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Behavioral Treatment + Naltrexone Reduces Drug Use and Legal Problems in the Republic of Georgia

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Abstract

Background—Known drug-users in the Republic of Georgia are 99% male. Georgian social context includes close family social structure, intense police scrutiny over daily life, and minimal social service infrastructure. Drug use is dangerous and individuals rely on family support to address socially-stigmatizing problems.

Objectives—To examine the changes in problem severity over time experienced by 40 adult opioid-injecting men with drug-free female partners in the Republic of Georgia who participated in a randomized clinical trial examining the feasibility and efficacy of a 22-week comprehensive intervention that paired behavioral treatment with naltrexone.

Methods—This secondary data analysis study examined results from a project that had randomized participants to either a comprehensive intervention that paired behavioral treatment with naltrexone or usual care and examined changes in Addiction Severity Index (ASI) composite scores.

Results—The comprehensive intervention showed three times the decline in ASI Drug Use and Legal composite scores than did the usual care condition in males in the Republic of Georgia, both *p*s<.009.

Conclusion—Results suggest that the use of a comprehensive behavioral intervention paired with naltrexone leads to significant reductions in drug use and legal problems in opioid-injecting males in the Republic of Georgia.

Scientific Significance—A comprehensive intervention that paired behavioral treatment with naltrexone provides a promising approach to protect drug users against relapse and legal risks.

Introduction

Prior to 2004, home-made opium and heroin were the main injection drugs in Georgia (1). In 2004 injection use of buprenorphine (Subutex®), available only illegally in Georgia, rose dramatically. Georgian drug user's attraction to buprenorphine may be due to its moderate clinically (externally) visible signs and its lack of inclusion in drug tests (2). In 2005, 39%

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of all inpatient-treated drug users in Georgia were buprenorphine injectors (3), mostly injecting buprenorphine for self-medication (2). It is currently estimated that there are about 40,000 injecting-drug users in Georgia and 99% are male (4). At the time of the present study, Georgia had six addiction (narcologic) clinics that had detoxified 841 patients (capacity was 1,000 patients per year). With limited aftercare referral, relapse risk was high; however, no data are currently available to document relapse rates. Methadone maintenance, introduced in 2005, was provided to 552 patients in 2008 (5). Introduced in January 2010, buprenorphine (Suboxone®) treatment is currently available to some 100 patients. Almost all treatment procedures, except methadone maintenance, are paid for by patients. Thus, Georgia, like many other countries, currently lacks the capacity to treat all drug-dependent individuals in need (6). It is against the background of changing use of opioids in the population of Georgian men and a clear need for treatment for opioid dependence that the present study was conducted.

Because of the fact that the vast majority of opioid-injecting males did not have the opportunity to enter opioid agonist treatment, together with the fact that naltrexone treatment had been unsuccessful in achieving continued illicit opioid abstinence, a behavioral therapy intervention was developed for Georgian males, based on a successful intervention model developed in the US which showed, on average, increased treatment retention and decreased heroin use among men receiving the intervention compared to the usual care condition (7). This intervention was chosen based upon its potential culturally-compatibility. For example, using a family/social support structure to reinforce drug abstinence fits well with Georgians close family-orientation. Moreover, Georgians are typically non-confrontational in their communication and interaction styles; thus, motivational interviewing provided a suitable counseling approach. The behavioral intervention was paired with rapid detoxification entry followed by initiation onto naltrexone maintenance. Upon detoxification completion, male participants received counseling comprised of both Motivational Interviewing (MI) focused on fostering aftercare treatment engagement (8–10) and couples MI sessions to improve the spousal support of the male participant's treatment and sustained recovery. To sustain drug-abstinence, participants received monetary value rewards following submission of drug-negative urine samples (11).

