Compliance to naltrexone treatment after ultra-rapid opiate detoxification: an open label naturalistic study

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Received 23 December 1996; accepted 20 May 1997

Abstract

Studies have found that naltrexone, a long-acting opiate antagonist, owing to poor patient compliance, is of limited value in preventing relapse. The current study investigates compliance with a 9-month course of naltrexone (25–50 mg daily) given with counseling after ultra-rapid opiate detoxification which uses clonidine and naltrexone under general anesthesia. Eighty-three of 113 randomly selected patients (out of 640), who were detoxified more than 1 year prior (average 1.5 years), responded to phone interviews. Phone questionnaire asked about patients’ compliance with naltrexone, counseling and drug use since detoxification. Similar interviews were also conducted with patients’ significant other. Non-relapse patients \( n = 47, 57\% \) took naltrexone an average of 2 months longer than did relapse patients \( n = 36, 43\% \). About half of the non-relapse patients completed at least 5 months of naltrexone, 30\% completed at least 7 months and about 20\% completed 9 months. Fifty-five percent of the relapse patients stopped using naltrexone by the end of the 3rd month, and by the end of 7th month 10% continued to take it. After the first 2 months the decline in naltrexone compliance was about the same for relapse and non-relapse patients. These results are more encouraging about the use of naltrexone for relapse prevention than previous studies. This method of using naltrexone should be further tested in prospective random assignment controlled studies. © 1997 Elsevier Science Ireland Ltd.

Keywords: Naltrexone; Relapse; Opiate detoxification

1. Introduction

Naltrexone, a long-acting antagonist that blocks the subjective and objective responses to opiates, is potentially beneficial for relapse prevention after detoxification. However, previous studies have found it to be of limited therapeutic value owing to low retention rates; most patients stop taking naltrexone within 2 months. Table 1 presents a comparison of studies published over the last 25 years that report on patient compliance with taking naltrexone after opiate detoxification. The studies in the table are ordered by retention rates, i.e., the number of months that patients continued to take naltrexone, which was reported in most studies. The first column presents the author, year, sample size and dosage (presented in parentheses). The second column presents the 2-, 4-, 6- and 8-month retention rates. The last column reports variables associated with retention and, when reported, relapse rates. Notable features of studies are also mentioned in this column.

Looking at the second column of Table 1 it can be seen that retention rates on naltrexone are low in most studies, less than 20\% at 4 months. The first three studies are notable exceptions (Gold et al., 1984; Ling and Wesson, 1984; Washton et al., 1984). The favorable results in these studies may be attributable to the fact...
Table 1
Studies of naltrexone in treating opiate addictions (ordered by rates of retention)

