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Opioid Addicted Buprenorphine Injectors: Drug Use During and After 12-Weeks of Buprenorphine–Naloxone or Methadone in the Republic of Georgia ☆

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ABSTRACT

Aims: The aim of this study is to assess the prevalence of non-opioid drug use among opioid-addicted, buprenorphine injecting individuals in Georgia, during and after a 12-week course of buprenorphine–naloxone (Suboxone®) or methadone.
Methods: Randomized controlled trial with daily observed Suboxone® or methadone and weekly counseling, urine tests and timeline followback (TLFB) in weeks 0–12 and 20, and the Addiction Severity Index (ASI) at weeks 0, 4, 8, 12, 20.
Results: Of the 80 patients (40/group, 4 women), 68 (85%) completed the 12-weeks of study treatment and 66 (82.5%) completed the 20-week follow-up. At baseline, injecting more than one drug in the last 30 days was reported by 68.4% of patients in the methadone and 72.5% in the Suboxone® groups. Drug use was markedly reduced in both treatment conditions but there were significant differences in the prevalence of specific drugs with more opioid (1.5 vs. 0.2%; $p = 0.03$), less amphetamine (0.2 vs. 2.8%; $p < 0.001$) and less marijuana (1.7 vs. 10.2%; $p < 0.001$) positive urine tests in the methadone vs. Suboxone® groups.
At the 20-week follow-up, TLFB results on the 34 that continued methadone or the 3 on Suboxone® showed less opioid (5.6 vs. 27.6%; $p < 0.001$), illicit buprenorphine (2.7 vs. 13.8%; $p = 0.005$), benzodiazepine (13.5 vs. 34.5%; $p < 0.001$), and marijuana (2.8 vs. 20.7%; $p < 0.001$) use than the 29 who did not continue opioid substitution therapy.
Conclusions: Despite small but significant differences in opioid and other drug use, both treatments were highly effective in reducing opioid and non-opioid drug use.

1. Introduction

Opioid substitution therapy (OST) using buprenorphine and methadone has been introduced in some Former Soviet States including Ukraine (Bruce, Dvoryak, Sylla, & Altice, 2007; Dvoriak et al., 2013; Dvoryak & Grishayeva, 2008; Golovanevskaya, Vlasenko, & Saucier, 2012; Lawrinson et al., 2008) and Georgia (Gambashidze, Sikharulidze, Piralishvili, & Gvakharia, 2008; Otiashvili et al., 2010; Piralishvili, Gamkrelidze, Nikolaishvili, & Chavchanidze, 2012) and data are becoming available on its effectiveness in these cultural settings. Findings from the U.S., Western Europe, and Australia have consistently found that OST is associated with substantial reductions in illicit opioid use, criminal activity, and drug related mortality, and that it can play an important role in reducing the spread of HIV by reducing injection risk and improving adherence to antiretroviral therapy (Cornish, Macleod, Strang, Vickerman, & Hickman, 2010; Degenhardt et al., 2010; Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011; Kimber et al., 2010; MacArthur et al., 2012; Malta, Strathdee, Magnanini, & Bastos, 2008; Mattick, Breen, Kimber, & Davoli, 2003; Mattick, Breen, Kimber, & Davoli, 2007; Suntharasamai et al., 2009; Tilson et al., 2007).

These findings have led to an interest in comparing outcomes of patients being treated with methadone or buprenorphine since they have different pharmacologic properties, safety profiles, and conditions under which they can be prescribed. The largest and latest Cochrane

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systematic review of trials to 2013 by Mattick et al., which includes 31 RCT and 5430 participants to assess effectiveness of buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence, found that buprenorphine appears to be less effective than methadone in retaining people in treatment if prescribed in a flexible dose regimen or at a fixed and low dose (2–6 mg/day). Authors conclude that although buprenorphine prescribed at fixed medium (7–15 mg/day) or high doses (≥16 mg/day) was not different from methadone prescribed at fixed medium (40–85 mg/day) or high doses (≥85 mg/day) in retaining people in treatment or in suppression of illicit opioid use, fixed doses are rarely used in clinical practice so the flexible dose results are more relevant for patients' daily management (Mattick, Breen, Kimber, & Davoli, 2014).

Though highly effective in reducing opioid use, OST has no direct effect and was never intended to have an effect on alcohol and other drug use (Methadone Research Web Guide and Tutorial, 2006). However many opioid users seeking OST have a history of, and continue to use, alcohol, amphetamine, benzodiazepine, cannabis, cocaine and/or other drugs (Gollnisch, 1997; Marsch, 1998; Ward, Mattick, & Hall, 1998; Wasserman, Weinstein, Havassy, & Hall, 1998). This problem is important because it is associated with greater addiction severity, more contact with active drug users (Craig & Olson, 2004; Methadone Research Web Guide and Tutorial, 2006; Nyamathi et al., 2009), and less-than-optimal outcomes including HIV risk behavior, particularly regarding alcohol and stimulants (Li, Luojian, & Chunming, 2012; Nyamathi et al., 2009; Sherman et al., 2009; Stenbacka, Beck, Leifman, Romelsjö, & Helander, 2007; Zule, Costenbader, Meyer, & Wechsberg, 2007).