The parent study showed that compared to the usual care condition, a comprehensive intervention that paired behavioral treatment with naltrexone significantly increased the likelihood that participants in the comprehensive intervention condition would choose detoxification and initiation of naltrexone treatment (0% *v.* 60%) as well as producing minimum seven-fold reductions in benzodiazepine use and injection of buprenorphine relative to the usual care condition (12). The extent to which the comprehensive intervention may have positively impacted other areas of life functioning was not addressed. Thus, the purpose of the present secondary-data analysis study was to examine the 1-, 3-, and 6-month post-randomization treatment outcomes of males randomly assigned to either the comprehensive intervention condition or a usual care condition.

It was hypothesized that the comprehensive intervention that paired behavioral treatment, composed of MI and opioid-abstinent contingent vouchers, paired with detoxification followed by naltrexone, would result in significant decreases in drug-problem-related behaviors, as reflected in the Addiction Severity Index composite scores, compared to a usual care condition.

Methods

Treatment Setting

Union Alternative Georgia, an independent nonprofit research institution located in Saburtalo, a residential area in Tbilisi, Republic of Georgia, was the study site.

The Institutional Review Boards of both Johns Hopkins University and the Georgian HIV/AIDS Patients Support Foundation approved the project.

Treatment Conditions

Usual Care (UC)—Male participants visited the field site once/week for 22 weeks to participate in individualized manualized education sessions on topics related to drug use recovery (e.g., drug refusal skills, HIV/AIDS). Information about community resources for common crises (e.g., employment, legal) drug users face was given if requested. Referrals were made to detoxification and aftercare programs, upon request (12).

Behavioral Treatment+Naltrexone (BT+N)—BT+N condition male participants attended a 22-week program with 4 major components: (1) the opportunity for 14-day detoxification (in-patient pharmacological treatment with clonidine in combination with abstinence-oriented psychological counseling) during the first two weeks of treatment followed by a 22-week supply of oral naltrexone, as a maintenance medication upon completion of the detoxification program, with individualized dosing regimens based upon participant response and need for supervision; (2) once weekly observed urine testing with participants receiving $9US upon demonstration of results being negative for opioids and buprenorphine; (3) beginning in the first week, 6 once-a-week individual Motivational Interviewing (MI) counseling sessions focused on engagement in treatment, followed by 12 once-a-week MI couples counseling sessions; (4) ending with 4 once-a-week individual MI sessions to reinforce changed behaviors.

Participants

Recruitment occurred through word-of-mouth, flyers, and advertisements distributed among the staff members of health and social service facilities commonly visited by drug users (e.g., harm reduction sites, detox clinics, infectious desease clinics). Potential participants were screened through a face-to-face interview at the study's site. Between May, 2006 – January, 2009, 55 of 74 males who responded to recruitment effort were assessed for eligibility. Eligibility criteria were: 1) male; 2) minimum18 years of age; 3) a current drug-free female sex partner with regular contact; 4) current DSM-IV opioid dependence; 5) no significant psychiatric or cognitive impairment preventing them from informed consent and baseline assessment completion; and 6) no evidence of current physical abuse of their female partner.

Randomization

Among the 40 eligible participants, participants were assigned at random to either the BT+N (n=20) or the UC (n=20) condition. The data from these 40 male participants served as the basis for all analysis reported herein.

Procedures

The equivalent of $9US was paid to all participants for completing the baseline interview and each of the 1-, 3- and 6-month post-treatment completion interviews. Participants earnd the equivalent of $9US for every completed study visit. Participants received a study-

developed community resources guide. Medical and social care refferals were offered to all male participants to overcome potential study participation barriers (12).

Measures

Addiction Severity Index (ASI) (McLellan et al., 1992) is a semi-structured interview measuring both lifetime and past-30 day events and behaviors in seven domains (Medical, Employment, Drug, Alcohol, Legal, Family/Social, and Psychiatric). Scores range between 0 (no problems) to 1 (severe problems), inclusive. It was translated into Georgian and then back-translated into English to ensure correct interpretation in the Georgian language.

The ASI was chosen to measure problem behaviors because: (1) it has been used extensively in Russia, a country with which Georgia shares some common history; (2) given the ASI's extensive use in the US and Russia, its continued use in Georgia allows for future cautious examination and interpretation of cross-national differences.

