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HIV Treatment Access and Scale-Up for Delivery for IDU in Ukraine with Opiate Substitution Therapy with Buprenorphine - Programme Description and Policy Implications

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Abstract

Background—Injection drug use (IDU) accounts for 70% of HIV cases in Ukraine. Until buprenorphine maintenance therapy (BMT) was introduced, few effective strategies aimed at achieving reduction in illicit drug use were available as a conduit to antiretroviral therapy (ARV) among IDUs.

Description—In October 2005, BMT was scaled-up using Global Fund resources in six regions within Ukraine. Entry criteria included opioid-dependence, HIV-1 seropositivity, age ≥ 18 years and reported interest in BMT. All sites included a multidisciplinary team. To date, 207 patients have been initiated on BMT.

Lessons Learned—The existing infrastructure allows for further scale-up of and administration of BMT and the possibility of co-administration with ARV. The process for prescription and administration of buprenorphine and ARV is at times cumbersome and constrained by current regulations.

Recommendations—More IDU need BMT to improve overall health outcomes. Central to expanding access will be legislative changes to existing drug policy. Moreover, the cost of buprenorphine is prohibitively expensive. Sustainable substitution therapy in Ukraine requires lower negotiated prices for buprenorphine and/or the addition of methadone to the existing formulary for HIV+ drug users.

Keywords

HIV/AIDS; buprenorphine; substitution therapy

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Introduction

Injection drug use (IDU) accounted for 70% of HIV cases in Ukraine between 1987 and 2004.¹ In 2005, Ukraine was home to the fastest growing HIV epidemic in Europe and one of the most explosive in the world with over 40000 individuals infected with HIV, most of whom are IDUs.² There has arisen a need for the treatment of opioid dependence to facilitate the expansion of ARVs among HIV-infected IDUs. Although drug treatment programmes existed in Ukraine prior to opioid substitution therapy (OST), retention in these programmes was poor with two out of three individuals leaving treatment due partly to limited capacity for treatment and lack of evidenced based treatments in narcological centers.⁷ Until November 2006, due to Ukrainian federal regulations, buprenorphine was the only medication available for OST. Buprenorphine is a partial opiate agonist that has been used in multiple settings for substitution therapy,³ most widely within France.⁴ Additionally, ARV access for IDUs is low. Although not formalized in policy, both clinicians and policymakers have tended to refuse ARVs to active IDUs, owing to the perception that IDUs would be poorly adherent. As a result, a buprenorphine maintenance treatment (BMT) programme was piloted with the goal of bringing HIV-infected IDUs onto buprenorphine to reduce further transmission of HIV, and to begin HIV-infected IDUs on ARV treatment.

There are several distinguishing aspects of opioid use patterns in Ukraine. Most IDUs use homemade opioids called *shirka*, which is prepared from poppy straw in a common container that is shared among a group of IDUs. Because *shirka* is a solution by nature, those IDUs purchasing ready-made *shirka* can buy it in preloaded syringes that tend to be unsterile. Critically, almost 30% of IDU respondents in Ukraine stated that they shared syringes with other IDUs.⁵

OST with sublingual buprenorphine was unavailable in Ukraine until 2004 when the WHO, UNAIDS and others recommended OST as a way to address the growing HIV incidence rate among IDUs.⁶ To gain experience and inform future programmes, a pilot BMT programme was conducted in two cities in 2004. A total of 70 patients (40 in Kiev and 30 in Kherson) participated in this one year project.⁷ Following this feasibility pilot, expansion of OST to additional sites began as described subsequently.

Methods

The national BMT project began in October 2005 and this report details lessons learned over the first 9 months. There are 207 patients on BMT in Ukraine and approximately 114 (55%) are HIV-infected with approximately 28 (25%) of the HIV-infected individuals on ARVs. This cohort is disproportionately male (21% women), but is consistent with substance use in Ukraine.⁸ The average age is 39 years and the average length of IDU is 16.8 years. The cohort was recruited through needle exchange sites, HIV/AIDS healthcare providers and narcological centers (Ukrainian drug treatment centers).

Originally, inclusion criteria for BMT required being HIV antibody positive, age > 18, opioid dependence, two or more non-pharmacological drug treatment attempts, and interest in buprenorphine. HIV-infected IDUs were targeted due to a Ukraine Ministry of Health order; however, this restriction was removed in late 2006 to allow both HIV-infected and HIV-uninfected. The only exclusion criteria is an inability, in the opinion of the narcologist, to adhere to the required directly observed method of daily administration which is required by Ukrainian federal regulations. There is no formal screening or evaluation of this and so it is interpreted widely.

Due to strict regulations, a special order from the Ministry of Health was required to allow expansion of the previous BMT pilot. Prior to expansion, physicians and staff visited the Yale

University AIDS Program where they underwent an intensive week long training on OST and harm reduction in HIV-infected IDUs. Subsequently, BMT expansion began in October 2005 at 6 sites.

