

Efficacy of Naltrexone in Preventing Relapse in Opioid Dependent Patients

SADAF RASHID, FATIMA SALEEM, SARAH HANIF, HAIDER IMAM, SYED MUHAMMAD OMER, MUHAMMAD FAROOQ*, ABBAS ALI WARIS, MARYAM HAROON RASHID

ABSTRACT

Objective: To assess efficacy of Naltrexone in preventing the relapse among opioid-dependent pts.

Place of study: Departments of Psychiatry, Fatima Jinnah Medical College, Lahore and Khyber Medical College, Peshawar.

Research design: Interventional design: Prospective, open-label, clinical trial.

Sampling technique: Non-probability: Purposive Sampling.

Study period: Six months: April, 2006 to October, 2006.

Material & methods: Forty five male drug addicts; 25 from Lahore and 20 from Peshawar were included in the study. After detoxification, each patient was given 50 mg of Naltrexone daily under supervision of a care giver. Each patient was followed for 24 weeks.

Results: On completion of the trial, 13 patients (28.9%) had relapsed while 71.1% were still abstinent as judged by Thin Layer Chromatography of urine. LFTs remained normal in all cases. Headache was the most frequent (29.7%) side effect followed by anxiety (27.4%) and loss of energy (25.3%).

Conclusion: A high rate of abstinence (71.1%) coupled with a low incidence of side effects makes Naltrexone an acceptable mode of treatment for opioid dependence.

Key words: Naltrexone, opioid,

INTRODUCTION

Drug addiction is a complex but treatable brain disease. It is characterized by compulsive drug craving, seeking, and use that persist even in the face of severe adverse consequences. Though treatment tailored to individual needs, people with drug addiction can recover and lead productive lives¹

Most opioid-dependent persons seek treatment to "control" the drug use, whereas the society demands and defines "control" as abstinence. This demand has lead governments to support detoxification programs, because detoxification is the most immediate and direct way of disentangling an individual from heroin. However, the problem of relapse still remains there. Another study using the data from National Institute on Drug Abuse, USA has reported a relapse rate of 22.75% among opioid users².

Naltrexone blocks opioid receptors on the surface of cells. As a result, opiates will not produce euphoria and their effect on pain may be less predictable. It is thought that when very small doses are used, naltrexone will increase natural endorphins in the body which play a role not only in mood regulation but also in the level of immune functioning^{3,4}.

*Department of Psychiatry FJMC/ Sir Ganga Ram Hospital Lahore. * Emergency Laboratory, SIMS/SHL, Lahore. Correspondence to Dr. Sadaf Rashid, Assistant Professor*

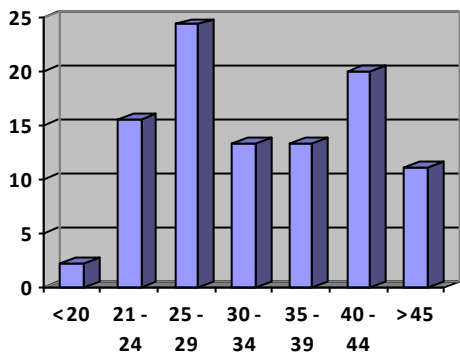
METHODOLOGY

Forty five male drug addicts; 25 from Lahore and 20 from Peshawar were included in the study. After detoxification, each patient was given 50 mg of Naltrexone daily under supervision of a care giver. Each patient was followed for 24 weeks. Patients between 19-50 years of age, free of heroin and other opioids for 7 -10 days, or 10 days for methadone, before commencing naltrexone maintenance treatment, free from acute hepatitis and abnormal LFT were included in the study. People who were given consent and are highly motivated to be opioid free or have support from family and/or friends.

RESULTS

Forty five patients were included in the study. 25 from Department of Psychiatry, Fatima Jinnah Medical College, Lahore and 20 from Department of Psychiatry, Khyber Medical College, Peshawar. The study was conducted under the supervision of Heads of the Departments of Psychiatry of both medical colleges. The laboratory work was done at PMRC centre of Pakistan Medical Research Council, Fatima Jinnah Medical College, Lahore. Thirty two patients completed the study of six months. The age of the patients ranged from 19 to 50 years (Figure-1). The mean age was 33.1±8.4 years. The maximum number of patients were between 25-29 years (24.4%) followed by 40-44 years (20%).

Fig 1: Distribution of cases according to age duration of drug abuse.



The duration of abuse ranged from 6 months to 22 years. The mean duration was 7.9±8.2 years. Majority of the patients (42.5%) were using the drug for one to five years.

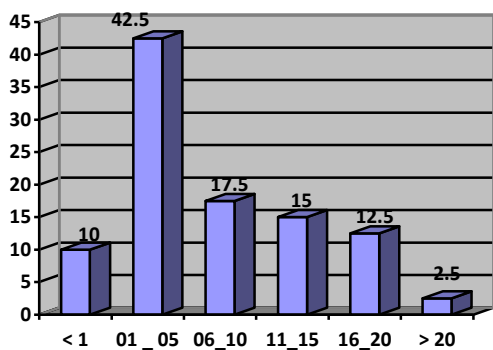


Fig 2: Duration of drug abuse.

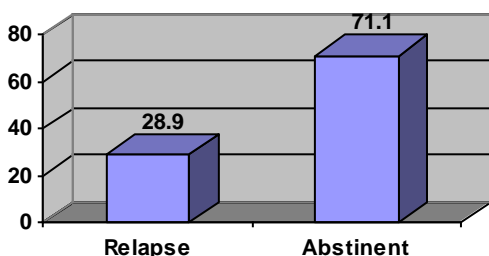


Fig. 3: Status of the patients at the end of study.

