

# A Double-Blind, Placebo-Controlled Study of the Opiate Antagonist, Naltrexone, in the Treatment of Kleptomania

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# ABSTRACT

**Background:** Kleptomania is a rare psychiatric disorder characterized by recurrent stealing and for which there exist no empirically validated treatments. This study examined the efficacy and tolerability of the opioid antagonist naltrexone in adults with kleptomania who have urges to steal.

**Method:** An 8-week, double-blind, placebo-controlled trial was conducted to evaluate the safety and efficacy of oral naltrexone for kleptomania. Twenty-five individuals with DSM-IV kleptomania were randomized to naltrexone (dosing ranging from 50mg/day to 150mg/day) or placebo. Twenty-three subjects (92%) completed the study. Subjects were assessed every two weeks with the Yale Brown Obsessive Compulsive Scale Modified for Kleptomania (K-YBOCS), the urge and behavior subscales of the K-YBOCS, the Kleptomania Symptom Assessment Scale (K-SAS), the Clinical Global Impressions scale (CGI), and measures of depression, anxiety, and psychosocial functioning.

**Results:** Subjects assigned to naltrexone had significantly greater reductions in K-YBOCS total scores ( $p=.001$ ), stealing urges ( $p=.032$ ) and stealing behavior ( $p<.001$ ) compared to subjects on placebo. Subjects assigned to naltrexone also had greater improvement in overall kleptomania severity (reflected in the CGI scores) ( $p<.001$ ). The mean effective dose of naltrexone was 116.7 ( $\pm$  44.4) mg/day.

**Conclusion:** Naltrexone demonstrated statistically significant reductions in stealing urges and behavior in kleptomania. Naltrexone was well tolerated.

# INTRODUCTION

Kleptomania is a disorder characterized by:

1. Recurrent failure to resist impulses to steal objects that are not needed for personal use or for their monetary value;
  2. Increasing sense of tension immediately before committing the theft;
  3. Pleasure, gratification, or relief at the time of committing the theft;
  4. Stealing is not committed to express anger or vengeance and is not in response to a delusion or a hallucination; and
  5. Stealing is not better accounted for by another disorder.
- Psychosocial problems are common in kleptomania and include legal consequences, reduced quality of life, and impaired functioning.
  - Kleptomania appears to share many phenomenological similarities to substance use disorders: urges or cravings, tolerance, withdrawal, repeated unsuccessful attempts to cut back or stop, and impairment in areas of life functioning.
  - The efficacy of opioid antagonists in the treatment of addictive disorders has been proposed to involve opioidergic modulation of mesolimbic dopamine circuitry. We hypothesized that naltrexone would reduce the severity of stealing urges and thereby improve behavior and patients' overall functioning.

## METHODS

### *Inclusion Criteria*

1. Men and women aged 17 to 75
2. Primary DSM-IV diagnosis of kleptomania using the clinician-administered Structured Clinical Interview for Kleptomania (SCI-K); and
3. Stole something within 2 weeks prior to enrollment.

### *Exclusion Criteria*

1. Infrequent stealing (i.e. less than one time per week) that did not meet DSM-IV criteria for kleptomania;
2. Unstable medical illness or clinically significant abnormalities on laboratory tests or physical examination at screening visit;
3. Current pregnancy or lactation, or inadequate contraception in women of childbearing potential;
4. A need for medication with unfavorable interactions with naltrexone (e.g., narcotics);
5. Lifetime history of bipolar disorder type I or II, dementia, schizophrenia, or any psychotic disorder;
6. Current or recent (past 3 months) DSM-IV substance use disorder; and
7. Initiation of psychotherapy or behavior therapy within 3 months prior to study.

The 25 randomized subjects reported a mean age of DSM-IV kleptomania onset of 23.4 ( $\pm$  15.9) years. Subjects spent 47.4 ( $\pm$  24.3) minutes each week stealing and an additional 114.3 ( $\pm$  102.4) minutes each week struggling with urges to steal. 23 subjects (92.0%) had been arrested at least once for stealing.

