# Naltrexone in the Treatment of Adolescent Sexual Offenders

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***Background:*** Naltrexone is a long-acting opioid used clinically in alcoholism, drug abuse, bulimia nervosa, obsessive-compulsive disorder, and impulse-control disorders. This study investigated whether naltrexone can decrease sexual arousal in legally adjudicated adolescent sexual offenders.

***Method:*** In an open-ended prospective study, naltrexone was given to 21 adolescents participating in an inpatient adolescent sexual offenders program who met any of the self-reported criteria of (1) masturbating 3 or more times per day, (2) feeling unable to control arousal, (3) spending more than 30% of awake time in sexual fantasies, or (4) having sexual fantasies or behavior that regularly intruded into and interfered with their functioning in the treatment program. After having been treated for more than 2 months, 13 patients had their naltrexone administratively stopped, thus providing a before, during, after, and resumption-of-treatment design. Behavioral changes were monitored daily with a fantasy-tracking log and a masturbation log. A positive result was recorded if there was more than a 30% decrease in any self-reported criterion that was applicable to each specific patient and this benefit lasted at least 4 months. Data were collected from July 2000 to December 2002. Leuprolide was given if naltrexone was not sufficiently helpful in controlling sexual impulses and arousal.

***Results:*** Fifteen of 21 patients were considered to have a positive result and continued to respond for at least 4 months to an average dose of 160 mg per day with decreased sexual fantasies and masturbation. Dosages above 200 mg per day were not more helpful. Administrative discontinuation of naltrexone in a subset of 13 patients resulted in reoccurrence of symptoms that began when the dose taper reached 50 mg per day. There were no changes in clinical chemistries. Five of 6 patients who did not benefit from naltrexone responded favorably to leuprolide.

***Conclusions:*** Naltrexone at dosages of 100 to 200 mg per day provides a safe first step in treating adolescent sexual offenders. It is possible that the benefits observed here will generalize to the larger population of non–socially deviant hypersexual patients or "sexual addicts."

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With a few exceptions, there are no reliable outcome data revealing successful treatment of sexual offenders. The Task Force on Sexually Dangerous Offenders concluded that psychodynamic treatment in general has been ineffective.[1] Most of the verifiable psychological treatments have used a cognitive model of relapse prevention.[2] Reliable data have come from the use of hormonal compounds to lower testosterone, such as cyproterone and medroxyprogesterone, which have substantially reduced recidivism.[1] However, these compounds, as well as leuprolide, which is longer acting, have significant potential side effects necessitating regular, expensive medical monitoring.[3] Naltrexone is a long-acting opioid that has been used clinically in alcoholism,[4] drug abuse,[5] bulimia nervosa,[6] obsessive-compulsive disorder (OCD),[7,8] and impulse-control disorders.[9]

In adults, the term *compulsive sexual behavior* has been used to describe socially deviant (e.g., paraphilias) and non–socially deviant hypersexual behavior.[10,11] The following study investigated whether naltrexone should be considered in the management of socially deviant hypersexual behavior in adolescents.

## METHOD AND MATERIALS

Twenty-one male, legally adjudicated sexual offenders had been admitted to a 36-bed inpatient adolescent sexual offenders program for an average of 1.2 years at the time this study was begun. The program is a behavioral modification and didactic program associated with a therapeutic school. The patients were 13 to 17 years of age, with a mean age of 15.2 years. They had offended against children 2 to 12 years of age and had a range of 1 to 37 victims. One patient also had offended against his dog, and 1 had offended against his mother. Nineteen were heterosexual, 1 was homosexual, and 1 was bisexual. Two were involved in self-injurious behavior. Nine patients had been discharged from the program before completion of this study. They had been in the program an average of 26 months.

