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Experiences with an Outpatient Relapse Program (Community Reinforcement Approach) Combined with Naltrexone in the Treatment of Opioid-Dependence: Effect on Addictive Behaviors and the Predictive Value of Psychiatric Comorbidity

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Key Words
Addiction · Treatment · Naltrexone · Opiates · Relapse prevention

Abstract

Background: There is increasing interest in naltrexone, an opiate antagonist, in the treatment of opiate addicts. The effects of naltrexone are often compromised by a lack of compliance and drop-out. The effects of this compound are probably more favorable when combined with a psychosocial intervention such as the Community Reinforcement Approach (CRA). ***Aim:*** To explore the effects of a combination therapy (naltrexone plus CRA treatment) and the predictive value of sociodemographic and psychopathologic characteristics. ***Method:*** Using a before-and-after design, heroine addicts (n = 24) receiving a combined naltrexone plus CRA treatment are compared with a group (n = 20) on methadone maintenance therapy (reference group). ***Results:*** Over a period of 6 months, 58% (14/24) did not relapse, after 1 year at least 55% (12/22) still met the initial goal of continuous abstinence. At baseline, the treatment group and the reference group were similar on nearly all variables except for the number of times clients were arrested. Within the treatment group, a comparison was made between the continuous abstinent and those who relapsed into frequent opioid use. Differences were significant in the cluster-B personality disorders and in polydrug users. ***Conclusion:*** The combination of naltrexone plus intensive CRA in an outpatient setting appears to be promising. A high score on cluster-B and polydrug use is associated with relapse.

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Introduction

In the field of opiate addiction treatment, there has been an increase in the use of pharmacological compounds such as naltrexone. After induction, this agent can be effective in the prevention of recurrent heroin use. During naltrexone maintenance treatment, the effects of heroine will be blocked, leading to lesser anticipation of the desired effects and a decrease in the relapse rate. Similar to other forms of therapy aimed at abstinence, patient compliance is often a problem and many patients relapse after having discontinued taking medication [1].

One study [2] showed good results with naltrexone (61% abstinence after 6 months) with highly motivated participants, such as business people and doctors. In addition, in southern Europe, good results with naltrexone (40% abstinence after 6 months treatment) have been reported [3]. The result is attributed to the traditional family structure and other forms of social interactions that increase treatment compliance.

These findings suggest that a combination of naltrexone maintenance and psychosocial therapy may lead to an increase in therapy compliance and a decrease in the relapse rate.

A promising approach is the Community Reinforcement Approach (CRA) [4]. CRA encompasses elements such as social network and enhancing motivation and is often supported by a variety of pharmacological interventions (i.e. naltrexone) and procedures to enhance compliance with the recommended medication regimen. First, there are interventions aimed at enhancing the social network (for example interventions including partners and parents, aimed at compliance). CRA pays attention to the expectations, motivation, coping skills, social, labor and recreational elements.

However, combined forms of therapy also suffer often from early dropout and lack of therapy compliance. An important factor which effects compliance and dropout is psychiatric comorbidity [5]. In general the severity of psychiatric symptoms worsens the prognoses [6]. Research suggests that the prevalence of psychiatric disorders among heroine addicts is high. There is a relationship between drug addiction and depression, anxiety and personality disorders [7]. Personality disorders are seen as negative predictors of treatment outcome [8].

The aim of this open-label study is to optimize the effects of using a combination of CRA and naltrexone.

The present study consists of a naturalistic follow-up study with before-and-after comparison without a control group. In order to assess a possible generalization of the study, a comparison on relevant variables was made with a group of heroine addicts participating in a methadone maintenance program.

The following questions were addressed: (1) is the study population comparable to the group of addicts participating in a methadone maintenance program; (2) what is the outcome in heroin addicts treated with naltrexone plus CRA, and (3) what is the predictive value of the sociodemographic characteristics and psychiatric comorbidity in patients treated with naltrexone plus CRA?

Table 1. Retention characteristics of the treatment population

	Naltrexone plus CRA population
Number of clients who relapsed	10/24 (42%)
Number of clients who were abstinent after:	
Mean ≥ 6 months	14/24 (58%)
Mean ≥ 12 months	12/22 (55%)
Mean length of treatment, months	16.6 (SD = 5.3; min 6, max 24)
Mean time to first relapse, months	3.8 (SD = 2.4; min 1, max 7)

Displayed are numbers, percentages, means, standard deviations, minimal and maximal values.