**Funding: Internal Funds**

## ***Study Design***

- Subjects were randomized to either naltrexone or placebo in a 1:1 fashion and seen every two weeks for the 8-week period.
- Subjects were started on naltrexone 50mg/day or matching placebo for 2 weeks. At week 2, the dose was increased to 100mg/day, and at week 4 was increased to 150mg/day unless clinical improvement was attained at a lower dose.

## ***Efficacy and Safety Assessments***

The primary outcome measure was the Yale Brown Obsessive Compulsive Scale Modified for Kleptomania (K-YBOCS), a reliable and valid, 10-item, clinician-administered scale that rates symptoms within the last seven days.

### ***Secondary measures used at each study visit included:***

- Kleptomania Symptom Assessment Scale (K-SAS)
- Clinical Global Impression - Severity (CGI)
- Sheehan Disability Scale (SDS)
- Hamilton Anxiety Rating Scale (HAM-A)
- Hamilton Depression Rating Scale (HAM-D)

## ***Data Analysis***

Primary and secondary measures were examined using repeated measures ANOVA in an intent-to-treat population (LOCF). A Bonferroni correction was used; tests were two-tailed and an alpha level of .006 was used to determine statistical significance. A retrospective power analysis was performed using a bootstrap approach with 10,000 resampling iterations. Significance at  $p=.05$  was achieved in 97.7% of the 2-level active/placebo dichotomy for the primary outcome measure, the K-YBOCS (significance at  $p=.006$  was achieved in 77.7%). Effect sizes were calculated using Cohen's effect size index  $d$ . A  $d$  of .2 is considered a small effect size, .5 is medium, and .8 is large.

## **DISCUSSION**

- This randomized, double-blind, clinical trial found naltrexone to be superior to placebo in the treatment of kleptomania across a spectrum of illness-specific and global outcome measures.
- The efficacy of naltrexone lends further support to the hypothesis that pharmacological manipulation of the opiate system may target core symptoms of kleptomania. Opioid antagonists have been hypothesized to influence dopamine neurotransmission in the nucleus accumbens and linked motivational neurocircuitry, dampening stealing-related excitement and cravings.
- Naltrexone's efficacy in kleptomania lends support to the hypothesis that kleptomania in particular and impulse control disorders in general may be related to substance addictions.

# RESULTS

## *Subject Characteristics*

TABLE I. Baseline Comparison of Kleptomania Subjects Assigned to Naltrexone or Placebo

Variable <sup>a</sup>	Baseline		Test <sup>b</sup>	df	p-value
	Placebo (n=13)	Naltrexone (n=12)			
Age, years	41.4 ± 12.7 [17-64]	44.3 ± 12.2 [22-65]	.575	23	.571
Sex, female, n (%)	10 (76.9)	8 (66.7)	f	n/a	.673
White, n (%)	12 (92.3)	12 (100.0)	f	n/a	.999
Married, n (%)	6 (46.2)	3 (25.0)	f	n/a	.267
Subjects currently taking an antidepressant, n (%)	10 (76.9)	9 (75.0)	f	n/a	1.000
K-YBOCS total score	15.69 (5.44) [7-25]	20.08 (7.79) [12-36]	1.646	23	.113
K-YBOCS urge/thought subscale	9.69 (3.17) [4-15]	10.67 (4.79) [3-20]	.604	23	.552
K-YBOCS behavior subscale	6.00 (4.67) [0-11]	9.42 (5.21) [1-19]	1.728	23	.097
Kleptomania Symptom Assessment Scale (K-SAS) total score	22.62 (10.21) [10-41]	29.42 (5.38) [21-41]	2.105	18.489	.049
Clinical Global Impression (CGI) – Severity Scale	4.15 (0.69) [3-5]	5.00 (0.95) [4-7]	2.559	23	.018
Hamilton Depression Rating Scale	6.69 (4.96) [0-17]	5.58 (3.45) [0-10]	-.644	23	.526
Hamilton Anxiety Rating Scale	6.46 (5.24) [0-16]	4.92 (3.97) [0-13]	-.826	23	.417
Sheehan Disability Scale	8.69 (7.60) [0-24]	14.33 (8.95) [0-27]	1.704	23	.102

<sup>a</sup> All variables are mean (±SD) [range] unless otherwise indicated

<sup>b</sup> t-test unless otherwise indicated (f=Fisher's Exact Test)

K-YBOCS = Yale Brown Obsessive Compulsive Scale Modified for Kleptomania

## *Safety and Tolerability*

The incidence of adverse experiences in naltrexone-treated subjects was consistent with prior studies and no unusual experiences were reported. There were no statistically significant differences in the incidence of adverse events between groups.