Statistical Analyses

α was set at .05. This choice runs the risk of increasing the cumulative error rate. However, given both the relatively small sample size and the exploratory nature of the study, the choice of a more conservative rate runs the risk of failure to detect some small but potentially important difference between treatment conditions.

Treatment Condition (Behavioral Treatment+Naltrexone *v.* Usual Care), a dichotomous fixed factor, together with a fixed repeated-measures factor, assessment Time point (baseline *v.* 1-month follow-up *v.* 3-month follow-up *v.* 6-month follow-up), and the Treatment Condition X Time interaction, were the explanatory variables in the statistical model. A general linear mixed model (GLMM) approach was employed to analyze each ASI composite score. The model assuming a normal distribution, a Huynh-Feldt error structure, and error degrees of freedom calculated by the Kenward-Roger method (sometimes producing fractional error *df*). Tests of simple main effects were used to follow up any significant Treatment X Time interaction. Interpretation was based on examination of model-derived least squares means (standard errors).

Results

Participant Characteristics

Participants, all White, Age M=35.6 (SD=6.7), all married to their drug-free female partners; 60% were hepatitis C positive at baseline, a rate consistent with that found in Georgia (13–14)(12). 40/40 (100%) reported misusing buprenorphine (Subutex®) in the past 30 days before study entry with exclusive injection use of buprenorphine in 39/40 (98%). All participants used opioids other than buprenorphine. Buprenorphine was injected more frequently than other opioids for some participants, while for others, buprenorphine was the secondary injection opioid of use.

Attempts to assess participants who had left treatment were limited to follow-up telephone calls asking that they return for follow-up assessment. The 19 participants for whom 6-month follow-up data were unavailable did not differ from the 21 participants for whom 6-month follow-up data were available on any of the seven ASI composite scores (all ps > .05).

Outcomes

Table 1 summarizes the results of the inferential analyses evaluating the impact of Treatment Condition across Time. Table 2 presents the least squares means for the Treatment Condition, Time, and Treatment Condition X Time effects.

BT+N impacted two composite scores. The Treatment Condition X Time interaction effect was significant for both Drug and Legal (both ps < .009).

Tests of the simple main effects for the Drug composite revealed that the two treatment conditions did not differ at baseline (p>.06), and the Time simple effect was significant for both BT+N [F(3, 72.6)=24.1, p<.0001] and UC [F(3, 70.5)=3.2, p<.03], indicating that, on average, both groups experienced fewer drug problems over the course of treatment. However, Table 2 indicates a more than seven-fold reduction in drug problems for the BT +N condition while there was only a two-fold reduction in such problems for the UC condition. [Given the presence of a significant Treatment Condition X Time interaction effect for the Drug composite, the significant Treatment Condition and Time main effects for the Drug composite will not be interpreted.]

Tests of the simple main effects for the Legal composite revealed that the two treatment conditions did not differ at baseline (p>.3). The Time simple effect was significant for BT +N [F(3, 65.7)=4.2, p<.01] but not UC (p>.1), with a greater than three-fold reduction in legal problems for the BT+N condition, on average, from baseline to 6-month follow-up assessment (see Table 2).

There were two Time main effects. In the total sample employment problems increased slightly, while family/social problems showed almost a three-fold mean decrease, from baseline to 6-month follow-up (Table 2).

Finally, there were two Treatment Condition main effects. Collapsed over Time, both family/social and psychiatric problems were approximately 50% more reduced in the BT+N than the UC condition.

Discussion

Study results show that, among participants who remained in treatment, a comprehensive intervention that paired behavioral treatment with naltrexone dramatically reduces drug problems compared to usual care, given that changes in ASI Drug use composite scores for the comprehensive intervention reduced drug use problems at more than three times the rate of usual care for the period from treatment entry to 6-month follow-up. The reductions in self-reported ASI drug use severity are affirmed by the significant reductions in the proportion of opioid-negative urine samples seen in the BT+N condition relative to the UC condition previous reported (12). These results are also notable in that they both partially replicate and extend the efficacy found with this intervention when tested with US drug-using men in partnerships with drug-using women (7).

