Brief Report

Treatment Outcome Predictors in Flexible Dose-Duration Methadone Detoxification Program

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Abstract

Methadone detoxification is among the widely used treatment programs for opioid dependence. The aims of this study were to identify which patient baseline factors and treatment regimen features are predictors of the treatment outcome in an outpatient flexible dose-duration methadone detoxification program.

We studied 126 opioid dependents in a naturalistic nonexperimental clinical setting. The patients were assessed for baseline demographic characteristics, and drug abuse characteristics. Treatment regimen features were recorded during the program. Successful treatment completion was defined as the last daily dose of methadone being less than 15 mg, negative urine analysis in the last two weeks of treatment, and based on the final clinician-client's decision.

Out of 126 patients, 60 patients completed detoxification successfully. Younger age, longer duration of the opioid abuse, and higher subjective opiate intoxication severity before treatment entry were all significantly associated with negative treatment outcome. Among treatment regimen features, higher maximum methadone dose had a marginally significant independent effect on treatment failure. Patients with maximum methadone dose of more than 75 mg per day had around ten times worse success rate when compared to those who received lesser doses.

The study findings could be used to predict treatment outcome and prognosis in a more individualized and patient-tailored approach in the real clinical setting. Guideline development for treatment selection and outcome monitoring in addiction medicine based on similar studies could enhance treatment outcome in clinical services.

Keywords: Detoxification, methadone, opiate addiction, treatment outcome

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Introduction

Treatment of opioid dependence is a crucial step in addressing health, social, and economic consequences associated with opioid addiction. Methadone detoxification program has been among widely used programs because of its brevity, lower cost, and resulting in resource capacity to treat more patients than other methods such as long-term methadone maintenance treatment.

Studies have also shown that various baseline patient factors affect the outcome of detoxification programs, such as age, sex, socioeconomic factors, or pattern of drug consumption.[1] Apart from these baseline variables, aspects of the treatment regimen also influence the outcome of a detoxification program. An inverse exponential reduction of methadone causes higher withdrawal symptoms during the acute phase of the opiate withdrawal curve in comparison to a linear reduction.[2] Also, greater withdrawal symptoms in patients coming off higher doses of methadone are reported.[3]

In this study, clinicians working in a naturalistic nonexperimental clinical setting were allowed to adjust dose and duration of methadone detoxification based on medical judgment of patient needs (what actually happens in clinical settings) regarding staring dose limitation and intoxication surveillance according to the national and international protocols.[4,5] Thus, we were in the position of 1) examining features of a treatment regimen that leads to lower retention rates, and 2) investigating patient factors that predict detoxification outcome.

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Materials and Methods

A naturalistic prospective study in a nonexperimental outpatient treatment setting was conceived to recruit 130 opiate- dependent subjects. Opioid-dependent patients were eligible for inclusion in this study if aged 18 years or older, using street opiates or prescription opioids as confirmed by morphine metabolites in a urine sample taken at the first assessment, and meeting opioid dependence criteria based on DSM-IV TR.[6] The study sample included 126 patients. Methadone detoxification characteristics was based on Iranian national treatment protocol for methadone detoxification and other internationally accepted treatment protocols.[4,5]

Completion or noncompletion (failure) of treatment was considered the main outcome of treatment. Treatment was taken as completed successfully if the following criteria were met: the last daily dose of methadone being less than 15 mg (most of the patients (88.3%) completed the program with the daily dose equal to 5 mg or less), negative urine analysis in the last two weeks of treatment, and final clinician-client's decision. Absent cases were considered to have failed or unsuccessful (most of the failed cases (78.7%)

Table 1. Effect of baseline variables on treatment outcome (top). Effect of treatment regimen features on treatment outcome (controlling for the effect of baseline variables) (bottom).

Predictor variable (n = 126)		Odds ratio	Confidence interval (2.5%–97.5%)	P
Baseline variables				
Age (years)		1.077	1.012–1.160	0.030
Duration of opioid abuse (years)		0.850	0.759–0.938	0.002
Subjective opiate intoxication severity		0.882	0.803–0.961	0.006
Injection history	Yes	0.299	0.080–0.954	0.052
	No	—	—	—
Opiate withdrawal severity		1.025	0.996–1.056	0.087
Education (years)		0.861	0.736–1.000	0.055
Main drug of abuse	White heroin (hydrochloride)	—	—	—
	Opium	3.416	1.022–12.485	0.052
	Brown heroin (base)	0.732	0.187– 2.678	0.642
	Prescription opioids	5.420	0.428–79.860	0.185
Treatment regimen features				
Maximum dosage		0.977	0.953–0.999	0.058
Age (years)		1.076	1.021–1.144	0.010
Duration of opioid abuse (years)		0.894	0.805–0.980	0.024
Subjective opiate intoxication severity		0.918	0.848–0.988	0.028
Injection history	Yes	0.314	0.086–0.973	0.056
	No	—	—	—

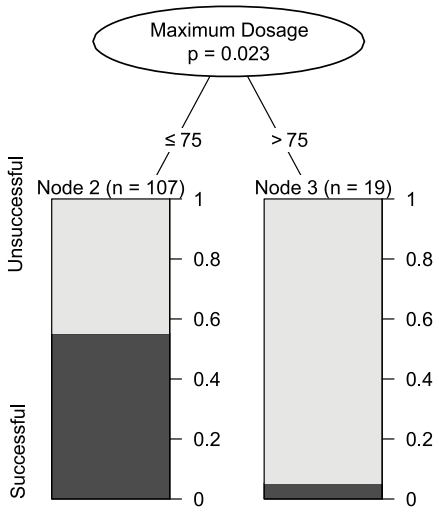

Figure 1. Classification of the subjects according to the prescribed dosage during methadone detoxification treatment. P values are computed using permutation tests, and 'n' represents number of data points in each group

were dropped out at the daily dose equal or more than 30 mg).

