REVIEW ARTICLE

From Addiction to Infection: Managing Drug Abuse in the Context of HIV/AIDS in Africa

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Abstract

People who use drugs are at higher risk of HIV: directly through the sharing of injecting equipment, indirectly through associated risk behavior, and physiologically through the substances' impact on the immune system. Drug users, especially people who inject drugs (PWID) are a bridge to the general population. The treatment of drug addiction and provision of harm reduction interventions have impact on HIV transmission and incidence. Addiction treatment reduces the frequency of drug-related risky behaviors and enhances access and adherence to HIV treatment, resulting in fewer new infections. However, the drug policies of many African countries are punitive and hostile to harm reduction programs. These fuel criminalization of drug use and discrimination against the drug user thereby preventing individuals with drug addiction from accessing treatment programs. There is need to formulate policies aimed at protecting the rights of people with drug addiction and address the ethical aspects of treatment. *(Afr J Reprod Health 2014; 18[3]: 47-54)*

Keywords: Drug users, Drug addiction, Substance use, HIV infection, Africa

Résumé

Les toxicomanes sont plus à risque d'être atteints par le VIH: directement à travers le partage de matériel d'injection, indirectement par l'intermédiaire des comportements à risque associés, et physiologiquement par l'impact des substances sur le système immunitaire. Les usagers de drogues, en particulier les personnes qui s'injectent des drogues (PSiD) sont un pont à la population générale. Le traitement de la toxicomanie et de la fourniture des interventions de la réduction des méfaits ont un impact sur la transmission et l'incidence du VIH. Le traitement de la toxicomanie réduit la fréquence des comportements à risque liés à la drogue et améliore l'accès et l'adhésion au traitement du VIH, ce qui entraîne moins de nouvelles infections. Cependant, les politiques pharmaceutiques de nombreux pays africains sont punitives et hostiles à nuire à des programmes de réduction. Ceux-ci alimentent la criminalisation de l'usage des drogues et la discrimination contre les usagers de drogues qui empêchant ainsi les toxicomanes d'avoir accès aux programmes de traitement. Il est nécessaire d'élaborer des politiques visant à protéger les droits des toxicomanes et d'aborder les aspects éthiques du traitement. *(Afr J Reprod Health 2014; 18[3]: 47-54)*

Mots-clés: Les usagers de drogue, de la toxicomanie, de toxicomanie, infection par le VIH, l'Afrique

Introduction

Africa remains the continent most affected by the Human immunodeficiency virus (HIV) and the Acquired Immune Deficiency Syndrome (AIDS). As of 2013, about 71% of the people living with HIV in the world resides in sub-Saharan Africa, a region with only 13% of the global population[1,2]. The burden of this epidemic varies among countries and regions. The worst hit are countries in the eastern and southern African region: Kenya, Uganda and South Africa[1]. The lower infection rate of 4.1% in Nigeria, a West African country, still translates to a large number of people due to its large population[3].

Recent efforts in the prevention of HIV transmission have emphasized the need to scale up antiretroviral therapy and focus attention on key populations[4]. These are groups of individuals that are more vulnerable to HIV infection due to a variety of factors such as: more frequent exposure to the virus, involvement in risky behaviors, potentially weak social support systems, marginalization, lack of resources, inadequate access to health-care services and poor health seeking behaviors[5,6]. Most at risk populations include female sex workers (FSWs), men who have sex with men (MSM) and people who inject

drugs (PWIDs).The use of illicit drugs is of public health concern in Africa. Data from many countries on the continent show that drug use and addiction is prevalent[7]. Also, there are reports of injecting drug practices in Kenya, Mauritius, Nigeria, Tanzania and South Africa[7,8]. It appears Africa has evolved from a drug-transit to a drug-using continent.

Drug Use and Addiction

Drug use tends to commence with occassional or recreational use. This may continue in a manner that is harmful to the user and initiate long-lasting changes in the reward pathway within the brain. The hijack of the mesocorticolimbic reward system is the basis of drug and alcohol dependence[9]. This is the stage at which the decision to use drugs is no longer voluntary and the drug user is transformed to a '*drug addict'.*

Addiction is a chronic relapsing disease characterised by compulsive, often uncontrollable, drug seeking and drug use despite its adverse consequences[10]. It is characterised by periods of remissions and exacerbations, and may result in significant morbidity and mortality[7].