Subjects were placed on naltrexone if they (1) masturbated excessively (i.e., 3 or more times per day), (2) felt they could not control their arousal (i.e., became sexually excited with erections spontaneously when seeing or thinking about children, girls, women, or men), (3) spent more than 30% of their awake time in sexual fantasies, or (4) had sexual fantasies or behavior that regularly intruded

  

**Table 1. Comorbid Diagnoses in a Group of 21 Adolescent Sexual Offenders**

| Diagnosis | N |
|---|---|
| ADD or ADHD | 11 |
| Sexual abuse of a child where the patient was the victim | 6 |
| Depressive disorder NOS | 5 |
| Substance abuse | 5 |
| Intermittent explosive disorder | 4 |
| Frotteurism | 3 |
| Posttraumatic stress disorder | 3 |
| Major depression with psychotic features | 2 |
| Learning disability | 2 |
| Oppositional defiant disorder | 2 |
| Self-injurious behavior | 2 |
| Physical abuse of a child where the patient was the victim | 2 |
| Psychotic disorder NOS | 1 |
| Bipolar disorder NOS | 1 |
| Schizophreniform disorder | 1 |
| Tourette's disorder | 1 |
| Paraphilia NOS (zoophilia) | 1 |
| Social anxiety disorder | 1 |
| Dysthymic disorder | 1 |
| Sexual abuse of an adult | 1 |

Abbreviations: ADD = attention-deficit disorder, ADHD = attention-deficit/hyperactivity disorder, NOS = not otherwise specified.

**Table 2. Concomitant Medications in a Group of 21 Adolescent Sexual Offenders**

| Medication | Dose, mg/day | N |
|---|---|---|
| Bupropion | 150–300 | 6 |
| Methylphenidate slow release (SR) | 20–54 | 5 |
| Risperidone | 0.5–6.0 | 5 |
| Valproate sodium | 500–1250 | 5 |
| Oxcarbazepine | 450–2400 | 4 |
| Clonidine | 0.1 | 3 |
| Guanfacine | 0.5–1.0 | 3 |
| Lithium carbonate SR | 600 | 3 |
| Topiramate | 100–300 | 3 |
| Dextroamphetamine mixed salts | 25–40 | 2 |
| Clonazepam | 0.5 | 2 |
| Sertraline | 50–100 | 2 |
| Paroxetine | 20–40 | 2 |
| Desmopressin | 0.2 | 2 |
| Citalopram | 40 | 1 |
| Nefazodone | 200 | 1 |
| Fluoxetine | 40 | 1 |
| Venlafaxine | 225 | 1 |
| Imipramine | 25–50 | 1 |
| Fluvoxamine | 200 | 1 |
| Haloperidol | 2 | 1 |
| Olanzapine | 5 | 1 |
| Ziprasidone | 160 | 1 |
| Propranolol | 30 | 1 |
| Minocycline | 200 | 1 |
| Mecamylamine | 7.5 | 1 |

into and interfered with their functioning in the treatment program. Subjects were selected out of a cohort of 39 consecutively admitted patients, 18 of whom did not meet these criteria.

The study was approved by the local internal review board, and parental or guardian informed consent was obtained in all cases. However, in the 13 cases (after these patients had each been on naltrexone treatment for at least 2 months) following the first case, the hospital administratively decided to discontinue naltrexone for 11 to 26 days, during which time a more extensive informed consent statement was obtained from each parent or guardian. This discontinuation allowed a serendipitous before-, during-, after- (i.e., 11 to 26 days), and resumption-of-treatment prospective design with and without naltrexone. One patient was discharged before this administrative decision, and 7 of the 21 patients were admitted after. The latter 7 were started on medication prospectively, allowing observations before and during treatment. All diagnoses were made during a clinical diagnostic interview, which is available from the authors by request.

In addition to the diagnosis of sexual abuse of a child, 11 had been diagnosed with attention-deficit disorder or attention-deficit/hyperactivity disorder (ADHD); 6, with sexual abuse of a child where the patient was the victim (1 of these patients was also physically abused); 5, with depressive disorder not otherwise specified (NOS); 5, with substance abuse; 4, with intermittent explosive disorder; 3, with posttraumatic stress disorder (PTSD); and 3, with frotteurism. Two patients each were diagnosed with major depression with psychotic features, learning disability, oppositional defiant disorder, self-injurious behavior, and physical abuse of a child where the patient was the victim; 1 each was diagnosed with psychotic disorder NOS, bipolar disorder NOS, schizophreniform disorder, Tourette's disorder, social anxiety disorder, paraphilia NOS (zoophilia), sexual abuse of adult, and dysthymic disorder (Table 1).