Findings have been mixed on the impact of OST on non-opioid substance use as some studies found a decrease (Fairbank, Dunteman, & Condelli, 1993; Maremmani, Pani, Pacini, & Perugi, 2007) while others found an increase (Chen et al., 2011; Powers & Anglin, 1993; Srivastava, Kahan, & Ross, 2008). Some systematic reviews and the large Treatment Outcome Perspective Studies (TOPS) were conducted to clarify this issue. In the TOPS ($N = 4{,}184$ patients), methadone maintenance treatment (MMT) was associated with reductions in any illicit opioid use (from 63% pretreatment to 17% 1 year post-treatment), any cocaine use (from 26 to 18%), and any marijuana use (from 55 to 46%). Alcohol use remained almost steady, declining slightly from 25 to 24% (not significant; Hubbard et al., 1989).

A systematic review examining the impact of methadone dose on cocaine use found that higher doses are associated with less cocaine use (RR = 1.81 [1.15, 2.85]) (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003), and a systematic review on alcohol use while on MMT found that it likely does not change (Srivastava et al., 2008). For example, of 15 studies that were reviewed three found an increase, three a decrease, and nine found no change in alcohol use. However among these studies, those that found no change or a decrease in use were stronger methodologically (3 randomized trials and 7 prospective cohorts) than those that found an increase in consumption, which were all retrospective and subject to recall bias.

Information about the impact of OST on opioid and non-opioid use is particularly important in a country such as Georgia that has a very low prevalence of HIV (Otiashvili et al., 2013) but is geographically close to Former Soviet States where injecting opioid use is contributing to one of the most rapidly growing HIV epidemics in the world (Bobrovsky et al., 2012; Carrieri et al., 2006). Though HIV prevalence has been low in Georgia, the prevalence of Subutex® injection and sharing of injection equipment has been high during the last decade as Subutex® was commonly smuggled in from France (Gamkrelidze et al., 2004; Javakhishvili et al., 2006). In one survey, conducted in 2007, Subutex® was named as the most commonly injected drug in terms of lifetime (95.5%) and last-month (75%) prevalence although buprenorphine treatment was not legal until 2008 in Georgia (Otiashvili et al., 2010). The main reasons given by drug injectors for Subutex® use were self-treatment to cope with withdrawal from other opioids (Otiashvili et al., 2010), increased police activity with random urine drug testing at a time that buprenorphine was not part of the drug testing panel (Otiashvili, Srosi, & Somogyi, 2008), and its relatively long-lasting effect and less obvious signs of intoxication compared to other opioids.

Here we report data from a study in which opioid addicted Subutex® injectors were randomized to a 12-week course of daily-observed Suboxone® or methadone and discuss possible reasons for the low level of drug use during OST in Georgia as compared to the U.S. Study details and the primary outcomes of opioid use and HIV risk have been reported elsewhere (Otiashvili et al., 2013). Conclusions were that daily observed methadone or buprenorphine–naloxone treatments were effective for non-medical buprenorphine or other opioid use and likely to be useful for preventing HIV infection.

2. Methods

2.1. Setting

The study was done at the medical center Uranti, a program located near the center of Tbilisi that provides medication-assisted therapy and psychosocial support for drug and alcohol addicted citizens of Georgia. The Center for Mental health and Prevention of Addiction (CMHPA) in Tbilisi coordinated treatment at Uranti, and the Addiction Research Center-Union Alternative Georgia provided administrative and scientific support. IRBs at the University of Pennsylvania and the Georgian National Council on Bioethics approved the study.

2.2. Study population

As per Georgian regulations, participants had been opioid dependent with physiological features for the past three or more years according to *ICD-10* criteria and were 25 to 50 years of age. Study admission criteria were that they had been injecting buprenorphine (Subutex®) 10 or more times in the past 30 days; had not been on methadone or buprenorphine maintenance in the last 4 weeks; were living in the Tbilisi area; literate in Georgian; and not psychotic, suicidal, homicidal, or had a medical of psychiatric problem that would prevent them from participating in the study or providing informed consent.

2.3. Recruitment

A brochure describing the study was developed and approved by the Georgian and Penn IRBs and distributed through medical treatment centers and harm reduction programs in Tbilisi; recruitment also occurred by word of mouth.

2.4. Randomization

Patients were randomized 1:1 to methadone or Suboxone® in blocks of four and stratified according to gender and age (over 30/30 or below).

2.5. Procedures

Methadone and Suboxone® were administered 7 days/week under direct observation since Georgian regulations prohibit take-home doses except for extreme emergencies and in those cases, program staff usually take the medication to the patient. A 3-week outpatient dose taper, transfer to methadone or the Suboxone® program in Tbilisi, or inpatient detoxification was offered to all patients at the end of the 12-weeks of study treatment. All patients were offered weekly group therapy and manual-guided individual drug counseling using procedures described on the NIDA Web site (http://archives.drugabuse.gov/TXManuals/IDCA/IDCA1.html).

Self-report and urine testing results were confidential and available only to clinical staff, and not to outside authorities. Research assistants collected data on case report forms that were linked to patients only