HIV Transmission Among Drug-using Populations

Drug users have a high risk of HIV infection. The sharing of injecting equipment is a direct and highly efficient method of transmitting HIV, along with other blood borne viruses like Hepatitis B and C[7]. Recent reports from Africa indicate an increase in the practice of '*flashblood*' in which drug users inject themselves with another addict's blood, in an effort to share the 'high' or stave off the pangs of drug withdrawal[11].

The risk of HIV transmission is not limited to injecting drug use. Inhaled or orally ingested drugs can indirectly expose the user to multiple risk factors for HIV. Male drug users have reported that stimulants and alcohol increased their sexual desire while cocaine enhanced their sexual performance[12]. Under the influence of these substances, the individual may experience impaired judgment that may likely reduce commitment to condom use and the practice of safer sex. Also, multiple sexual partners and the practice of transactional sex either for drugs or money to buy drugs are common among drug users[13].

In addition, co-morbid psychiatric disorders commonly associated with drug use may contribute to impaired judgment and sexual disinhibition. The presence of these disorders has the capacity to potentiate risky sexual behaviours that can lead to HIV infection.

Beyond individual's risk of HIV infection, drug users are possibly the bridge connecting the most at risk populations with the larger public. PWID are sexually active and many sex workers also inject drugs[8]. Most male clients of these sex workers have other sexual partners, including wives and steady girlfriends that can vertically transmit the virus through maternal routes[14]. Additional exposures include healthcare workers who are accidentally exposed in the course of caring for these groups. So, HIV may trickle down from PWID and commercial sex workers to their regular sex partners and the general population who have no other risk of exposure to the virus.

Drug Use and HIV Susceptibility

Beyond promoting risky sexual behaviours, drugs of abuse including cannabinoids, opiates, cocaine and amphetamines may function as co-factors for susceptibility to HIV. There are reports suggesting that these drugs alter the biology of the virus itself and adversely impact on a number of immune parameters[14].

Laboratory studies exploring these biological alterations have made attempts to provide insight into important questions such as:

1. Do drugs of abuse influence viral entry, integration, replication and latency?
2. Do the drugs of abuse directly or indirectly make the immune cell lines relatively susceptible or resistant to infection i.e. by their ability to induce and / or regulate the expression of viral co-receptors such as CCR5 or CXCR4?

Cocaine and methamphetamine have been found to increase the ease with which HIV entered immune cells in laboratory cultures[15,16]. To investigate this observation further, a recent study collected blood samples from healthy human donors, isolated quiescent CD4 T cells, exposed

these to cocaine and subsequently infected them with HIV[17]. The investigators observed that in comparison with cocaine-untreated blood; the quiescent CD4 T cells in the study sample were more susceptible to HIV, resulting in significant infection and new virus production.

The susceptibility of immune cells to HIV may be mediated in part by the influence of drugs of abuse on receptor mechanisms. There are reports of cocaine use increasing the production of one of the receptors (DC-SIGN) that dendritic cells use to capture invading organisms[16]. Similarly, methamphetamine use increases activity in the gene for a receptor, CCR5, which the virus exploits to enter cells[15]. In addition, receptors for opioids have been found on immune cells and the activation of these receptors leads to the modulation of cellular activities pertinent to immune function[18].

Further evidence supporting the receptor-mediated mechanism in HIV susceptibility was demonstrated by an earlier study in which peripheral blood mononuclear cells from normal humans were co-cultured with morphine in the presence of HIV-infected lymphocytes[19]. The researchers observed an increase in HIV-1 infectivity, which was reversible with the administration of a specific opiate receptor antagonist indicating a receptor-mediated effect for morphine.

Other laboratory studies reported that drugs of abuse impact negatively on immune functions[14]. For example, morphine has been shown to inhibit a number of immune functions including those involved in innate and adaptive immunity such as bone marrow cells, macrophages, natural killer cells (NK), thymocytes, T and B cells[18,20-22], as well as induce apoptosis of macrophages[23]. However, some of these laboratory findings appear controversial and paradoxical. If drugs of abuse suppress the immune response by preventing T cell activation, how does this explain the ability of drugs of abuse to increase viral loads since viral replication requires T cell activation?

Laboratory studies may not be readily extrapolated to clinical settings. These studies did not control for other factors that may impact on the immune system of drug users. Aside HIV, drugs of abuse are known to predispose to other infectious diseases including hepatitis and tuberculosis[24]. As these co-morbidities equally depress the immune system independent of drug use[24], laboratory studies may not be able to extricate the contribution of individual variables to immune depression.