Each BMT is allowed to screen for ongoing substance use, but no universal protocol exists in their use of these measures to improve clinical outcomes. Many of the programmes struggle to do urine toxicology due to funding limitations.

Discussion

Despite the project still being in its infancy, several points regarding the efficacy of BMT, lessons learned starting BMT, and remaining obstacles require discussion. First, after six months, retention is approximately 75%. This stands in contrast to drug free programmes (non-OST) in Ukraine where retention after 6 months is 33.3%.⁷ It is hoped that improved access to ARV will follow the improved retention in BMT. Second, average addiction severity index (ASI) scores on drug use have decreased between baseline and six months consistent with improvements in opioid use over the last six months. Specifically, the average score of drug use by ASI at baseline was 0.3238 ± 0.1208 and had decreased at 6 months to 0.0944 ± 0.0866 . Additionally, individuals have experienced other personal successes such as weight gain, improvements in interpersonal relationships, and obtaining and keeping employment. Third, the average dose of buprenorphine was approximately 9.3 mg, which is lower than the average dose in the largest prospective cohort in the United States where the average dose is 16 mg/day [personal communication with R. Douglas Bruce]. Despite the difference in dosing, anecdotal reports from Ukraine do not suggest that they are inadequately dosed. The differences in pharmacological requirements are beyond the scope of this paper, but may reflect the difference in potency between *shirka* and heroin. Fourth, potential drug-drug interactions exist and must be explored. At least one subject reported increased craving and subjective symptoms of withdrawal every morning. This subject was on buprenorphine at 10mg/day and also taking nevirapine for HIV and rifampin for tuberculosis. Understanding the shared metabolic pathway of each medication, a drug-drug interaction is possible.⁹ Finally, after the project started, more HIV-infected IDUs came to the BMT programmes seeking treatment than programme slots would allow; as a result, these individuals seeking treatment were turned away and their names added to a growing list.

There exist many difficulties in the continued implementation and eventual expansion of BMT. First, although cheaper and equally as effective, methadone was unavailable in Ukraine, until recently. Although recently available in a pilot project, its future expansion remains to be determined. Second, federal regulations require extensive measures of control to supervise buprenorphine's administration. For example, buprenorphine is administered only in government or community based treatment centers and only in the presence of medical staff. Other agencies are not allowed to provide BMT regardless of expertise and safeguards. Third, only narcologists (physicians with specialized training) can prescribe buprenorphine. This is an obstacle for integration. Models of care delivery within the United States allow for integrating services: a physician can treat opioid dependence with buprenorphine while treating HIV.³ Fourth, all buprenorphine is administered daily by direct observation and is discontinued if the patient is incarcerated, admitted to an inpatient facility for any treatment (e.g., medical hospitalizations), or moves to another city (even temporarily), as other programmes cannot provide buprenorphine to visiting patients. To avoid administration on weekends, patients are given a double dose on Friday with no opportunity for take-home doses. The reported purpose of these measures is the prevention of diversion. Ironically, in discussions with the medical directors of various BMT sites, it is apparent that the major reason for administrative discharges is for diversion. In focus groups with patients, the main purpose of diversion was to create a home supply of buprenorphine to allow 'days off'. Such days off are used by patients for various

activities including family holidays. Unfortunately, strict supervision has a selection bias in some sites towards healthier individuals (e.g., do not meet criteria for ARVs). This bias occurred due to system-level barriers where bringing buprenorphine to hospitalized patients can be extremely problematic if not impossible.

Recommended Response

Although barriers and difficulties exist, the reality that 207 individuals have entered into BMT in Ukraine, with high levels of retention in treatment, remains promising. The outcomes of these subjects over the next several years will be closely monitored. Given the demand for OST, deregulation is necessary, including a new order from the Ministry of Health allowing for the expansion of BMT to non-narcologist physicians with adequate training. Buprenorphine should be transferred from the List of Narcotic Drugs to the List of Psychotropic Drugs. Additionally, the availability of methadone must be addressed. The cost differential between methadone and buprenorphine is significant: if the money allocated for buprenorphine was shifted to methadone, 7 seven to 8 eight times as many patients could be treated with methadone [personal communication with Sergey Dvoryak]. Price negotiation which was successful in lowering ARV prices must be used to lower the cost of buprenorphine; this will require both national and international pressure. All changes are desperately needed if OST is to expand from 207 to 6000 by 2008 and, most importantly, the estimated goal of 60000 necessary to impact the HIV epidemic in Ukraine.⁶ Without such changes to expand access to substitution therapy in a meaningful way, injection drug use will continue to fuel the HIV epidemic in Ukraine and will continue to stand in the way of life-saving antiretroviral therapy.

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