## DISCLOSURES

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## Efficacy Results

**TABLE 2. Treatment Responses of Kleptomania Subjects Assigned to Placebo or Naltrexone (intent-to-treat population)**

Variable <sup>a</sup>	Baseline		Endpoint		Treatment F (df) p-value	Visits F (dfb) p-value	Treatment by Visits F (dfb) p-value	Effect Size Cohen's d <sup>c</sup>
	Placebo	Naltrexone	Placebo	Naltrexone				
K-YBOCS total score	15.69 (5.44)	20.08 (7.79)	11.46 (7.76)	3.83 (2.86)	0.16 (1,23) P=.691	17.80 (2.94,67.7) P<.001	6.07 (2.94,67.7) P=.001	1.14
K-YBOCS urge/thought subscale	9.69 (3.17)	10.67 (4.79)	6.38 (3.62)	3.17 (2.33)	0.25 (1,23) P=.619	17.24 (2.27,52.25) P<.001	3.29 (2.27,52.25) P=.039	0.80
K-YBOCS behavior subscale	6.00 (4.67)	9.42 (5.21)	5.08 (5.01)	0.67 (2.02)	0.06 (1,23) P=.805	8.52 (4,92) P<.001	5.61 (4,92) P<.001	0.89
K-SAS total score	22.62 (10.21)	29.42 (5.38)	16.54 (9.99)	7.50 (6.70)	0.01 (1,23) P=.942	20.64 (3.15,72.37) P<.001	7.21 (3.15, 72.37) P<.001	1.09
CGI – Severity	4.15 (0.69)	5.00 (0.95)	3.31 (1.38)	1.75 (0.75)	0.54 (1,23) P=.470	22.73 (4,92) P<.001	7.64 (4,92) P<.001	1.89
HAM-D	6.69 (4.96)	5.58 (3.45)	4.38 (4.54)	1.50 (2.75)	2.07 (1,23) P=.164	6.02 (2.67,61.32) P=.002	0.84 (2.67,61.32) P=.465	0.67
HAM-A	6.46 (5.24)	4.92 (3.97)	3.38 (3.50)	1.42 (2.71)	1.65 (1,23) P=.212	6.96 (2.82,64.90) P=.001	0.39 (2.82,64.90) P=.746	0.42
Sheehan Disability Scale	8.69 (7.60)	14.33 (8.95)	5.00 (5.51)	1.83 (3.10)	0.65 (1,23) P=.427	9.35 (2.27,52.19) P<.001	2.79 (2.27,52.19) P=.064	0.38

<sup>a</sup> All variables are mean (±SD)

<sup>b</sup> When Mauchly's Test of Sphericity was significant the Greenhouse-Geiser correction was used (fractional degrees of freedom)

<sup>c</sup> Cohen's d at endpoint calculated using the pooled standard deviation of the 2 baseline groups