<table>
<thead>
<tr>
<th>Author (year), n =</th>
<th>Naltrexone retention in months</th>
<th>Correlates of retention; relapse data; and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gold et al. (1984), n = 114 (?)</td>
<td>?-? - 80% - ?, mean = 132 days</td>
<td>Half of subjects in job jeopardy or legal consequences program. They remained in treatment longer (185 vs. 101 days). After 12-18 months 64% opiate free. Longer NX treatment lower relapse.</td>
</tr>
<tr>
<td>Washon et al. (1984), n = 114 (?)</td>
<td>?-? - 63% - ?</td>
<td>Physicians longer retention. 64% (n = 93) opiate free (12-18 months). 17.8% re-addicted, re-hospitalized. Study of physicians and business executives, 4-10-week inpatient program.</td>
</tr>
<tr>
<td>Ling and Wesson (1984), n = 60 (?)</td>
<td>?-71% - 53% - 13%, mean 8 months</td>
<td>Older patients and physicians did best. Unknown. Study of health care professionals.</td>
</tr>
<tr>
<td>Klieber and Kosten (1984), n = 160 (?)</td>
<td>65% - 40% - 35% - 25% (final at 7 + )</td>
<td>None</td>
</tr>
<tr>
<td>Anton et al. (1981), n = 25 with family therapy</td>
<td>90% - 80% - 30% - 28%</td>
<td>Comparison of NX, standard psycho social intervention program with and without 90-min weekly family therapy. Family therapy was associated with better compliance. No difference in urine tests during first 2 months of study.</td>
</tr>
<tr>
<td>n = 40 without (A)</td>
<td>30% - 10% - 5% - 0%</td>
<td></td>
</tr>
<tr>
<td>Garcia-Alonso et al. (1989), n = 113 (A)</td>
<td>68% - 50% - 40% - ?</td>
<td>Opiate dependents compared to opiate abusers results for dependents reported here, no difference between groups.</td>
</tr>
<tr>
<td>Gutierrez et al. (1995), n = 123</td>
<td>77% - 56% - 36% - ? 72% - 42% - 38% - ?</td>
<td>67 patients induced inpatient vs. 56 outpatient, results similar. Outpatients treated 1 year later to rule out novelty effect on outcomes.</td>
</tr>
<tr>
<td>San et al. (1991), n = 50 (28 NX vs. 22 placebo) (A)</td>
<td>50% - 40% - 20% - ?, no significant difference between groups</td>
<td>At 1 year 32% NX drug free. 36% in placebo group, and 46% of NX and 27% in placebo met criteria for opiate dependence.</td>
</tr>
<tr>
<td>Bradford et al. (1976), n = 883 in 17 centers (?)</td>
<td>45% - 37% - 20% - 15% 48% - 28% - 20% - 12% 40% - 20% - 18% - 12%</td>
<td>NX (n = 776, lines 1 &amp; 2) vs. placebo (n = 107) 1 NIDA study sight, 2 - 3 National Academy of Science sight.</td>
</tr>
<tr>
<td>Schifano and Marra (1990), n = 99 (A)</td>
<td>57% (2weeks) - ? - 16% - ?</td>
<td>Results recalculated by removing nine patients who left treatment under medical advice and 15 still being treated for less than 6 months.</td>
</tr>
<tr>
<td>National Research Council Committee on Clinical Evaluation of Narcotic Anagatagonists (1978), n = 124 (NX n = 60, placebo n = 64) (A)</td>
<td>42% - 35% - 20% - 10% 38% - 18% - 15% - 10%</td>
<td>Rates slightly better for naltrexone group.</td>
</tr>
<tr>
<td>Osborn et al. (1986), n = 30 NX vs. 30 methadone (?)</td>
<td>NX ?-27% (3 months) - ?-? MT ?- 87% (3 months) - ?-?</td>
<td>Four of each group attained complete abstinence, 50% of urine dirty during study in both groups.</td>
</tr>
<tr>
<td>O'Brien et al. (1975), n = 54 (A)</td>
<td>28% - 7% - ? - ?</td>
<td>On NX 85% of urine all clean (643 tests), 5% with opiates.</td>
</tr>
<tr>
<td>Tennent et al. (1984), n = 160 (A)</td>
<td>26% - 17% (3 months) - ?-?</td>
<td>Weekly urine screens and needles found 3% use of opiates on NX.</td>
</tr>
</tbody>
</table>
that patients were highly motivated to succeed as they were health care professionals (Ling and Wesson, 1984; Washton et al., 1984) or in job jeopardy or legal consequences programs (Gold et al., 1984). Another exception is Anton et al. (1981) who reported high retention associated with providing family therapy as a supplement to the usual psychosocial treatment program. However, the other study to test the added benefit of psychosocial treatment, Callahan et al. (1980), did not report significant differences in retention between the groups. It should be noted that in most studies patients were given some kind of psychosocial intervention in addition to naltrexone.
Studies that compared the use of naltrexone to the use of a placebo found similar retention and relapse rates (Bradford et al., 1976; National Research Council Committee on Clinical Evaluation of Narcotic Antagonists, 1978; San et al., 1991; Shufman et al., 1994). Grey et al. (1986) found that patients who were given methadone had longer retention than did patients who were given naltrexone. However, relapse rates were similar in both groups. Most studies did not report variables associated with naltrexone retention.

