A Non-opioid Protocol for Outpatient Opioid Detoxification and Transition to Antagonist Treatment

Vania Rudolf, MD, MPH; Jim Walsh, MD; Paul Gianutsos, MD, MPH; Kaitlan Baston, MD; Gregory Rudolf, MD
Addiction Recovery Service, Swedish Medical Center, Seattle, WA

Background

Opioid use disorder represents a critical public health problem associated with growing morbidity and mortality in the United States and throughout the world (1).

Injectable extended-release naltrexone (XR-NTX) therapy is a long-acting FDA approved formulation that increases adherence and offers efficacy in opioid relapse prevention (2).

XR-NTX is an alternative approach to opioid substitution treatment for people highly motivated to achieve abstinence, for younger patients with a short history of opioid dependence, and for those confined to drug-free environments.

Adequate management of opioid withdrawal plays a key role in the initiation stage of antagonist therapy, and can contribute to successful early recovery (3).

While different opioid agonist tapers and other medication strategies for medically supervised withdrawal have been described, there is no standard evidence-based treatment protocol for opioid withdrawal and induction to XR-NTX (3, 4).

Effective therapies to facilitate transition to injectable naltrexone are greatly needed.

Study Objective

Using a case series design, the study examines a novel non-opioid and non-benzodiazepine approach to transition patients from active opioid addiction to XR-NTX treatment in an outpatient office setting.

This work is modeled after a similar inpatient protocol found to be effective for opioid detoxification and XR-NTX induction (5).

Design

Retrospective analysis and review of clinical data stored in electronic medical record system reflecting standard patient care.

Method

- Twenty opioid dependent DSM-IV treatment-seeking individuals evaluated and treated between 1/1/2012-3/31/2014 at the Addiction Recovery Service Clinic, Swedish Medical Center, Seattle, WA.
- Outpatient detox and XR-NTX induction 7-10 day procedure based on severity (physical dependence), type of opioid, anticipated withdrawal and timing of opioid cessation.
- Severe dependence/long-acting: 5-7 day scheduled medications (detoxification and NTX induction).
- Moderate dependence/short-acting: 3-5 day scheduled medications (detoxification and NTX induction).
- A 2-3 day home NTX induction with scheduled oral NTX (12.5 mg every twelve hours-> 25mg every twelve hours-> 50 mg daily until XR-NTX).
- In office XR-NTX (> day 5).
- Subsequent 5-7 day taper of detoxification medications (every six-eight hours as needed).
- Protocol detoxification medications included scheduled tizanidine, hydroxyzine and gabapentin and ancillary mirtazapine and dicyclomine.

Protocol Medications

Symptoms	Drug class	Medication (dosage)
Autonomic arousal (sympathetic)	A2-adrenergic agonist	Tizanidine (4 mg Q6-8H)
Anxiety/restlessness	Anticonvulsant	Gabapentin (300 mg Q6-8H)
Anxiety	Antihistamine	Hydroxyzine (50 mg Q6-8H)
Insomnia	Sedating antidepressant	Mirtazapine (15 mg HS)
	Anticonvulsant	Gabapentin (300 mg HS)
GI distress	Antispasmodic	Dicyclomine (20 mg Q6-8H)
	Aggressive oral hydration	Water, sport drinks (electrolytes)

- Daily telephone follow up visits with patient and support person verifying proper dispensing and treatment response.
- Office visits on Day 3-7-14-28.
- Counseling and referral to inpatient/outpatient treatment programs.
- Urine drug screening for opioids/other substance at each office visit.
- Screening for adverse events, medication tolerability, withdrawal, and precipitated symptoms or XR-NTX complications.
- Opioid withdrawal/SOWS- mild, moderate, severe.