Patients were receiving concomitant medications given prior to the initiation of naltrexone. Eleven received various forms of stimulant medication, with 6 of these patients also receiving guanfacine or clonidine for sleep or agitation. Eight patients also received various combinations of antidepressants, mainly bupropion. There was no clear effect seen with the SSRIs on sexual arousal or masturbation in this population. Five patients were receiving combinations of valproate, lithium, oxcarbazepine, and topiramate (topiramate was often added as a mood stabilizer when there was excessive weight gain). Five patients received risperidone, and 1 patient with Tourette's disorder received mecamylamine and low-dose haloperidol. Finally, 1 patient was receiving imipramine and desmopressin for enuresis (Table 2).

All patients received an average maintenance dose of 170 mg of naltrexone per day, with a range of 100 to 200 mg per day. They were started on naltrexone treatment at 50 mg per day for 4 days, and the dose was increased every 4 days until a clinical response occurred. Behavioral changes were monitored daily with a fantasy-tracking log, in which all daily sexual fantasies (deviant and nondeviant) were transcribed by each patient and reviewed by staff, and a masturbation log, in which the number of masturbation episodes per day was noted.

Any changes in clinical chemistries were assessed monthly for 3 months and then every 6 months with a complete blood count (CBC) and 20 general chemistries, which included liver function profile testing. A positive result with naltrexone was recorded if there was more than a 30% decrease in self-assessed sexual fantasies and masturbation and if this benefit lasted at least 4 months. Data were collected from July 2000 to December 2002.

Leuprolide, 3.75 to 7.50 mg IM per month, was given if naltrexone was not sufficiently helpful in controlling sexual impulses and arousal, and especially if the patient was an assaultive or aggressive offender.

## RESULTS

Clear clinical benefits were not seen at naltrexone dosages of less than 100 mg per day, and only 2 patients were successfully maintained at this dose. All patients except 1 noted an initial benefit of decreased arousal, masturbation, and fantasies at 100 mg, which quickly diminished in all but 2 patients; the dosage was accordingly increased to 150 mg/day given in divided doses. However, 11 patients reported that this dose was not sufficient clinically, and 200 mg per day was given in divided doses. Six of these 11 patients felt that naltrexone's benefit eventually "wore off" after an average of 3 months, while the other 5 reported ongoing benefit.

Three patients in whom the benefits with naltrexone diminished reported the return of nocturnal emissions. At 150 to 200 mg, all patients except 1 reported initial benefit. This 1 patient later admitted he was lying because naltrexone interfered with his ability to masturbate and fantasize "about little kids." Dosages above 200 mg per day in divided doses were not found to be more helpful. Masturbation decreased initially from an average of 2 times per day (range, 1–11 times) to 2 times per week. Of the 15 patients successfully continuing naltrexone, the average frequency of masturbation was 3 times per week. The patient who had been masturbating the most before treatment asked for help because his penis was too painful to touch and he had begun anal digital stimulation.

The concomitant decrease in sexual fantasies was more difficult to quantify because the fantasies were more numerous, not all written down because they were "embarrassing," or so frequent that they couldn't all be remembered. Prior to treatment, a few patients had spent the majority of their day in sexual fantasy, which interfered with their ability to function in school or in the program. On the average, there was a decrease in reported fantasies from approximately 5 times per day (with a range of 2 times per day to almost continuous fantasizing or more than 50% of the day) to an average of once a day. This result was also found in those 15 patients (71%) who continued to respond to naltrexone at the average dose of 160 mg per day.