The current study is a retrospective naturalistic open label investigation reporting on compliance rates with a 9-month course of naltrexone prescribed for relapse prevention after UROD (ultra-rapid opiate detoxification). In UROD, patients are detoxified in 6–8 h under general anesthesia with intubation using a combination of naltrexone, which blocks opiate receptors, and clonidine, a hemodynamic stabilizer. The day after detoxification patients are started on a daily dosage of naltrexone combined with counseling. Possible advantages of this protocol are that detoxification takes place almost immediately which effectively eliminates dropout, and naltrexone is started rapidly. In other studies naltrexone was started after conventional detoxification. This meant that many patients did not even begin naltrexone as they failed to complete detoxification. For example, in Schifano and Marra (1990) only 99 out of 207 patients completed detoxification. Another difference between the current study and previous studies is that many of the previous studies were singly focused on retention. Only half of the 24 studies presented in Table 1 reported relapse rates. In six of the studies patients were followed for 6 months or less.

2. Ultra-rapid opiate detoxification (UROD) procedure

UROD is a variation of what has been reported elsewhere (Legarda and Gossop, 1994; Gossop, 1995). Patients are detoxified in an intensive care unit under general anesthesia with intubation using a combination of naltrexone and clonidine. The treatment is offered in a private for pay clinic run by CITA (Center for Investigation and Treatment of Addictions), and is provided at several major teaching hospitals in the United States and abroad. The treatment was not covered by health insurance at the time of the current study. The cost of the treatment package, which covers the detoxification and 15 out-patient sessions, was $4500.

2.1. Intake

Patients are seen for an intake interview to which they are accompanied by a significant other, typically a family member. The intake includes medical screening, which helps to rule-out contraindications, such as danger of acute psychiatric decompensation, alcohol abuse, acute or progressive hepatitis, liver cirrhosis, with and without esophageal varices, immunosuppression, acute infectious disease, and chronic not compensated diseases (e.g., respiratory or cardiac disease). The medical screening includes complete blood cell count, blood chemistry (BUN, Creat, Glucose, and Electrolytes), liver function tests (enzymes + bilirubin), hepatitis profile (A, B, C and D), HIV status, VDRL, pregnancy test, a chest X-ray, and an electrocardiogram.

Based on the exclusion criteria, most of the patients belong to American Society of Anesthesiology categories I and II, for whom anesthesia-related complications for planned procedures are extremely rare. According to recent estimates anesthesia-related mortality for all patients, including those in poor physical health treated under emergency situations, is low (1 in 400 000 (Voelker, 1995); 1 in 20 000 (Warden and Horan, 1996); 1 in 11 000 (Warner et al., 1993)). In the event of contraindications attempts are made to refer patients to other appropriate care.

On the morning or evening before detoxification, patients are admitted to a hospital. Patients are instructed to fast for 6 h, not to use drugs for 4 h, and to use prescription medications until the day of detoxification.

2.2. Procedure

The UROD procedure is performed on an intensive care or intermediary care unit. The patients are kept there until after the treatment and a recovery period. The procedure takes 6–8 h. Preparation includes giving patients an enema and giving fluids in i.v. line according to the hydration requirements of the patient.

Intravenous anesthesia is induced using midazolam and propofol in doses dictated by patient response followed by intubation. The opiate antagonist regimen of naltrexone, administered via a gastric tube, accompanied with clonidine is then given. To verify that detoxification has been completed, naloxone, an opiate antagonist, is given diagnostically as a challenge test. If the test fails to elicit withdrawal symptoms the UROD procedure is terminated. A anesthesia is discontinued and the trachea extubated. As the patient recovers from general anaesthesia, additional medication like clonidine, a benzodiazepine and loperamide are given as needed.

2.3. Post-procedure care

The day after the procedure patients are given an oral dose of naltrexone. Two hours later, the degree of abstinence is checked using the 5-point scale of Blachly (1966). If the degree is low, the patient is released. In
less than about 10% of cases patients are kept in the hospital an additional night after detoxification to treat uncontrolled severe diarrhea or vomiting, anxiety, aggressiveness or exhaustion.