Method

Study Population

Treatment Group. The treatment group consist of 24 heroin addicts treated with naltrexone in a CRA program from February 1996 until evaluation in May 1998. The treatment took place at the outpatient treatment center for addiction Kentron in Roosendaal (<100,000), the Netherlands. Subjects were recruited from methadone programs through newspaper articles and via addiction clinics throughout The Netherlands. During the research period 60 persons showed interest in participating by at least one contact. 24 persons were included (40%).

All 24 subjects were opiate-dependent and 21 of these were participants in a methadone program. Subjects were included during a 24-month period. Table 1 shows that follow-up varied between 6 and 24 months (mean length of treatment 16.6; s.d. 5.3 months).

Detoxification of 19 subjects consisted of a rapid detoxification procedure [9]. In this procedure naltrexone was administered in increasing dosage: 12.5 mg/day on day 1, 25 mg/day on day 2, and up to 50 mg/day on days 3 and 4. To ameliorate withdrawal symptoms, clonidine, diazepam, midazolam and ondansetron were used as indicated. The other 5 patients were detoxified by a methadone-tapering procedure either in a regular clinic or at home. Patients from the latter group had to pay a fee of Eur 227.00 (n = 5), and patients from the rapid detoxification program had to pay an extra fee of Eur

1,818.00 (n = 19). Detoxification was followed by naltrexone maintenance. Subjects were stimulated and expected to bring a non-using partner, spouse or good friend to assist as a coach during detoxification and aftercare treatment.

Reference Group. To check selection bias, a reference group of 20 participants randomly drawn from a regular methadone program was selected.

Intervention

After naltrexone induction, all subjects received a maintenance dosage of naltrexone of 25 mg/day. The treatment consisted of medical support, psychosocial interventions followed by a consistent and strict policy towards compliance (naltrexone) and control of substance abuse by urine analysis. The importance of the social network was emphasized. CRA implemented: diagnostic interview (functional analysis), psycho-education, pharmacotherapy, compliance therapy, urine analyses/monitoring, marriage/relation therapy, and support of the social network, career orientation, job counseling, education and hobbies, problem solving, social skills and cognitive restructuring.

The therapist (first author) has several years experience in the addiction setting. On regular basis, he received supervision from the second author and from multidisciplinary coworkers. The CRA program was tailored to the work of Meyers and Smith [10]. Treatment integrity was guarded on the basis of monitoring forms and stored in files. Data collection, extraction and interviewing was done by an independent researcher.

During the first month of treatment, counseling sessions averaged 2–3 sessions of 45 min/week, which was reduced to 1 weekly session of 45 min after 3–6 months, and, during the last phase, to monthly sessions. After 9 months the dosage of naltrexone was reduced to 12.5 mg/day. Abstinence was verified by means of controlled urine analyses.

Assessment Procedure

Subjects in the treatment group were interviewed prior to detoxification regarding baseline characteristics. The reference group was assessed in the same way.

Instruments

The following questionnaires and tests were included in this study: (a) SCL-90 (Symptom Check List) [11]; (b) ABV (Amsterdamse Biografische Vragenlijst) [12]; (c) VKP Questionnaire on Personality Traits (Vragenlijst kenmerken van de persoonlijkheid) [13], and (d) the VGIT, the shortened version of the GIT (Groningse Intelligentie Test) [14].

(a) The SCL-90 is a multidimensional self-report on mood and somatic complaints. This list has been translated into Dutch [15]. There is a relationship between the scales of depression and anxiety in the SCL-90 and relevant categories in the DSM-III(R) [16]. The SCL-90 has proven to be a reasonable indicator of the severity of psychopathology among psychiatric patients [17].

(b) The ABV is a personality questionnaire measuring the dimensions: N = neurotic instability; NS = neurotic somatic complaints; E = social extravertism, and T = test attitude. The T dimension ranges from a self-criticizing attitude (low score) to a self-defending attitude (high score) in answering the questionnaire. The N and NS scales are highly inter-correlated. The test-retest index is satisfactory [18].