Equally important was the continued decrease in sexual arousal, as well as improved self-esteem and a feeling of self-mastery and control that was reported by the 15 patients who responded to 160 mg per day. One patient was relieved that he no longer had to cut pictures of women and girls out of magazines to hide in his room. Another noted, "my sexual arousal is no longer controlling me." The 1 homosexual patient was observed by staff to stop "swishing" his hips and exhibiting other seductive behaviors after naltrexone was begun. These behaviors resumed when naltrexone was discontinued and then stopped again upon reinitiation of medication. This unconscious change in behavior was more convincing to the staff than anything the patient reported. When naltrexone was administratively discontinued in 9 other responders, all of their former behaviors began to return to baseline levels during a discontinuation taper at 50 mg per day. At initiation of naltrexone, both patients with self-injurious behavior stopped cutting and scratching; this behavior resumed with the discontinuation of naltrexone treatment and stopped with treatment reinitiation. Two patients who had spontaneous erections for no apparent reason ceased having them at initiation of naltrexone. Naltrexone responders had an average of 3 victims and an approximately 25% decrease in morning erections.

There were no changes in clinical chemistries, including the liver function profile, or the CBC for the duration of this study. The patients who continued taking naltrexone did so for an average of 12.1 months, with a range of 4.5 to 21.0 months, while those who discontinued did so after an average of 3.0 months.

All 6 patients who were not responsive to naltrexone began leuprolide, which they all found initially helpful at 3.75 mg IM monthly. This benefit diminished in 5 patients, and the dose was increased to 7.5 mg IM monthly with continued benefit in 4 patients and no benefit in 1. As a group, these patients had more victims (average = 8 victims), were hospitalized longer (average = 31 months), were violent or had violent fantasies (N = 4 of 6), had thought process problems (N = 2 of 6), and had both adult and child victims (N = 1) compared with the 15 responders to naltrexone treatment.

## DISCUSSION

The mean age of patients in this study was 15.2 years (range, 13 to 17 years) when they entered the inpatient program. However, they had offended an average of 2 years earlier, with various types of outpatient treatment and court proceedings occurring in the interim. Accordingly, none of these patients committed their offenses when they were 16 years or older. DSM-IV criteria[12] are therefore difficult to apply since "age 16 years or older"[12(p527)] is a criterion for pedophilia. There are obvious reasons for hesitating to label adolescents, but the

  

available diagnoses do not easily educate the reader or adequately describe the pathology in most adolescents (i.e., ages 12 to 16 years). Paraphilia not otherwise specified is "for coding Paraphilias that do not meet criteria for any of the specific categories."[12(p532)] This diagnosis is nonspecific enough and could clearly be applied to all of these patients and, specifically, to the 1 patient who also sexually abused his dog (i.e., zoophilia). Impulse-control disorder not otherwise specified is also vague but is technically applicable here. More clarity is potentially available in the section of DSM-IV describing other conditions that may be a focus of clinical attention. All 21 patients in this study qualify for the diagnosis of sexual abuse of a child, perpetrator (V61.21), with 5 having been sexually abused (995.53), 1 having been sexually and physically (995.54) abused, and 2 having been physically abused. One patient also had raped his mother, thus fulfilling criteria for a diagnosis of sexual abuse of adult, perpetrator (V61.1).

In a study of 36 adult male sexual offenders who were "admitted from prison, jail, or probation,"[13(p414)] had a mean age of 33 years, and had been convicted as adults (i.e., ages 25 to 41 years) 1 to 9 times, McElroy et al.[13] found a 36% incidence of bipolar disorders. In the present study, only 1 of 21 patients had a diagnosis of bipolar disorder; however, it has been reported that "the average age of onset for both major depressive disorder and bipolar disorders falls between the ages of 20 and 40 years."[14(p1084)] Hirschfeld et al.,[15] using a screening tool, reported the highest rate of bipolar disorders in those aged 18 to 24 years and in those earning less than $20,000 per year. Four patients in the present study who received mood stabilizers had rage reactions (which is a mood swing), but none were manic or hypomanic. It is possible that these patients could become overtly bipolar as adults.