2.4. Relapse prevention

The day after detoxification, patients are initiated on a 9-month maintenance dose of daily oral naltrexone (25–50 mg). The 9-month course was selected based on clinical experience. Patients' liver function is checked before treatment (baseline) and at 3-month intervals due to the small chances of liver complications relating to naltrexone use (Hetrick, 1993). A part of the treatment package patients are given 15 sessions of psycho-social counseling, including individual and family interventions as needed. Counseling consists of supportive psychotherapy to help the patient make the transition to a drug-free life. It also includes a psycho-educational component on the use and role of naltrexone. In addition, relapse prevention techniques focusing on coping with craving cues are taught. Two other foci of counseling are stabilization of family and helping patient become gainfully employed.

3. Method

3.1. Sample

A simple random sample of 120 male patients, who were detoxified in Israel at least 1 year prior to March 1995, were drawn from the list of 640 such patients. The sample was drawn using a table of random numbers.

3.2. Interview contents

Separate telephone interviews were held with patients and significant others (usually family members). Interviews included questions about patient use of opiates and other drugs, use of naltrexone and attendance at counseling. Naltrexone use questions included asking how many months, and how frequently, naltrexone had been taken. The opiate use questions included asking if patients had used opiates since their UROD detoxification, if so when was the first time, if they were taking opiates routinely, and when was the last time that they had taken opiates. A similar set of questions was asked about use of alcohol and other substances.

Consistent with the literature (Hubbard and Marsden, 1986; Gossop et al., 1989; Harrison et al., 1991; Unnithan et al., 1992), relapse was defined as a patient or significant other responding that patient had used opiates routinely since detoxification (at least 2 weeks of daily use). Non-relapse was defined as the patient and significant other reporting that the patient had not returned to a period of routine opiate use, but may have had episodes of opiate use.

The patient interview included a few additional questions regarding service use. This included asking how many of the post-UROD counseling sessions they had attended, about their contact with other help sources (mental health clinic, N A, social welfare agency, methadone clinic, private therapist and others) and if they had undergone additional detoxifications. Patients were also asked about life changes since UROD such as starting to work or go to school, changes in their relationship with their family and whether or not their major social contacts were with addicts.

3.3. Data collection

Interviews were conducted by one of the authors (H.C.). Considerable efforts were made to locate and interview respondents. An average of eight phone calls were placed to reach patients (range 1–19). The average patient interview took 27.3 min (range 18–52). An average of five phone calls were placed to reach significant others (range 1–11). The average significant other interview took 18.5 min (range 12–35 m). Patients and significant others gave informed consent to be interviewed orally at the time of the interview. Also, as part of the intake process patients are asked to sign a consent form to participate in follow-up studies. Demographic, clinical and substance abuse history variables were extracted from structured patient intake records. A list of these variables is presented in Table 2.

3.4. Statistical analysis

The first step of the analysis focused on attempting to validate patients' responses. This was done by comparing them to the responses of significant others. Additionally, this was accomplished by cross-checking consistency of patients' responses to opiate use questions. The major part of the analysis focused on (a) describing and comparing naltrexone compliance of relapse and non-relapsed patients, (b) exploring the proximal relationship between first use of opiates and course of naltrexone therapy and (c) identifying variables associated with naltrexone compliance.

The specific analytic methods used were as follows. To validate patient self-reported responses these were compared to significant other responses using cross tabs for categorical variables and correlations for variables on an interval scale. The relationship between naltrexone compliance (i.e., the number of months that patients took naltrexone) and relapse (i.e., patients returning to routine opiate use) was explored using the Kaplan-Meier method of survival analysis. For that analysis, the number of months that patient took nal-
naltrexone was defined as time until event. The proximal relationship of first opiate use and course of naltrexone therapy were explored by creating a variable which was the difference between time until first opiate use and number of months that naltrexone was taken. A negative value means that the patient challenged the naltrexone, i.e., took opiates while using naltrexone, and a positive value that opiates were first used only after patient stopped taking naltrexone. To compare time until first opiate use of the patients who had relapsed and those non-relapse patients who had episodes of opiate use, survival analysis was done (for analysis time until first opiate use was rescaled to begin at 0).