Also, it is not clear if the reported immune suppression is dependent on the types of drugs, route of drug administration, recurrent drug withdrawal symptoms, gender of the drug user and other factors inherent in the drug user.

Drugs of Abuse and HIV Progression

Active substance use is associated with non-adherence to ARV medications, resulting in failure of viral suppression and reduced CD4 cell count[25]. Further investigation of individual drugs, including cocaine, amphetamines and marijuana, on antiretroviral adherence support an association between active cocaine use and antiretroviral non-adherence[25,26]. There have been mixed results on marijuana in this context. Tucker et al[25] demonstrated an association between marijuana use and poor adherence, while de Jong et al[27] found improved adherence in HIV-infected individuals using marijuana for nausea. Among studies, there is a consensus that adherence affects virological and immunological response to therapy.

Prior to widespread use of highly active antiretroviral therapy (HAART), researchers did demonstrate an independent association between drug use and diagnosis of AIDS[28]. In the era of HAART, research on the effects of drug use on HIV progression has been hampered by the difficulty in separating the effects of non-adherence to medications from the physiologic effects of illicit drugs. Despite available data on ARV medication adherence, crack cocaine was found to increase the risk of progression to AIDS by accelerating the decline of CD4 cell count independent of adherence to ARVs[29]. In addition, there is compelling evidence from both animal and in vitro studies that illicit drugs and alcohol use have a direct effect on intracellular HIV multiplication, progression to AIDS, and death[30].

Beyond medication adherence, there may be factors mediating the relationship between drug

use and HIV progression. However, the investigation of these intermediate variables has been problematic. The difficulties in studying drug-using populations, such as enrollment, compliance, use of multiple drugs, lack of access to ARVs, co-morbid nutritional deficits and other issues, have led to less than definitive data on this subject. Nonetheless, a review of available laboratory and clinical studies suggest that the relationship between drug use and HIV disease progression may be mediated by several key factors. These include immunologic and virologic conditions affecting host susceptibility, underlying co-morbidities in drug users, use of antiretroviral therapy, and viral strain, as well as pharmacodynamic aspects of drug use, such as the pattern, type and route of drug administration[30].

Table 1: Interactions between drugs of abuse and ARVs[33]

Drug of abuse	ARV	Effects
Amphetamines	Ritonavir	2-3 fold increase in Amphetamine
Methamphetamine	Ritonavir / Saquinavir	Overdose with Methamphetamine
Ecstasy (MDMA)	Ritonavir	Overdose or death
GHB (liquid X)	Ritonavir / Saquinavir	Increased levels of GHB
Heroin	Ritonavir	Heroin levels may increase or decrease

Interactions Between Drugs of Abuse and Antiretroviral Medications (ARVs)

The introduction of antiretroviral medications in the treatment of HIV has significantly reduced AIDS-related morbidity and mortality[31,32], turning the tide around in the management of this epidemic. Nonetheless, there is a possibility that individuals with drug dependence may continue their drug use practices while on ARVs. This has raised concerns about potential interactions between ARVs and substances of abuse.

The margin of safety for many drugs of abuse is poorly defined, and the quality of their active ingredient is highly variable[33]. Therefore, factors that may lead to unpredictable drug concentrations can further increase adverse health outcomes. ARV medications can impact on the metabolism of drugs of abuse. There are documented case reports of ARVs reducing the metabolism of drugs of abuse and leading to drug intoxication, overdose and death[34,35].

On the other hand, drugs of abuse can also affect the metabolism of ARV medications[36]. An increase in ARV metabolism results in reduced antiviral efficacy, while a reduction of ARV metabolism could mean increased medication toxicity and dose dependent side effects.

The concomitant use of drugs of abuse with Ritonavir has produced pharmacokinetic interactions of clinical interest as depicted in Table 1. Potential interactions with cocaine use have not been investigated. A study involving cannabis reported pharmacokinetic interactions of no clinical significance[37].

Much of the available research findings are from in-vitro pharmacokinetic experiments, case reports, or animal model studies. As such, these may not be readily extrapolated to clinical practice settings.

Beyond the potential consequences of using ARV medications with drugs of abuse, there are major concerns about the recent reported use of ARV medications for recreational purposes. In South Africa, a drug of abuse called '*Whoonga'* has been reported to contain an ARV (Efavirenz) with heroin in addition to other illicit substances[38,39]. Efavirenz produces lysergic acid diethylamine (LSD)-like effects including hallucinations, dizziness, double vision and vivid dreams when ingested orally[40]. These can be aggravated by the concomitant use of other psychoactive drugs.