All patients in the present study were clearly in the socially deviant hypersexual behavior spectrum. Initially, most felt their behavior was neither excessive nor deviant. They were uncomfortable being addressed as legally adjudicated sexual offenders. They became more comfortable as they learned about their offending cycle, began to see themselves through their victims' eyes, and understood the errors in their thinking. However, even after the concomitant psychiatric disorders (e.g., ADHD) were successfully treated, there remained a hypersexualized state and orientation to others in 21 of 39 patients.

The finding of frequent episodes of spontaneous penile erections seen with several patients in this study is not dissimilar to spontaneous ejaculation without sexual stimulation seen in opioid withdrawal, during which time there is sometimes greater than normal sexual activity.[16] It has been suggested that low endorphin levels may play a role in the disinhibition of sexual activity in Tourette's disorder.[16] Naltrexone inhibition of dopamine release in the nucleus accumbens has been posited as a possible reason for its beneficial role in impulse-control disorders[9]; however, chronic naltrexone also significantly increases serum beta-endorphin levels[17] and brain methionine-enkephalin and preproenkephalin messenger RNA.[18] Administration of d-ala$^2$-met$^5$-enkephalinamide or beta-endorphin into a lateral ventricle of a male rat inhibits sexual behavior.[19] Although dopamine release in the nucleus accumbens increases with exposure to the bedding material of a receptive (i.e., hormonally available for impregnation) female rat, this release is blocked by naloxone.[19] It has also been suggested that opioid system activation occurs before or at the same time as dopamine release in response to sexually relevant stimuli[19] and that opioid release activates dopamine neurons innervating the nucleus accumbens.[19] Thus, a certain endogenous opioid level appears crucial for arousal and sexual functioning. It is thus not surprising that phospho-Leu-Phe, the enkephalinase inhibitor, prolongs intromissions and mount latency in rats.[19]

High levels of opioids, however, inhibit dopamine release. Enkephalins also have a considerable affinity for mu-opioid receptors.[19] The infusion of the mu-opioid receptor agonist morphiceptin into the medial preoptic nucleus in the male rat produced a marked delay in the initiation of sexual behavior.[19] Accordingly, it is feasible to propose that the delayed or inhibited sexual behavior observed in the present study is in part related to naltrexone-induced accumulation of opioid peptides. Chronic morphine and heroin addicts have significantly inhibited sexual behavior including impotence, lack of orgasm, and loss of sexual desire.[16] It may be that a high circulatory level or accumulation of opioids has an action similar to that of naltrexone. However, a more complete controlled study is necessary to define and substantiate these findings.

Nevertheless, it is suggested that naltrexone (at doses of 100 mg per day or higher) may have a role in the treatment of paraphilic compulsive sexual behavior and provides a safer, less expensive, and less intrusive first step compared with antiandrogens in the majority of adolescent offenders. Although this study lacked a true experimental design and was based on self-report, it is possible that the benefits observed may generalize to the larger population of non–socially deviant hypersexual behavior.[20]

*Drug names:* bupropion (Wellbutrin and others), citalopram (Celexa), clonazepam (Klonopin and others), clonidine (Clorpres, Catapres, and others), desmopressin (DDAVP, Stimate, and others), dextroamphetamine mixed salts (Adderall and others), fluoxetine (Prozac and others), guanfacine (Tenex and others), haloperidol (Haldol and others), imipramine (Tofranil, Surmontil, and others), leuprolide (Viadur, Lupron, and others), lithium (Lithobid, Eskalith, and others), mecamylamine (Inversine), medroxyprogesterone (Provera and others), methylphenidate (Methylin, Ritalin SR, and others), minocycline (Vectrin, Minocin, and others), morphine (Kadian, Avinza, and others), naloxone (Narcan and others), naltrexone (Revia), nefazodone (Serzone and others), olanzapine (Zyprexa), oxcarbazepine (Trileptal), paroxetine (Paxil and others), propranolol (Innopran, Inderide, and

others), risperidone (Risperdal), sertraline (Zoloft), topiramate (Topamax), valproate sodium (Depacon and others), venlafaxine (Effexor), ziprasidone (Geodon).

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