible transmission.

The concern about relapse to high risk behaviors has been examined in a variety of populations. Recent reports indicate increases in high-risk sexual behaviors, anal/rectal gonorrhea, and HIV seroincidence among gay and bi-sexual populations in the HAART era [124,125]. Other studies have reported decreased concerns about HIV infection and diminished caution with sexual and drug-use behaviors associated with new HIV therapies [126,127,128,129, 130,131]. A recent study found HAART use among gay men to be significantly associated with subsequent increased high-risk sexual behaviors [132]. Few studies, however, have reported on reported risk behaviors among IDUs after initiating HAART. A study of HIV-infected French IDUs showed a significant association between HAART use and decreased sexual risk [133]. However, another study, among IDUs in Baltimore, reported increased sexual activity, including unprotected sex, among HAART users in the 6-month period after HAART initiation, compared to declines in these activities among those who did not initiate HAART [134]. HAART initiation, however, was not associated with resumption of drug injection or needle sharing.

The Baltimore study also considered whether this increase in risky behavior might have been due to "feeling better" or to belief in reduced transmissibility. The data showed no significant difference in the probability of engaging in sex or unprotected sex after HAART when comparing those whose HIV-associated symptoms decreased after HAART to those whose did not [135]. This may suggest that engaging in any sex and unprotected sex may not be a result of improved clinical health or functional status. However, the perception that sexual transmission of HIV is less likely because of HAART and consequent undetectable viral loads was an important factor associated with unprotected sex among HIV-seropositive individuals in the Baltimore study [136]. This supports current concerns raised by the public health community that high-risk populations have become complacent about behaviors that reduce the risk of transmission of HIV and other blood-borne pathogens. This study also supports results obtained in studies of gay/bisexual populations [131], which have experienced a more significant impact of HIV treatments due to greater awareness and higher utilization of HAART. More recently, a meta-analysis examined this question across studies and concluded that relapse to risky behaviors was not a widespread problem [137].

Drug resistance transmission risk

The dual issues of HAART effectiveness with poor adherence and possible relapse to high risk sex raises not just the issue of transmitting HIV, but also of transmission of drug resistant HIV to needle sharing or sexual partners, which can limit treatment options in those who become infected with these strains [138]. A recent case in New York City of drug resistant HIV infection and rapid progression to AIDS in a gay man who used methamphetamine drew considerable attention [139]. How often this occurs is difficult to assess, but several studies have measured the prevalence of genotypic and/or phenotypic resistance among recent HIV seroconverters (who by definition should not have been previously exposed to HAART) [138,140,141,142,143,144,145,146,147,148,149]. The strongest evidence for transmission of drug-resistant HIV comes from studies showing that up to one-quarter (27%) of HIV seroconverters have drug resistance mutations [141,142,143,144,145,146, 147,148]. For someone to become infected with drug-resistant HIV, that individual must engage in high-risk behavior with a partner who has drug resistance and a viral load that is high enough to allow for HIV transmission. In a study of IDUs in Baltimore [150], among HIV-infected IDUs who engaged in high-risk behavior and had an elevated viral load, 13% had clinically significant resistance, placing their partners at risk for acquiring a drug-resistant HIV strain. The extent to which this is or will become a problem needs to receive attention not only in targeted surveillance but also through HIV prevention messages.

Conclusion

The use of HAART for HIV infected illicit drug users remains a complex medical, social and legal issue. Issues of adherence and relapse to risky sexual behavior and development of transmittable resistance to medications all need to be simultaneously addressed. However, reduced access to medication can not be an *a priori* condition, for once barriers to access are resolved through various means, treatment should be considered. Although some studies have shown effectiveness of HAART in drug users was worse than others patients [79,80], not all studies report differences between risk groups [76] and definitions of HAART have varied. In a recent report, dramatic improvement in survival was identified in IDUs in pre- vs. post-1996 analyses (85% reduction in risk) and to a lesser extent in the data restricted to the HAART era that compared treated vs. untreated (50% reduction in risk) [71]. Some literature suggests that the discrepancy between HAART clinical trials showing 90% improvement [65] and clinical studies that show 50-70% improvement was likely due to problems with adherence. Such a conclusion has obvious implications for recommendations for treatment. Epidemiologic studies that showed improvement based on pre- vs. HAART era comparisons in fact might be due to confounding or biasing factors such as survival or frailty biases (rather than perhaps a true improvement due to the medical regimen). However, a recent analysis of putative bias and confounding factors [71] noted that the difference in results noted above was related not only to a dramatic improvement (from pre- to HAART era) among those who received HAART but also among those who had not received HAART after 1996. Further analyses suggested that the differences were more likely to be due to treatment selection (who gets treated and what medications are prescribed), and that effectiveness was not affected by type, frequency or duration of illicit drug use or drug abuse treatment. The implications are that treatment

can be effective in persons who have used illicit drugs.

While there is significant reluctance among medical care providers to begin HAART therapy with active drug users, the evidence base supporting this decision is quite limited. In our review of the existing literature, the data are not terribly clear on the benefit/risk ratio of commencing HAART therapy earlier rather than suspending initiation until the substance abuse problem in dealt with through replacement therapy. The few reports with empirical data on substance use and HIV therapy effectiveness in general do not show any additional risk and treatment appears to have excellent impact on both viral load and CD4+ cell count gains. Overcoming residual stigma and discrimination towards drug users by the medical community is essential for optimal treatment to occur. Data to date suggest that drug use is not an automatic exclusion criterion for prescribing HAART.

Resumo

Os usuários de drogas injetáveis (UDI) ainda representam um importante grupo de risco para a infecção pelo HIV no mundo em geral, além de constituir o grupo central das epidemias de HIV na Ásia e no Leste Europeu e Rússia. Os programas de prevenção do HIV variam, desde a testagem sorológica e aconselhamento, educação, intervenções comportamentais e em redes, tratamento da dependência química, desinfecção de agulhas com água sanitária, troca de agulhas e ampliação do acesso a seringas, além da redução da transição ao uso injetável e a prevenção primária da dependência química. Com o advento da terapia antiretroviral altamente potente (HAART), em 1996, houve uma melhora clínica dramática. Além disso, o impacto do tratamento sobre a redução da carga viral de HIV (e, portanto, da transmissão do vírus por todas as vias) fornece uma forte justificativa para a ampliação do escopo da prevenção, no sentido de enfatizar a identificação e tratamento precoce de indivíduos infectados. Entretanto, o tratamento dos UDI apresenta inúmeros desafios, inclusive em relação à aderência, resistência e recaída para comportamentos de alto risco, todas as quais têm impacto sobre questões de acesso e, na última análise, da eficácia da HAART. Um importante desafio para o enfrentamento atual da epidemia do HIV gira em torno da busca de uma abordagem apropriada para o tratamento do HIV/AIDS em UDIs.

Terapia Anti-retroviral de Alta Atividade; Uso Indevido de Substâncias Parenterais; Infecções por HIV

Contributors

D. Vlahov & D. D. Celentano both identified and abstracted the literature, contributed writing sections for the first draft, and both completed writing, review and approval of final draft. As this was a literature review, no ethics review was undertaken. The authors have no conflict of interest.

Acknowledgments

Supported in part by the National Institute on Drug Abuse (DA 04334).

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Submitted on 4/Jul/2005
Approved on 28/Jul/2005