It is also the case that legal problems, as measured by the ASI Legal composite score, declined much more precipitously in the comprehensive intervention condition than in the usual care condition. However, this reduction may in part be due to the relative difference between the treatments in the decline in drug use, given the strong relationship between drug use and legal problems. This is a highly important finding in the context of Georgian society that has experienced disproportionately large increase in recorded minor drug-related crimes compared to almost no increase in what is classified as major crime during the time period in which the study was conducted (6). The primary reason for this increase in minor drug-

related crimes is likely the fact that drug legislation was amended in 2006 that included the addition of stricter enforcement measures, with a resulting increase in police activity targeting drug users. The fact that BT+N, relative to UC, on average reduced the severity of legal problems suggests that the participants made meaningful and sustained behavioral changes even in the face of intensified police activity related to the practice of massive random searches of young men and their testing for presence of illegal drugs and metabolites in body fluids (6).

The general increase in employment problems are likely related to Georgian economic declines. The Georgian economy was impacted by global economic problems during the conduct of the study.

In contrast, the decrease in family/social problems that occurred irrespective of treatment condition may well be related to the fact that simply entering drug abuse treatment may lead to less family friction and its attendant problems. Such a finding is common in drug abuse research.

The study has several limitations. First, the sample was relatively small for a clinical trial. However, this was the first clinical trial involving the behavioral treatment of opioid-dependent males in the Republic of Georgia, primarily focusing on feasibility rather than power to detect differential treatment effectiveness. Second, the attrition over the 6-month post-treatment period was marked, with 48% of the participants lost to follow-up at 6-months. However, comprehensive intervention condition changes were pronounced at 1-month follow-up, when data for 75% of these participants was available. This fact suggests that the findings were not simply the result of the fact that the ‘successful’ participants were the ones who remained in the study to 6-month follow-up, leading to an overestimate of differential treatment effectiveness. Third, because the treatment conditions differed markedly in both intensity and score, it is not possible to determine the effective ingredients associated with the behavioral intervention. Fourth, the sampling procedure did not intend to collect a random sample of the population of opioid-dependent sample of males seeking treatment for opioid dependence in the Republic of Georgia; rather, the sample was a convenience sample of opioid-dependent males with a stable female partner, limiting the ability to effectively generalize.

This study represents an important and necessary first step in the development of a culturally-compatible behavioral intervention for Georgian men. Such a behavioral intervention may serve as a foundation for future studies aimed at ways to best address the capacity demands for drug treatment in Georgia.

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Table 1

Tests of Significance for Time, Treatment Condition, and Treatment Condition X Time Effects for the 7 Addiction Severity Index (ASI) Composite Scores

ASI Composite Score	**Time Main Effect**		**Treatment Condition Main Effect**		**Treatment Condition X Time Interaction Effect**	
	F	***p***	***F***	***p***	***F***	***p***
Medical	$F(3, 63.7) = 2.3$	.08	$F(1, 25.7) = 2.5$	.12	$F(3, 63.7) = 1.2$	.30
Employment	$F(3, 62.5) = 2.8$	.047	$F(1, 36.3) = .5$	.47	$F(3, 62.5) = 1.3$	.28
Drug	$F(3, 71.7) = 21.3$	<.0001	$F(1, 27.2) = 4.3$	.048	$F(3, 71.7) = 4.9$	.004
Alcohol	$F(3, 78.7) = 1.8$	.15	$F(1, 41.4) = .1$	.80	$F(3, 78.7) = 1.7$	.18
Legal	$F(3, 64.7) = 2.3$	.09	$F(1, 25.9) = 2.9$	.10	$F(3, 64.7) = 3.9$	.014
Family/Social	$F(3, 65.3) = 18.4$	<.0001	$F(1, 25.8) = 6.1$	.020	$F(3, 65.3) = 1.8$	.15
Psychiatric	$F(3, 69.9) = .7$	.54	$F(1, 32.9) = 4.9$	.034	$F(3, 69.9) = 2.5$	.07