To identify variables associated with the number of months that patients had used naltrexone, bivariate (t-tests and correlations) and then multivariate analysis (multiple regression) were done. Relapsed and non-relapsed patients were analyzed separately. Variables included in the analysis were the background characteristics, as extracted from patient charts (listed in Table 2), and the information gathered during the phone interview (see above section on phone interviews for a list of items). All analyses were performed using SPSS (Statistical Package for the Social Sciences) version 7 for Windows.

3.5. Respondents

Of the 120 patients randomly selected, seven were excluded because they lived overseas. Of the remaining 113, 19 significant others could not be located and two refused to respond, leaving 92 significant others (81.4% response rate of families). Eighty-three of the patients were interviewed (73.4% response rate), one refused and 29 could not be located. Average follow-up time was 1.48 ± 0.19 years (range 1.12–2.05 years).

Characteristics of respondents are presented in Table 2. These suggest that for the most part respondents were marginal members of the society. Almost 80% of them had been arrested, more than half of them had been imprisoned and about half did not complete compulsory military service. In Israel completing military service is considered to be an essential right of passage. The army makes special efforts to accommodate even conscripts requiring rehabilitation, with the hope of making them contributing members of the society.

Using background variables obtained from the patient record as reported at the intake interview, the only significant differences between the patients who did not respond to the phone interview, and those who did, was that more time had elapsed since detoxification (non-respondents, 1.63 ± 0.18 years vs. respondents, 1.48 ± .19 years, t = 3.2, df = 108, P = 0.002) and for those patients with a history of criminal activity, the non-respondent group had a later age of first criminal activity (n = 8, age = 15.5 ± 1.2; n = 48, age = 12.5 ± 7.7, unequal variances t = 2.53, df = 54, P = 0.01).

3.6. Validity of measures

Patients and significant others agreed about whether or not patients were routinely using opiates since detoxification. There was close agreement as to the number of months that patients took naltrexone (r = 0.91). In 56 cases there was agreement and in 25 cases disagreement. In two cases patients reported that they did not remember the number of months that they had taken naltrexone. In the 25 cases of disagreement the correlation between the two responses was r = 0.65 (patient estimate 5.2 ± 3.3, family 4.9 ± 3.11).

As a consistency check of patient reporting, their responses to the question about whether or not they had gone back to routine opiate use (i.e., had relapsed) were compared to their responses to the question about

<table>
<thead>
<tr>
<th>Table 2: Characteristics of respondent patients (n = 83)</th>
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</thead>
<tbody>
<tr>
<td>Characteristics of patients</td>
</tr>
<tr>
<td>Age at time of detoxification (years)</td>
</tr>
<tr>
<td>Place of birth</td>
</tr>
<tr>
<td>Age began abusing substances (years)</td>
</tr>
<tr>
<td>Have been arrested</td>
</tr>
<tr>
<td>Number of imprisonments</td>
</tr>
<tr>
<td>Siblings</td>
</tr>
<tr>
<td>Years of formal education</td>
</tr>
<tr>
<td>Army service</td>
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<tr>
<td>Reserve duty</td>
</tr>
<tr>
<td>Marital status</td>
</tr>
<tr>
<td>Number of children</td>
</tr>
<tr>
<td>Worked during the year prior to detoxification</td>
</tr>
<tr>
<td>Previous mental health treatment</td>
</tr>
<tr>
<td>Previous detoxifications</td>
</tr>
</tbody>
</table>

1-17 N number of patients with missing data.
recency of opiate use. The answers to these two questions are not mutually exclusive since relapse patients could now be abstinent and non-relapse patients could have had episodes of use without returning to routine use. However, it was assumed that most of the relapse patients would have used opiates in the last 24 h, and that most of the non-relapse patients would not have. Of the 36 patients who reported relapsing, i.e., returning to regular use of opiates since detoxification, 28 reported using opiates within the last 24 h, one within the last week, three in the last month, three in the previous 6 months, and one as not having used opiates for at least 1 year. Of the 47 patients who reported no relapse, 14 of them had episodes of opiate use. None of these patients had used opiates within the last week, five within the previous month, six during the previous 6 months, and three more than 1 year before. These results suggested consistency of the patients reporting. To help estimate the internal validity of the study, it should be noted that only 14 patients reported any contact with other treatment providers (mental health clinic, three; social welfare service, three; other detoxification, two; methadone clinic, one; N.A., one; and other, four).

