

Paxil (Paroxetine) in Complex Therapy in Heroin Addicts

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Summary

The efficiency of Paroxetine was studied in 27 males with heroin addiction (average age: 26.2 years, average disease duration: 3.4 years) undergoing detoxification. After 3-4 days of paroxetine (initial dose 20 mg/day, maximum dose 40 mg/day) the first improvement of affective symptoms were noticed. By the 14th day of treatment, affective discomfort had been arrested in most cases. On the whole paroxetine can be considered an effective medicine for contrasting affective discomfort of heroin addicts in the post-withdrawal stage, as long as agonist compounds are not available.

Key Words: Heroin Addiction- Affective Disorders -
Antidepressants – Paroxetine

Introduction

Affective symptoms are frequent and prominent among other psychopathological symptoms in patients with heroin addiction. Extensive research proved that affective disorders are present to a variable extent at every stage of the disease (8, 11, 18-20, 22, 23, 26-28): dysphoria and irritability are featured in chronic heroin intoxication and amplify during withdrawal, parallel to the somatic and vegetative symptoms. By the time acute

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symptoms of the withdrawal have faded (days), affective symptoms will loom in the foreground. In almost all cases low mood is accompanied by irritation, asthenia, general displeasure, dissatisfaction with treatment, proneness to aggressive and violent behavior, often in a psychopathic, unpredictable mode. During heroin-free periods, weakness, flabbiness and fatigability may prevail over properly depressive symptoms, while patients complain for low mood, lack of motivation and irritability accompanied by an attraction towards drugs. Emotional unsteadiness, enhanced sensibility and vulnerability are as well featured, patients becoming quite sensitive to even the smallest emotional discomfort and prone to distress for low levels of effort. Such a syndrome is known to be specifically responsive to opiate agonists, while it is expected to worsen under naltrexone treatment⁽¹⁵⁾. In Russia, methadone is not widely available for maintenance treatment of heroin addicts, so that the intervention upon drug addiction is limited to the intervention upon secondary symptoms. As for affective symptoms, antidepressants may be resorted to as means of discomfort reduction, hopefully retaining patients in treatment and contrasting their affective distress until methadone and buprenorphine patients are eventually available. In particular, selective serotonin reuptake inhibitors are safer and easier to manage. Moreover, some common biological grounds have been described. In man, the exhaustion of vein muscle produced by repeated inoculations of 5-hydroxytryptamine (5-HT) is antagonized by naloxone. During opiate withdrawal, the loss of vein sensitivity to 5-HT is observed together with the acute stress of opiate metabolism^(3,24). The same phenomenon is documented for migraine sufferers during and between headache attacks⁽²⁴⁾. Naltrexone is also effective in suppressing 5-HT-induced platelet aggregation⁽⁵⁾. Therefore, at least to some extent, 5-HT and opioid metabolism seem to be directly related. The impairment of 5-HT-metabolism is present in detoxified heroin addicts, regardless of psychiatric axis I or II comorbidity⁽⁶⁾. On clinical grounds, SSRIs are known to increase the likelihood of retention in naltrexone-based programs^(7, 9, 12, 14, 25). Lastly, buspirone was effective in reducing symptoms of opiate discontinuation in a double blind setting⁽²¹⁾. On the other hand, SSRI do not seem to be effective in preventing relapsing behaviour in non-abstinent, methadone maintained heroin addicts, and does not produce any significant improvement in depressive symptoms in these patients⁽²⁾.

Paroxetine^(4,10,16,17) is one of the most specific inhibitors of serotonin reuptake, and the most potent. Its action on muscarin, and α and β adrenoreceptors is not significant. Paroxetine's half-life is between 16 and 21 hours, which allows once-a-day prescription, and has no active metabolites. Meals do not influence absorption of the medicine.

We reasonably expected that, in the absence of any specific agonist treatment, paroxetine may provide with some improvement of endogenous opioid function, or at least replace for failing opioid-mediated functions through the enhancement of 5HT metabolism. Such a property may be hypothesized for temporarily abstinent heroin addicts who have recently undergone detoxification, rather than in active users.

Methods

This study comprised 27 males with DSM-IV TR-rated heroin addiction who were consecutively admitted for treatment at the Unit for Clinical Research on Drug Addictions at the National Scientific Centre for Drug Addiction of the Ministry of Health of the Russian Federation, during the period from February to December 2003. Patients with other known concomitant psychiatric disorders were excluded from the study. Patients were aged 19-34 years (average: 26.2 years). The disease lasted between 8 months and 10 years (the average disease duration: 3.4 years). Patients underwent the traditional detoxification schedule (Clonidine, Tramal, Tiopridal, Diazepam) followed by two weeks of paroxetine alone.

Patients were assessed at treatment entrance by a special rating scale including the most widespread symptoms of affective disorders typical of heroin addiction (see table 1). Each sign was registered according to a 0-3 grading scale (0 = absent; 1 = mild or moderate; 2 = marked). Subsequently, each patient's conditions were assessed on a daily basis during inpatient treatment, twice a week in the out-patient setting.

Paroxetine was prescribed from the 4th-8th day of inpatient treatment, after the extinction of the acute withdrawal syndrome was achieved. For all patients, the initial dose was 20 mg per day. Dosages could be increased on a clinical basis.

Results and comment

Retention was complete for the 27 patients enrolled, and all appointments scheduled on an outpatient basis were attended. Maximum administered dose was 40 mg per day. Increased dosages were administered to those patients, who showed symptoms of greater severity. In no case was paroxetine discontinued due to side effects or intolerance.