Notes. N=40 at baseline [20 in the Behavioral Treatment+Naltrexone (BT+N) Condition, 20 in the Usual Care (UC) Condition], 25 at 1-month follow-up (15 in BT+N, 10 in UC), 23 at 3-month follow-up (12 in BT+N, 11 in UC), and 21 at 6-month follow-up (12 in BT+N, 9 in UC). There were 15 BT+N and 11 UC participants who showed for their second week of treatment (the second week of inpatient treatment for participants in the BT+N condition).

Table 2

Addiction Severity Index (ASI) Composite Scores Least Squares Means (Standard Errors) for Time, Treatment Condition, and Treatment Condition X Time Effects

ASI Composite Score	Time Main Effect				Treatment Condition Main Effect		Treatment Condition X Time Interaction Effect			
	Baseline	**1-month Follow-up**	**3-month Follow-up**	**6-month Follow-up**			**Baseline**	**1-month Follow-up**	**3-month Follow-up**	**6-month Follow-up**
Medical	.26 (.05)	.39 (.06)	.23 (.08)	.18 (.08)	Behavioral+Naltrexone	.34 (.06)	.39 (.06)	.48 (.08)	.33 (.11)	.15 (.10)
					Usual Care	.19 (.07)	.14 (.06)	.29 (.10)	.12 (.12)	.21 (.12)
Employment	.58 (.05)	.65 (.05)	.69 (.05)	.62 (.05)	Behavioral+Naltrexone	.67 (.06)	.63 (.07)	.68 (.07)	.68 (.07)	.69 (.07)
					Usual Care	.60 (.06)	.53 (.07)	.63 (.07)	.70 (.08)	.55 (.08)
Drug	.26 (.02)	.15 (.02)	.12 (.02)	.08 (.02)	Behavioral+Naltrexone	.13 (.02)	.29 (.02)	.10 (.02)	.08 (.03)	.04 (.03)
					Usual Care	.17 (.02)	.23 (.02)	.19 (.02)	.16 (.04)	.12 (.03)
Alcohol	.30 (.08)	.19 (.07)	.20 (.08)	.11 (.06)	Behavioral+Naltrexone	.21 (.06)	.41 (.11)	.21 (.09)	.19 (.11)	.04 (.07)
					Usual Care	.19 (.06)	.20 (.11)	.17 (.10)	.20 (.12)	.19 (.09)
Legal	.26 (.03)	.15 (.04)	.22 (.06)	.24 (.06)	Behavioral+Naltrexone	.16 (.05)	.29 (.05)	.11 (.05)	.13 (.08)	.09 (.08)
					Usual Care	.28 (.05)	.23 (.05)	.19 (.06)	.31 (.09)	.39 (.09)
Family/ Social	.44 (.03)	.23 (.04)	.18 (.04)	.15 (.04)	Behavioral+Naltrexone	.19 (.03)	.44 (.05)	.15 (.06)	.11 (.05)	.05 (.05)
					Usual Care	.31 (.04)	.44 (.05)	.30 (.07)	.25 (.06)	.25 (.06)
Psychiatric	.24 (.03)	.24 (.04)	.25 (.04)	.19 (.03)	Behavioral+Naltrexone	.19 (.03)	.25 (.04)	.23 (.05)	.17 (.05)	.11 (.04)
					Usual Care	.27 (.03)	.23 (.04)	.25 (.05)	.34 (.05)	.27 (.05)

Notes. N=40 at baseline [20 in the Behavioral+Naltrexone Intervention (BT+N) Condition, 20 in the Usual Care (UC) Condition], 25 at 1-month follow-up (15 in BT+N, 10 in UC), 23 at 3-month follow-up (12 in BT+N, 11 in UC), and 21 at 6-month follow-up (12 in BT+N, 9 in UC).