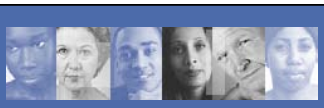


Short-Term Opioid Withdrawal Using Buprenorphine

Findings and strategies from a
NIDA Clinical Trials Network Study

Clonidine

- Clonidine - Catapress®
- Inpatient and outpatient settings
- A centrally acting alpha 2-adrenergic agonist
- Partially suppresses peripheral symptoms of opioid withdrawal (e.g., nausea, vomiting, sweating, diarrhea) by decreasing autonomic nervous system activity

Why Use Clonidine?

- Not a scheduled medication
- No special license required
- Alleviates autonomic mediated signs and symptoms
- Standard clinical medication for opioid withdrawal
- Not effective in alleviating subjective effects of opioid withdrawal (e.g., body aches, abdominal cramps, cravings, etc.)

Contraindication for Use of Clonidine

- Pregnancy
- Liver damage
- History of auditory hallucinations of delirium
- Systolic blood pressure < 90 mm Hg
- Recent myocardial infarction
- Chronic renal failure
- History of hypertension, hypotension, fainting, or dizziness on rising

Medically-Assisted Withdrawal

(a.k.a. Dose Tapering; a.k.a. Detoxification)

The Research: CTN Protocols 0001 and 0002

The Two Buprenorphine-Naloxone Protocols

NIDA-CTN 0001:

Buprenorphine-Naloxone vs. Clonidine for Short-Term Inpatient Opiate Detoxification

NIDA-CTN 0002:

Buprenorphine-Naloxone vs. Clonidine for Short-Term Outpatient Opiate Detoxification

Initiated in 8 Regional Nodes and
12 Community Treatment Programs

NIDA CTN 001/002 Buprenorphine-Naloxone Detoxification Protocols

- Two, open-label, randomized clinical trials
- Compared Buprenorphine-Naloxone (BUP/NX) and Clonidine for Short-Term (2 weeks) opioid Detoxification in Residential or Outpatient Settings

Study Schema

1. Obtain Informed Consent
2. Perform Screening/Baseline Assessments

Randomize (2:1) and Enroll

N=240	N=120
Buprenorphine/Naloxone	Clonidine
13 days detoxification	13 days detoxification

Follow-up at 1 month

Follow-up at 3 months

Follow-up at 6 months

Primary Efficacy Endpoint

- It is hypothesized that BUP/NX detoxification, compared to clonidine, will be associated with a better treatment response.
- A treatment responder = anyone who completes the 13-day detoxification and whose last urine specimen is negative for opioids.

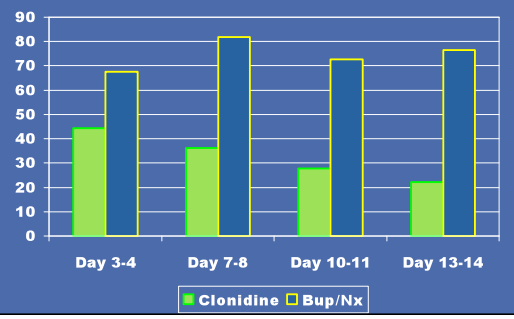
Demographics 0001 (Inpatient)

	Bup/Nx	Clonidine	Total
Sex No. (%)			
Male	61	58	60
Female	39	42	40
Race No. (%)			
White	56	56	56
Black	19	19	19
Hispanic	12	17	16
Other	9	8	9
Age in Years: Mean (Range 21-61)	35.6	37.4	-
Employed (%)	-	-	66
Mean Education in Years (SD)	-	-	12.8 (1.7)
Mean Years of Heroin Use (SD)	-	-	6.6 (8.1)

Present and Opioid Negative 0001 (Inpatient)

Present and opioid neg	Bup/Nx (N)	%	Clonidine (N)	%
N	77		36	
Day 3 or 4	52	67.5	16	44.4
Day 7 or 8	63	81.8	13	36.1
Day 10 or 11	56	72.7	10	27.8
Day 13 or 14	59	76.6	8	22.2

Present and Opioid Negative 0001 (Inpatient)



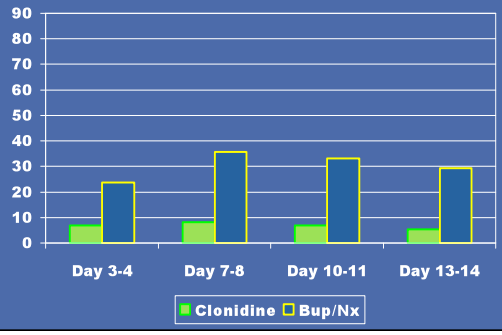
Demographics 0002 (Outpatient)

	Bup/Nx	Clonidine	Total
Sex No. (%)			
Male	73	69	72
Female	27	31	28
Race No. (%)			
White	40	40	40
Black	36	28	37
Hispanic	21	13	20
Other	3	3	3
Age in Years: Mean (Range 21-61)	38.3	40.0	-
Employed (%)	-	-	56.8
Mean Education in Years (SD)	-	-	12.4 (2.1)
Mean Years of Heroin Use (SD)	-	-	9.4 (9.6)

Present and Opioid Negative 0002 (Outpatient)

Present and opioid neg	Bup/Nx (N)	%	Clonidine (N)	%
N	157		74	
Day 3 or 4	37	23.6	5	6.8
Day 7 or 8	56	35.7	6	8.1
Day 10 or 11	52	33.1	5	6.8
Day 13 or 14	46	29.3	4	5.4

Present and Opioid Negative 0002 (Outpatient)



Lessons from Additional Analyses : Predictors of Treatment Success

- Medication was the best predictor of treatment outcome for opiate detoxification regardless of treatment setting
- Inpatient treatment was a strong predictor of treatment success
- Those with greater reduction in opioid withdrawal severity from baseline to day 3 was were more likely to have positive treatment outcome
- Those who did the best with clonidine had low severity withdrawal symptoms at baseline

Ziedonis, et al., 2009, *Drug and Alcohol Dependence*, 99, 28-36.

Lessons from a Study of Longer and Shorter Taper Schedules

- Differences in being drug free at end of taper did not differ for 7 or 28 day groups (after 4 week stabilization)
- A relatively quick taper may be advantageous and did not result in relapse to drug use at greater rates than longer tapers
- Patients stabilized physiologically on a range of buprenorphine doses can be tapered successfully over 7 days
- There was no advantage to prolonging the tapering schedule for weeks.

Ling, et al., 2009, *Addiction*, 104, 256–265.

Additional Research

- More research is needed to answer questions such as:
- To what degree do these patients return to opioid use following taper.
- What counseling is best coupled with this taper?
- What difference would it make if the treatment were provided in a physician's office rather than in a substance abuse treatment program or clinic where other ancillary services are available?