Although the effects of smoking Efavirenz are unclear, there are potential implications of recreational use of ARVs in the development of ARV pretreatment resistance. Other implications include poor adherence to ARV treatment, limited access to treatment, stealing of ARVs and further stigmatisation of HIV[39,41].

Drug Addiction Treatment as HIV Prevention

Drug users are a difficult to reach population.

They often live on the fringes of society, away from family and friends and beyond the reach of health education or treatment programs[42]. These individuals do not utilise primary care services and would rather present in emergency departments[43,44]. They do not see themselves as vulnerable to HIV infection, do not test for the virus, and underutilise HIV-specific medical services[45,46]. Lack of access, their disorganized and marginalized lifestyle, discrimination, lack of medical insurance and the cost of treatment constitute barriers excluding drug users from 'mainstream' health services.

Recommended strategies for the prevention of HIV among drug users include: education about HIV transmission, counseling and testing, HIV treatment, access to sterile injections, provision of condoms and post-exposure prophylaxis, and treatment of drug addiction[47-49]. For individuals living in the shadows of the society due to drug use, the most important strategy would be the treatment of drug addiction. Within the confines of drug treatment centres, the other strategies may be easier to implement.

The goals of drug addiction treatment include abstinence, reduction in problematic use and reduction of harms caused by drugs[50]. Although goals can guide intervention strategies, there are questions regarding the participation of the drug users in their own treatment. Are these goals client-driven or provider-driven? Where is the client in treatment intervention? What about people who do not seem to respond to any type of treatment?

The relapsing nature of drug addiction has opened the gates of controversies surrounding the effectiveness of abstinence-driven treatment approach. There is a gradual shift in focus from the therapeutic goal of abstinence to approaches that reduce harm to the individual and the larger society. Harm reduction is a pragmatic and progressive approach to the "drug problem"[51]. It recognises abstinence as an ideal outcome, but accepts other alternatives. Although the use of medications that are pharmacologically similar to drugs of abuse is a core component of harm reduction, this approach is more than drug substitution[52]. Needle exchange programs and the provision of condoms can reduce harm from drug use.

The treatment of drug addiction is an effective strategy for the prevention of HIV. Research has demonstrated that treated drug users had lower incidence of HIV infection, increased access to HIV treatment and better adherence to ARVs compared to untreated drug users[47]. In the same study, there was a significant reduction in frequency of drug use and drug–related risk behaviors among in-treatment subjects.

Policy and Ethical Considerations

Inadequate policy framework for the management of drug addiction remains a challenge in many African countries. Available policies are very punitive and tend to prioritize supply reduction and law enforcement over the provision of treatment services[53]. Resources are channeled towards the arrest and prosecution of drug users who end up in the criminal justice system rather than the health care system. This criminalization of people who use drugs present significant barriers to accessing existing programs where these do exist, and exacerbate unsafe injecting practices and HIV transmission among PWID[54,55].

Injecting drug use practices may be contributing to the sustained high prevalence of HIV infection on the continent. However, harm reduction strategies including Needle Exchange Programs are not common in sub-Saharan Africa[53].

There is need to formulate policies that will protect the rights of people with drug addiction. Such policies should protect against discrimination in accessing health care and social services, provide equal opportunities, include the option of treatment instead of prison, address both client-level and societal-level ethical dilemmas and provide framework for harm reduction interventions.

Conclusion

It is clear that increased availability of drugs, high prevalence of drug use and adoption of riskier methods such as injection drug use can undermine response to HIV/AIDS in Africa. One means of breaking this nexus is the treatment of drug addiction. This requires the provision of drug

abuse prevention and treatment services including harm-reduction, training and capacity building in the field of drug addiction, and provision of reproductive health-care services for drug users. Health promotion strategies via the print and electronic media need to highlight the relationship between drug abuse and increase in new HIV infections.

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Contributions of Authors

Taiwo Akindipe conceived the idea of the review, contributed towards the writing of the different sections and provided feedback on drafts of the review. Lolade Abiodun and Sylvia Adebajo were responsible for literature search and writing of its background sections. Rahman Lawal and Solomon Rataemane provided subject expertise and feedback on drafts of the review.

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