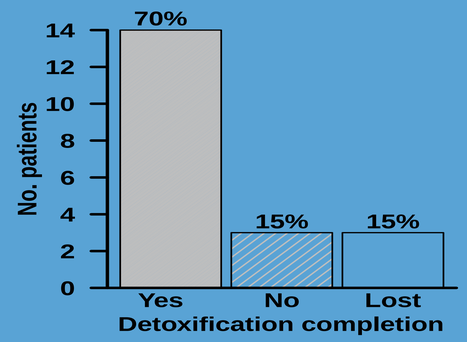
Outcomes:

- *Primary*- Completion of outpatient detoxification and successful XR-NTX induction.
- *Secondary*- Length of detoxification procedure, length of NTX and XR-NTX initiation, opioid and other drug use measured by urine drug screen (UDS), adverse events, and engagement in chemical dependency treatment prior to and post XR-NTX.

Results

Baseline characteristics:

Mean age 25. Caucasian 95%. Gender M 65%/F 35%, Employed 70%. Single 80%. Education: College grad 25%, >some college 35%, HSG/GED 40%. Tobacco use: 75%, HepC Ab+ 10%. Fam hx addiction 85%. Ins: private 85%.
Years of opioid use, mean (SD) [range] 4.6 (3.1) [1-13]
Nr of prior detox events- mean (SD) [range] 2.4 (1.6) [1-8]. History of past XR-NTX 55%. Level of physiological dependence: severe 55%, moderate 45%.
Opiate history: heroin IV 30%, heroin smoked 20%, oxycodone/hydrocodone oral 20%, oxycodone smoked 5%, methadone 1%, mixed 20%.
Sober support dispensing protocol meds 70%.



- Fourteen of the twenty subjects (70%) completed the detoxification protocol and transitioned to XR-NTX .
- Mean [range] of detoxification treatment was 6.8 [5-15] days, mean time to home oral NTX was 7 [3-25] days, and mean time to XR-NTX was 10 [4-25] days.
- No noted severe withdrawal; mild restlessness, muscle aches and anxiety 4 (20%), insomnia 1 (5%).
- Protracted NTX fatigue 4 (20%) 1-2 wks s/p XR-NTX.
- Treatment engagement (P=.016), rates of opioid (P<.001) and drug use for more than one substance (P=.002) significantly improved after detoxification and initiation of XR-NTX compared with baseline.
- Eight of the fourteen subjects (57%) received a second XR-NTX injection.
- Decreased cravings reported after XR-NTX.
- Tobacco, marijuana and alcohol use were not significantly different from baseline.
- Medications well tolerated, no adverse events.

Pre- and post-treatment urine drug analysis

	1st visit (n=14)	Post detoxification (n=14)		2 weeks (n=14)		4 week (n=14)	
	n (%)	n (%)	P[1]	n (%)	P[1]	n (%)	P[1]
Opioid use	14 (100%)	0 (0%)	<.001	0 (0%)	<.001	3 (17%)	<.001
>1 substance use	12 (60%)	0 (0%)	.002	0 (0%)	.002	0 (0%)	.002

[1]Compared to 1st visit, McNemar's test for paired proportions.

Conclusions

This retrospective study describes a novel pharmacologic approach with potential efficacy for outpatient management of opioid withdrawal and early XR-NTX initiation.

Induction rate was likely influenced by prior uncomplicated XR-NTX experience in eight out of the 14 receiving XR-NTX.

All participants reported feeling safe with daily telephone follow up, regular office visits and establishment of a support monitor during the acute withdrawal and induction phase of antagonist treatment.

The observed high percentages of urine samples negative for opioids and other tested substances support research that XR-NTX combined with engagement in treatment effectively decrease pathologic opioid use.

Study limitations: retrospective, uncontrolled design, small sample size.

There are no current studies that specifically evaluate the optimal dosing, efficacy and tolerability of a controlled substance-free protocol in managing opioid withdrawal and XR-NTX induction.

A controlled substance-free protocol that adequately manages withdrawal via safe, generic medications could have significant advantages over opioid or sedative-hypnotic approaches, including lower risk of adverse events, misuse, and reduced delay b/n opioid cessation and antagonist initiation while avoiding precipitated withdrawal upon NTX induction.

Further research into this novel approach is needed to identify its place within the spectrum of available therapies for opioid withdrawal and antagonist induction.

References:

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Contact:
Vania Rudolf, MD, MPH; vania.rudolf@swedish.org
Gregory Rudolf, MD; gregory.rudolf@swedish.org