The high concordance between the responses of patients and significant others, and internal consistency of patient responses, supports the validity of patient self-reported substance abuse. Others have had similarly encouraging findings about the validity of patients’ self-reported substance abuse (Freedberg and Johnston, 1980; Maisto et al., 1982; Polich, 1982; Verinis, 1983; Sobell and Sobell, 1986; Gossop et al., 1989). For example, in a similar study regarding relapse among detoxified opiate addicts, Gossop et al. (1989) report concordance of 99% between patient interview and urine testing regarding heroin use and 93% concordance for methadone use. Because patient and significant other reporting were almost the same in the current study, patient reporting is presented as the patient questionnaire contained more items.

4. Results

4.1. Relationship between naltrexone compliance and relapse

All 47 non-relapse patients (57% of respondents) had used naltrexone. Of the 36 relapse patients (43% of respondents), one did not use naltrexone at all and two were unable to say how many months they had used it. Fig. 1 compares survival curves of retention on naltrexone for patients who had not relapsed and for those who had. Survival analysis found a significant difference in retention rates of the two groups (Breslow = 6.92, df = 1, P = 0.008; Tarone Ware = 6.70, df = 1, P = 0.009). Patients who had not relapsed had taken naltrexone for an average of 2 months longer than patients who had relapsed (mean = 9 SD 3.8 vs. 5.9 ± 3.7, t = 2.7, df = 79, P = 0.009). After the first month 74% of relapse patients continued to take naltrexone, at 2 months 61.8, at 3 months 44% and at 8 months 9%. In contrast, at 1 month 98% of non-relapse patients were still taking naltrexone, at 2 months 89.4%, at 3 months 64%, and at 8 months 28%. Thus, the major loss of patients in the relapse group was during the first 2 months of naltrexone treatment. After this time the difference between the groups stabilized. The odds of relapse were greatest for patients who stopped taking naltrexone during the first 2 months (1
or less, OR = 20.2 (CI = 2.5-166), 2 or less, OR = 6.00 (CI = 1.92-18.7) after which time the odds remained about constant (OR’s approximately 2.5 and CI 1-6). As another indicator of compliance patients were asked about frequency of naltrexone use, 86.4% (n = 70) responded ‘once a day’, 12.3% (n = 10) ‘not regularly’ and one patient did not use naltrexone at all.

4.2. Relationship between opiate use and course of naltrexone

Fifty of the patients had used opiates since detoxification. This includes all relapse patients and 14 out of the 47 non-relapse patients who had episodes of opiate use. Fig. 2 shows the relationship between first opiate use and naltrexone use for these patients. A negative value means that opiates were taken that number of months before the patient quit naltrexone, zero during the month of quitting naltrexone and positive values are the number of months after quitting naltrexone that opiates were used. The survival curves for the relapse and non-relapse groups are very similar. This suggests that relapse patients did not challenge their naltrexone by taking opiates earlier than those non-relapse patients who had episodes of opiate use (Breslow = 0.02, df = 1, P = 0.89; Tarone Ware = 0.00, df = 1, P = 0.97; no re-lapse n = 14, -0.06 ± 3.6 vs. relapse n = 34, -0.32 ± 3.6; t = 0.23, df = 46, P = 0.82).

About 43% of the patients in both groups first took opiates while still taking naltrexone, 27% immediately upon stopping naltrexone and 30% during the month after quitting naltrexone. Thus close to half of the patients challenged naltrexone and many continued after challenge to take naltrexone for many months. The no-challenge group took naltrexone significantly longer than did the challenge group (5.1, SD 3.5, n = 28 vs. 3.2, SD 2.4, n = 20; t = 2.2, P = 0.04).