Baseline variables measured for each individual included age, education, gender, main drug of abuse, main route of abuse, injection history, imprisonment history, duration of opioid abuse (years), subjective opiate intoxication severity, objective opiate intoxication severity, and opiate withdrawal severity. Treatment regimen features measured included initial methadone dosage, maximum dosage, and raising duration (days taken for the dosage to reach its maximum).

Stepwise multiple regression analysis was used to determine the variables predicting outcome of the detoxification program and to control for potential confounding factors. Variance-inflation factors were calculated for detecting multicolinearity in the model. The Classification and Regression Tree (CART) method was used for partitioning treatment regimen features to different classes based on detoxification outcome.[7]

Results

Positive outcome evaluated on the whole data was 47.6% (60 patients out of 126). Regarding baseline variables affecting treatment outcome, Table 1 (top) presents results from the stepwise multiple logistic regression analysis that examined the predictors of the treatment outcome. All the baseline variables presented were included in the analysis. As the table shows, age, duration of opioid abuse, and subjective opiate intoxication severity were all predictors of the treatment outcome. These results indicate that older age (81.7% of the subjects were between 18 and 40 years old), predicts better completion of the detoxification treatment; whereas longer duration of opioid abuse and higher subjective opiate intoxication severity are predictors of the treatment failure. Overall, the regression model could classify 68.2 % (86 out of 126 patients) of the subjects correctly.

To investigate the effect of heroin dependence on treatment outcome, we grouped the main drug of abuse into two categories: heroin (white heroin and brown heroin) and nonheroin (opium and prescription opioid) categories. This analysis showed that if heroin was the main drug of abuse, this significantly would have predicted treatment failure ($P = 0.01$, odds ratio (OR) = 0.25, confidence interval (CI) = 0.07–0.77).

Also, Table 1 (bottom) shows effect of treatment regimen variables on the treatment outcome. The analysis was based on stepwise logistic regression analysis (assuming baseline variables as covariates). As the table illustrates, maximum methadone dosage affects the treatment outcome marginally significant ($P = 0.058$). That is, with a unit dose increase of the maximum methadone dosage, the odds of the treatment success decrease by a factor of 0.97. Overall, the regression model could classify 68.2 % of the subjects correctly.

We also investigated what is the critical dosage that if the maximum dosage exceeds that, there is significantly higher chance of being unsuccessful in the treatment. For answering these questions, we used a tree classification of the patients based on treatment regimen features. Results show that subject can be best classified into two groups: patients with maximum methadone dosage less than 75 mg (55.1% success rate) and patients with the maximum dosage greater than 75mg (5.2% success rate) ($P = 0.023$). This indicates that the number of successful treatments (positive outcome) differs significantly between these two groups (maximum dosage less than 75 mg, and greater than 75 mg).

Finally, we also investigated which baseline factors would predict treatment duration in successful cases. The results of univariate regression analysis showed that for the male subjects, the treatment duration was almost 16.2 days longer than the female subjects (r-squared = 0.064, $P = 0.050$).

Discussion

Consistent with previous studies,[8,9] we found that higher age is associated with higher treatment failure. It could be that older patients have less adventurous attitudes, have more stable lifestyles, and better social supports. Also, longer duration of drug abuse is the main aspect of addiction severity that had negative impact on treatment completion in this study. This is consistent with the previous study that reported addiction severity index (ASI) predicts negative treatment outcome.[10] Male subjects had longer duration of treatment among successful cases. Higher severity of dependence and better financial ability to cover extra charges for longer treatment duration for male subjects and tendency of female subjects for shorter treatment duration due to more severe stigmatization aspects of substance abuse among women could be possible reasons.

We also found a hierarchic effect of maximum methadone dose on the treatment outcome. Cases with maximum methadone dose of more than 75 mg per day had around ten times lower success rate than subjects who received lesser doses. Higher maximum doses of methadone albeit acceptable to some patients might lead to a more severe dependence that may in turn cause more difficulties during tapering phase in the next steps. Whereas in methadone maintenance treatment under-dosage and insufficient amount of doses are a cause for treatment failure,[11] our findings suggest that during methadone detoxification, being more conservative about methadone dosage is preferable.

One of the interesting findings of this study was the significant effect of baseline severity of opioid intoxication on the treatment outcome. Intoxication checklists are used, mainly not quantitatively, but just as a warning list to avoid possible life-threatening intoxication with higher methadone doses. Based on the findings of this study, lesser intoxication (subjective) at baseline before the treatment, were associated with better treatment completion. However, based on this study, quantitative measurement of intoxication severity with objective and subjective measurements could be considered as a possible treatment outcome predictor.

This study was based on a naturalistic nonexperimental setting, and thus the restrictions associated with such studies also apply here. For instance, the patients were not randomly assigned to the different treatment regimen, which makes the results less generalizable across populations. Other individual differences such as financial situation and ASI, treatment regimen features, and unmeasured confounds might also be responsible for the treatment outcome, which can be addressed in the future studies.

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