Out of 45 patients enrolled in the study, 13 patients (28.9%) had a relapse. Thirty two patients (71.1%) remained abstinent till the close of study. Out of 25 cases in Lahore, 10 patients had relapse (40%), while among 20 patients from Peshawar, only 3 had relapse (15%). The relapse rate was, thus, higher in Lahore as compared to Peshawar but statistically the difference was not significant ($P>0.05$). Thin later

chromatography (TLC) of the urine was done on monthly basis (Table 1)

Table 1 : Positive TLC test according to time of treatment

Month	=n	Positive TLC test	
		n=	%age
First	45	-	-
Second	45	-	-
Third	45	1	2.2
Fourth	44	7	15.9
Fifth	37	4	10.8
Sixth	33	1	3.1
Total	45	13	28.9

Fig. 7 shows the timing of the relapse. Weeks 14th to 18th, both inclusive, showed the maximum relapse rate, 2 cases per month.

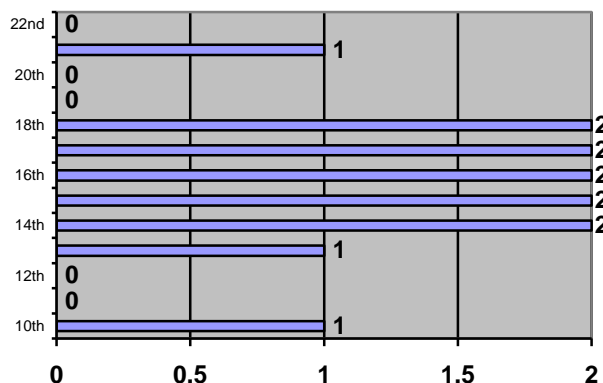


Fig. 4: Relapses according to week of treatment

DISCUSSION

Initial clinical studies about the efficacy of naltrexone in preventing relapse among opioid addicts were carried out in the 1980s, when the drug was first launched. However, number of patient in these studies is generally small and only a limited number of these trials are of a double-blind comparative design. As a consequence, in many studies the type of medication is self-selected and where blinding is performed, drop-out in the placebo group is much higher than in the naltrexone group⁸.

Recently, the use of naltrexone as an adjunctive treatment of opioid dependence has been assessed in numerous clinical studies, involving street addicts, methadone maintenance patients and reformed addicts^{5,6,7,9,10}

A decision-analytic model using Monte Carlo simulation was developed that compared naltrexone as an adjunctive therapy to no naltrexone group. The results suggest that naltrexone as maintenance therapy may be better than placebo in terms of retention in treatment but this was not statistically significant. A meta-analysis of seven included RCTs

gave the relative risk (RR) of loss of retention in treatment in the naltrexone arm as 0.94. The pooled hazard ratio (HR) reported in five of the RCTs for retention in treatment data followed up to 35 weeks was calculated as 0.90 in favor of naltrexone and also did not reach statistical significance. The risk of drug abuse in naltrexone versus placebo, with or without psychological support given in both arms, gave a pooled RR of 0.72, which was a statistically significant difference in favor of naltrexone. The pooled HR from three RCTs for opioid relapse-free rates was significantly different from placebo in favor of naltrexone 0.53; however, this fell off over time and may be of limited clinical significance. They concluded that following successful withdrawal from opioids, naltrexone may be administered on a chronic basis to block any future effects of opioids.

Krupitsky et al (2006)⁹, in a randomized placebo-controlled trial, tested the efficacy of oral naltrexone with or without fluoxetine for preventing relapse to heroin addiction. All patients received drug counseling with parental or significant-other involvement to encourage adherence. Patients totaling 414 were approached, 343 gave informed consent, and 280 were randomized (mean age, 23.6 +/- 0.4 years). At 6 months, two to three times as many naltrexone patients as naltrexone placebo patients remained in treatment and had not relapsed. Psychiatric symptoms and overall adjustment were markedly improved among all patients who remained on treatment and did not relapse.

Naltrexone is reported to be a reasonably effective treatment for relapse prevention in patients with opioid dependence. However, there is a lack of data on outcome and acceptability in patients from subcontinent. An open-label clinical trial was conducted by Malhotra et al (2003)¹⁰, in which 106 patients with opioid dependence were given naltrexone 50mg daily for 6 months. Fifty eight patients (55%) could be followed up and reassessed after 6 months. The follow up and drop-out groups were comparable. Using last outcome carried forward analysis; the overall abstinence rate was 52% (55 of 106 patients). The relapse rate among Indian patients was significantly higher ($P < 0.02$) than our study (28.9%). The relapse rate observed in our study is more close to 22% reported in NJDA's data¹⁰. The relapse rate noted in our study is significantly lower than 72% noted by Mufti et al (2004)¹² in a 5 year follow-up of the heroin addicts in Peshawar being treated with an extended in-patient detoxification for 30 days, motivational Interview, and training in coping strategies.

Early relapse is common after opiate withdrawal and deprives addicts^ important opportunities to develop new, opiate-free cognitive-behavioural

habits. The oral opiate antagonist naltrexone significantly reduces relapse only when rigorously supervised¹¹.

CONCLUSION

Naltrexone appears to be an acceptable treatment for opioid-dependent patients. There is, however, general agreement from drug professionals that the effectiveness of Naltrexone treatment is very much dependent on the persons particular situation, including their level of commitment to staying off heroin and the level of support available to them.

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