4.3. Variables associated with naltrexone compliance

For the patients who did not relapse the only variable that was related to retention was marital status. Married non-relapse patients tended to remain on naltrexone more time than non-married patients (n = 24, 7.1 ± 4.2 vs. n = 23, 4.6 ± 2.5, t = 2.4, df = 45, P = 0.02).

For the relapse group the variables related to retention were having worked the year before detoxification (worked, n = 6, retention = 6.3 ± 4.2 vs. not worked, n = 28, retention = 3.3 ± 2.6, t = 2.3, df = 32, P = 0.03), having worked since detoxification (worked, n = 6, retention = 6.7 ± 3.7 vs. not worked, n = 28, retention = 3.2 ± 2.7, t = 2.7, df = 32, P = 0.01), having had social contacts with addicts since detoxification (contact, n = 20, retention = 5.5 ± 3.4, t = 2.9, df = 32, P = 0.007), and time of first use of opiates after detoxification (r = 0.47, = 32, P = 0.007). Used together in a step-forward regression model the following variables were significant: (a) more time till first use of opiates after detoxification (B = 0.35, b = 0.44, t = 3.1, P = 0.004) and (b) having worked since detoxification (B = 3.02, b = 0.38, t = 2.6, P = 0.01), which together explained 33% of the variance in retention for the relapse group (adjusted R² = 0.33).

5. Discussion

This study, unlike most previous studies, offers encouraging results about the use of naltrexone for relapse prevention. These findings should be interpreted with caution as this was an open label study with no control group. To the extent to which comparisons can be made, compliance in the current study was better than reported in most of the literature. Comparing to Table 1, in the current study the 2-, 4-, 6- and 8-month
Retention distribution was 89%–51%–32%–28% for the non-relapse group. For the relapse group it was 62%–32%–21%–9%. These retention rates are similar to the first three studies in the table which were done on physicians, other health care providers and persons in job jeopardy programs. In contrast most patients in the current study were socially deviant. It is possible however that patients in the current study were more motivated than patients in some of the other studies where patients were treated for free, since they or their families had to pay for the treatment.

When making comparisons to other studies, it should be noted that most of the other studies used urine analysis to estimate opiate use during naltrexone therapy. In some studies patients had also taken naltrexone while being observed during clinic visits. These provided investigators with better point estimates of opiate and naltrexone use than in the current study. On the other hand routine urine testing and supervised naltrexone taking may have influenced outcomes and thus become part of the therapeutic method. These studies also had lower long-term response rates and follow-up than the current study. All but one patient in the current study was not initiated on naltrexone. Most other studies lost patients during detoxification and before beginning naltrexone. The favorable results in the current study may relate to the early and rapid initiation of naltrexone treatment. Another difference may relate to the daily dosage regimen, as compared to most studies, where it was prescribed to be taken two or three times a week.

Longer naltrexone use was associated with less chance of relapse. As in other studies, we were not able to identify many variables associated with retention on naltrexone. For the non-relapse group, the only variable associated with retention was being married, which was associated with longer retention. Lewis et al. (1978) report a similar finding. This relationship may be due to wives’ role in encouraging naltrexone use, although we have no data to test this hypothesis. For the relapse group marital status, however, was not related to retention. For this group contact with addicts was significantly related to retention. The lack of relationship for the non-relapse group on this variable was because none of the non-relapse patients had contact with addicts. For the relapse group, multivariate analysis found that more time till first use of opiates after detoxification and having worked since detoxification were positively related to retention.

It should be noted that while these results are more encouraging than previous studies about the use of naltrexone for maintenance, the role of ultra-rapid opiate detoxification in obtaining these results will have to be tested in prospective random assignment controlled studies. Such studies are currently being planned. Additional research is also being planned to explore optimal range of length for naltrexone therapy and ways of promoting its use. Another question to be considered are the reasons for the relationship between naltrexone use and non-relapse. It is possible that naltrexone use is an expression of motivation; thus, these same patients may have had similar results even without naltrexone. The possible role of early induction to naltrexone will also be explored.

Acknowledgements

The authors wish to thank the anonymous reviewers for their many helpful comments which greatly contributed to this paper.

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