Improvement of symptomatology is reported in table 1. The first signs of improvement in the patients' conditions were noticed as early as on the 3rd-4th day of paroxetine treatment. At the start of treatment the great majority of patients (n=21; 77.8%) reported marked depressed mood and melancholy, but by the 4th-7th day these symptoms were weakly or moderately expressed in a significant number of patients (n = 18; 89.9%). By the 14th day of treatment depressed mood was marked in 3 patients (11.1%) only, 12 (44.4%) had moderately depressed mood, and 12 (44.4%) showed no melancholy or depressed mood.

Some patients (n = 23; 85.2 %) had experienced a sense of guilt and aimlessness. By the 7th day of treatment only a few patients (n =10; 37%) alleged this symptom, which was absent by the 14th day of treatment in the great majority of patients (n = 24; 88.9 %).

Even more apparent changes were noticed in the analysis of symptoms such as anxiety and dysphoria. By the 4th day of treatment, anxiety was absent in 9 patients (33.3%), by the 7th in 12 patients (44.4%), and by the 14th in the great majority of patients (n=24; 88.9%). Dysphoria and irritability showed the same trend: by the 14th day both anxiety and dysphoria had extinguished in the vast majority of patients (n=24; 88.9%).

Table 1: Efficacy of Paroxetin on affective symptomatology in heroin addicts				
	Days			
	1st	4th	7th	14th
Depressed Mood				
Marked	21	10	8	3
Moderate	6	17	19	12
Absent	0	0	0	12
Melancholia				
Marked	21	7	8	3
Moderate	6	20	19	9
Absent	0	0	0	15
Anxiety				
Marked	7	9	0	0
Moderate	12	18	15	3
Absent	8	9	12	24
Disphoria				
Marked	8	0	6	0
Moderate	11	18	12	3
Absent	8	9	9	24
Irritability				
Marked	13	0	5	0
Moderate	9	21	14	3
Absent	5	6	8	24
Fatigability				
Marked	22	8	4	3
Moderate	5	19	23	11
Absent	0	0	0	13
Weakness				
Marked	12	7	4	0
Moderate	15	20	23	15
Absent	0	0	0	13

The great majority of patients claimed enhanced fatigability (n=22; 81,5%); some of them noticed weakness (n=12; 44,4%). Fewer patients claimed apathy and indifference (n=10; 37%). During the course of treatment fatigability significantly decreased: by the 14th day of treatment it was marked in 3 patients only (11.1%). By the 14th day of treatment 15 patients claimed slight weakness (55.6%), and 12 (44.4%) denied it.

Table 1: Efficacy of Paroxetin on affective symptomatology in heroin addicts				
	Days			
	1st	4th	7th	14th
Apathy				
Marked	10	0	4	5
Moderate	17	22	17	4
Absent	0	5	6	18
Psychomotor retardation				
Marked	3	3	0	3
Moderate	24	24	27	8
Absent	0	0	0	16
Agitation				
Marked	3	8	0	0
Moderate	14	5	18	6
Absent	10	14	9	21
Apathia				
Marked	19	13	11	3
Moderate	8	14	16	9
Absent	0	0	0	15
Sexual inhibition				
Marked	18	18	10	6
Moderate	7	6	17	9
Absent	2	3	0	12
Low concentration				
Marked	0	0	0	0
Moderate	21	21	21	9
Absent	6	6	6	18
Slow mental processes				
Marked	3	3	0	0
Moderate	19	19	19	8
Absent	5	5	8	19

As for apathy and indifference, it was absent in 18 patients (66.7%) by the 14th day of treatment. In a few patients (3 subjects: 11.1%) depressed mood was accompanied by slow psychomotor reactions, which disappeared by the end of treatment. Restlessness, alleged by 3 subjects (11.1%), also disappeared or was weak by the 14th day of treatment. A majority of patients (n= 19; 70,4%) showed low interest in activities of any kind. By the end of treatment 15 of them (55.6%) had become more active and

interested. A significant number of patients (18 subjects: 66.7%) complained for the absence of sex drive at the beginning of treatment. This symptom proved to be the least curable, consistently with paroxetine side-effects profile: it could only be improved by the 7th day; by the 14th day it was absent in 12 patients (44.4%), but persisted in 6 patients (22.2%). At the beginning, most of the patients (n=21; 77.8%) showed marked or moderate concentration or attention impairment. By the 14th day of treatment with Paroxetine the concentration of attention had been restored in 2/3 of patients (66.7%). The analysis of symptoms such as slow mental processes revealed the same trend. By the 14th day of treatment these disorders were absent. On the whole, the improvement observed was consistent with known paroxetine antidepressant properties on non addicted depressed and anxious patients. The latency of improvement was shorter than expected, which is usually between two and four weeks. In some of the patients remission was gradual, while in others (n=3; 11%), despite eventual improvement, it appeared to be unsteady. Among unsteady responders (n=2; 7.4%) patients experienced a relapse into narcotic use and a subsequent exacerbation of affective symptoms. In these cases the prescription of paroxetine was prolonged until the elimination of affective disorders was complete, by 3-4 months.

Results were consistent with previous observations about the possibility to improve affective state in detoxified heroin addicts ^(1,13).

Conclusions

Paroxetine provided short-term relief of symptoms of affective discomfort in opiate addicts recently detoxified from heroin, who could not receive opiate agonist compounds due to legal limitations. Improvement was rapid and noticeable by two weeks for all symptoms typical of the post-detoxification state, with special regard to aimlessness, dysphoria, anxiety, apathy and lack of motivational drive.

In the absence of any agonist treatment option for the control of addictive symptoms and relapsing behavior, paroxetine may be useful to contrast post-withdrawal affective discomfort, between and across relapses.

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