(c) For the presence and severity of personality pathology the VKP was used. This self-reporting questionnaire is based on the International Personality Disorder Examination (IPDE) of the WHO [19]. The VKP provides severity ratings on all 13 DSM-III-R [20] personality disorders. An important advantage of the VKP (next to cost-effectiveness) is the fact that during testing there is no systematic bias or interview tendencies [21]. Compared to an interview, the VKP has a high sensitivity and a low specificity.

(d) VGIT: in this study intelligence was tested by using the short version of the GIT [14] consisting of the 3 subtests: numerical, a card lay puzzler and a word puzzler. The short version correlates 0.91 with the complete version (10 subtests) of the GIT. The results can be translated into an IQ score [18].

Statistical Analysis

To assess the predictive value of psychiatric comorbidity comparisons were made between the abstinent and relapsed group concerning sociodemographic background, intelligence, juridical conflict, psychopathology and personality disorders.

Differences in the means of continuous variables were tested by using the Student's t test. χ^2 statistics and Fisher's exact test (two-sided) were used to test differences in categorical data. Because of the small sample size and the explorative nature of the study, the significance level was set at $p < 0.05$.

Results

Comparison of Treatment Group with Regular Methadone Clients

Table 2 shows that the 2 groups are similar on all variables except for the number of times clients were arrested (96% naltrexone vs. 57% methadone, $p < 0.05$).

Treatment Outcomes of the Naltrexone Group

After a 6-month treatment period, 14 of 24 clients were still abstinent (58%). After 1 year, 12 of 22 were still abstinent (55%). One client used heroin incidentally after detoxification without relapse into frequent opiate abuse. All 10 clients who relapsed into frequent opiate abuse, did so within 7 months after the start of treatment (table 1).

Of 11 frequent cocaine users, 9 used cocaine a couple of times during treatment. One of them had a period of some weeks of extensive cocaine use. In that scenario the treatment was intensified and adapted to cocaine use, which ceased. Three clients who regularly used amphetamines ceased using this drug. One of them started taking drugs again after 5 months in treatment, but ceased using the substance again after 9 months. Of 8 benzodiazepine users, 6 stopped their benzodiazepine use. One of them persisted in irregular use of benzodiazepines, another slowly decreased his use to a stable maintenance level. The use of cannabis remained the same for almost all clients.

Table 2. Characteristics and psychopathology among naltrexone- and methadone population

	Population				p
	naltrexone (n = 24)		methadone (n = 20)		
	mean	SD	mean	SD	
Age, years	30.5	6.4	29.9	7.1	NS
Age onset opiate addiction, year	21.7	4.5	23.0	5.3	NS
Duration addiction, years	8.8	6.0	7.0	8.0	NS
Daily amount heroine, g	0.6	0.7	0.8	0.8	NS
Daily amount methadone, mg	24.8	10.6	25.7	9.0	NS
Mean IQ	102	10.6	90	13.5	NS
Poly drug users, %	67		91		NS
Women, %	13		18		NS
Min. once arrested, %	96		57		<0.05
Min. once detention, %	58		43		NS
Min. once suicide attempt, %	35		29		NS
Clients with partner, %	63		57		NS
Clients with occupation, %	43		57		NS
Subscale SCL-90	(n = 24)		(n = 16)		
Anxiety	15.3	5.5	17.1	6.6	NS
Agoraphobia	8.7	3.0	10.6	4.7	NS
Depression	33.0	12.7	34.9	13.4	NS
Som. complaints	21.6	8.6	22.9	9.0	NS
Insufficiency	16.5	5.1	17.4	6.0	NS
Sensitivity	31.2	11.0	31.6	11.6	NS
Hostility	10.3	3.9	9.3	4.6	NS
Insomnia	6.9	3.3	7.2	3.8	NS
Other	14.3	4.9	14.8	5.6	NS
Total	157.6	47.8	165.8	54.1	NS
Subscale ABV	(n = 24)		(n = 16)		
N	69.5	31.6	55.3	27.8	NS
NS	24.3	9.1	23.3	8.9	NS
E	60.8	16.9	52.3	17.5	NS
T	32.7	7.9	37.3	8.3	NS

Displayed are numbers, percentages, meanscores, standard deviations and significant levels ($p < 0.05$) for subscales and total scores of the SCL-90 and ABV.