K-YBOCS = Yale Brown Obsessive Compulsive Scale Modified for Kleptomania

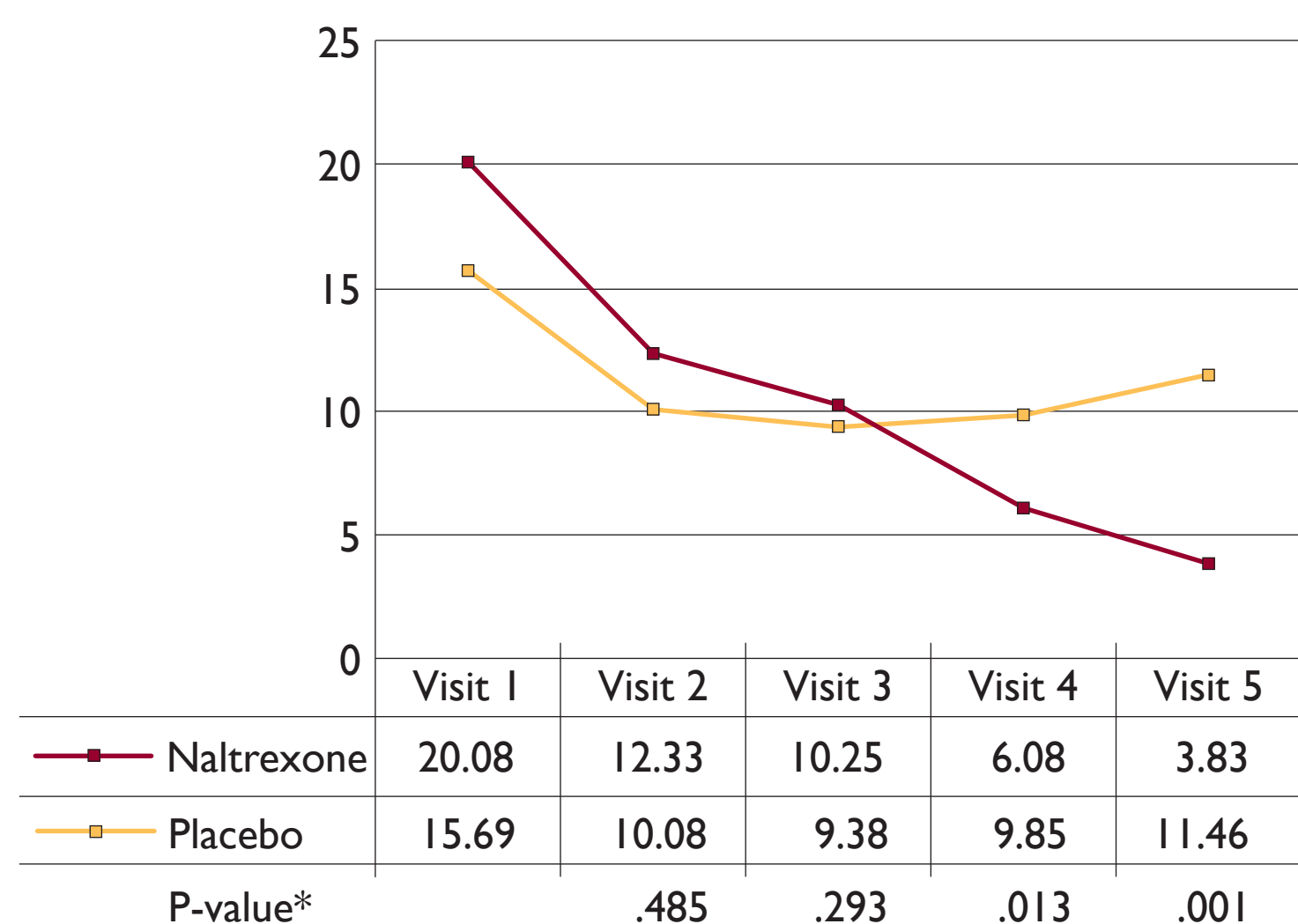
K-SAS = Kleptomania Symptom Assessment Scale