Predictive Value of Sociodemographic Characteristics and Psychiatric Comorbidity

The abstinent (n = 14) and relapsed clients (n = 10) were compared with regard to sociodemographic background, intelligence, social integration, juridical conflict, psychopathology and personality disorders. Of the 43 different comparisons made, only three showed statistical significance: (1) 90% of the relapse population were polydrug users compared to 50% in the abstinence group; (2) the T score of the ABV showed a small but significant difference, a highly critical self-evaluation indicates a risk of relapse, and (3) those who relapsed had a higher total score on the B-cluster personality disorder measured at a dimensional level (table 3).

Discussion

The results of this pilot study, 55% drug free for a period of at least 12 months, are promising considering that this group of heroine addicts had a long addiction history and a long-term history of failed attempts to become abstinent. These results were achieved by rapid detoxification and by means of psychosocial outpatient treatment with naltrexone support. For the interpretation of these results it is important to investigate the selectivity of the treatment group. A comparison with a reference group of methadone patients showed that both groups were similar. There was no difference as to drug abuse history and the amount and severity of (comorbid) psychopathology

Table 3. Personality pathology according to DSM-III(R) axis II as measured by VKP, among naltrexone-plus CRA group both in abstinent- and relapsed population

Disorder	Dimension score				p
	abstinent (n = 14)		relapsed (n = 10)		
	mean	SD	mean	SD	
Cluster A	5.2	3.8	5.6	4.7	NS
Schizoid	1.1	1.3	1.2	1.3	NS
Schizotypal	2.1	2.1	2.1	2.3	NS
Paranoid	2.1	1.3	2.3	1.6	NS
Cluster B	9.7*	5.0	15.8*	6.4	<0.05
Borderline	2.4	1.8	3.7	2.1	NS
Antisocial	5.1	2.7	7.1	2.8	NS
Histrionic	0.9	1.4	2.0	2.1	NS
Narcissistic	1.4	1.6	3.0	2.4	NS
Cluster C	7.7	7.0	9.5	7.9	NS
Dependent	1.8	1.9	2.8	2.4	NS
Avoidant	1.8	2.2	1.8	2.4	NS
Obsessive-compulsive	1.9	2.1	2.4	2.3	NS
Passive-aggressive	2.2	2.2	2.5	1.6	NS
Appendix A					
Sadistic	0.7	0.7	1.1	1.2	NS
Self-defeating	1.9	1.9	2.7	2.1	NS

Displayed are means, standard deviations and significance levels ($p < 0.05$) of the dimensional scores and cluster total scores.

* $p < 0.05$.

were not less in the naltrexone group. The only difference was the fact that the subjects participating in naltrexone treatment had been arrested more frequently than the subjects of the regular methadone program.

It is, however, likely that those subjects who applied for participation in the naltrexone group were more motivated than those participants following regular programs. Patients, in the treatment group could afford to pay a fee, or had a person in their network willing to pay for the treatment. Probably only a limited and selective proportion of heroin addicts maintain good contacts with non-addicts in order to find a non-drug using partner, spouse or friend willing to assist as a coach during treatment. In sum, participants in the naltrexone treatment group were probably better motivated and integrated in the community.

However, this can hardly be used as an objection against the study results, because motivating subjects is one of the key elements of treatment as a whole. When the fee was a problem, or when the patient or the network was incapable of financing the treatment (objective information supporting their claim), there was a possibility of raising the complete amount of money from a charity foundation, from the municipality or from social benefits as a gift. Prior to acceptance, potential candidates and their coaches took part in a couple of informative meetings where they were motivated and prepared for treatment. It is the experience of the authors that this preparation prior to detoxification should not be underestimated.

As to any connection between the type of addict and success rate, we found that the risk of dropout was greatest among polydrug users, although even here 7 of the 16 polydrug users (44%) benefited from the treatment. In addition, cluster-B personality disorder was found to be an indicator for dropout, but was insufficient to be a contraindication for participation [22].

Considering a 55% abstinence rate covering an average period of 12 months and comparing these results with other studies we find the results promising. Although it is tempting to credit the results to the applied intervention (naltrexone plus CRA), this is not possible until a randomized experimental design is followed.

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