CGI = Clinical Global Impression (Severity) Scale

HAM-D = Hamilton Depression Rating Scale

HAM-A = Hamilton Anxiety Rating Scale

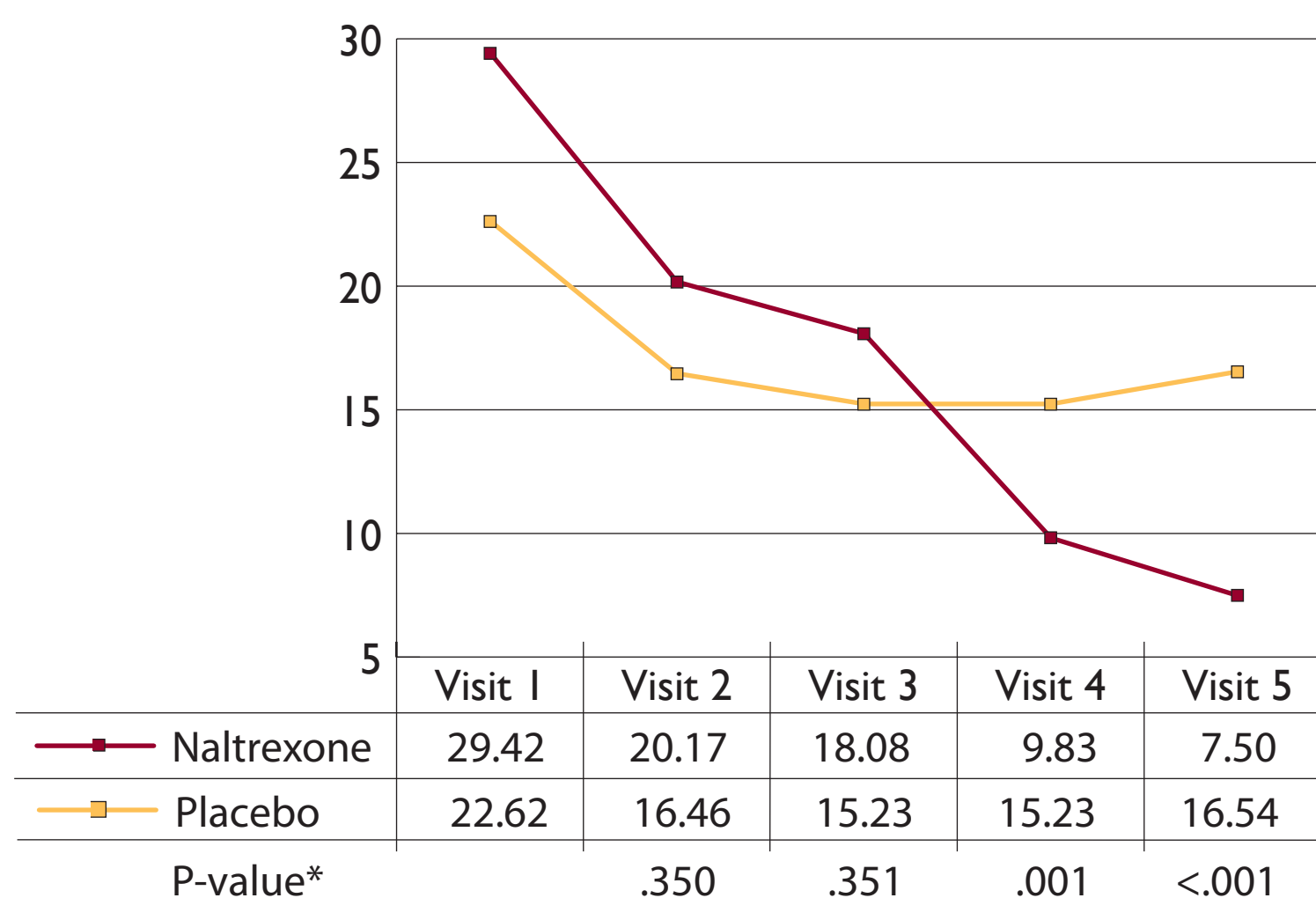
**FIGURE 1. K-YBOCS Total Scores Over Time in Subjects Assigned to Naltrexone or Placebo**



\*p-value is for the interaction of treatment group by contrast of each visit to baseline (df=1,23)

With 4 visits a Bonferroni adjusted p-value would be .0125

**FIGURE 2. K-SAS Total Scores Over Time in Subjects Assigned to Naltrexone or Placebo**



\*p-value is for the interaction of treatment group by contrast of each visit to baseline (df=1,23)

With 4 visits a Bonferroni adjusted p-value would be .0125