Heroin Addiction and Related Clinical Problems

the official journal of

European Opiate Addiction Treatment Association
EUROPAD

EUROPEAN OPIATE ADDICTION TREATMENT ASSOCIATION

EUROPAD formerly EUMA was founded in Geneva (Switzerland) on September 26, 1994. It shall remain independent of political parties and of any government. The object of EUROPAD is to promote, in the EU and elsewhere, the effective treatment of drug addiction, especially heroin addiction, in particular, but without prejudice to the generality of the foregoing:

1. to promote the development and acceptance of treatment with methadone and other prescribed medicaments (buprenorphine, LAAM, heroin, naltrexone) including long-term prescribing;
2. to enhance the provision and quality of services to drug abusers and their families, especially heroin addicts;
3. to promote a better understanding of methadone treatment by the general public and its elected representatives and officials;
4. to promote collaborative research and to provide a European research centre;
5. to work with the American Methadone Treatment Association to promote support for methadone treatment worldwide;
6. to promote good will and cooperation among the staff of methadone and other medical treatment services in Europe and elsewhere, and, in pursuit of any of the foregoing objects, to obtain financial support from government

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The promise of Opioid Receptor Antagonist drugs in the treatment of neuropsychiatric disorders

Joseph A. Deltito and Icro Maremmani

Summary

The endogenous opioid system, either directly or through its influence on other neurotransmitter systems, has far-reaching effects on normal as well as abnormal (maladaptive) behaviours, thoughts and mood states. Altering this system through the use of an opioid antagonist medication may not only be useful in treating recognized psychiatric illnesses, but may also prove to be valuable in elucidating psychophysiological abnormalities that could contribute to the foundation of these disorders.

Opioid Antagonists Naltrexone and Naloxone have been used in substance abuse illnesses (narcotics, alcohol, tobacco) but have also been administered in variety of psychiatric conditions, including Anorexia Nervosa, Bulimia, Schizophrenia, Self-injurious Behaviour (as part of Borderline Personality Disorder and other conditions), Autism, Obsessive-Compulsive Disorder, Tourette’s Disease and Trichotillomania.

A review of the clinical effectiveness of Naltrexone and Naloxone reveals many situations that call for a therapeutic trial on opioid antagonists in these conditions, despite the lack of a robust database demonstrating the clear efficacy of these medications in the global resolution of any of these conditions. A psychopathological reconceptualization of the conditions mentioned above, focusing on symptoms rather than syndromes, may prove to be of great clinical value.

Key words: Opioid Receptor Antagonists - Neuropsychiatric Disorder Treatment

Opioid Receptor Antagonists (ORAs) have been widely studied for use in various phases of the treatment of substance and alcohol abuse [3,4,5,7,8]. In addition, there is a growing body of evidence indicating the usefulness of this class of medications.
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in non-opiate and non-substance abuse Neuropsychiatric disorders such as Obsessive-Compulsive Disorder, Eating Disorders, Autism, Schizophrenia, Borderline Personality Disorder (Self-Injurious Behaviour), Gille de la Tourette’s Syndrome, and Trichotillomania.

In various countries around the world most current research and clinical usage has been accounted for primarily by three agents:

Naloxone, which has a very short elimination half-life, and is only available in injectable preparations.

Naltrexone, which has an elimination half-life two to four times longer than Naloxone, and is available in oral preparations.

Nalmefene, which has an elimination half-life similar to Naltrexone when given in oral form, and one of about ten hours after administration by injection.

There exists no comprehensive database supporting the use of any of the ORAs as monotherapy in the treatment of any of the above-mentioned neuropsychiatric conditions, but there does exist a rather broad database supporting the use of these agents as adjunctive agents in at least certain subsets of patients within these diagnostic categories. For discussion of this literature we refer the reader to the comprehensive review of this topic by Reneric and Bouvard [6].

The current system of Psychiatric Classifications now in use may not be optimally sensitive for purposes of noting true utility of certain novel pharmacological agents being employed in experimental paradigms or in novel clinical practices. That is because the ICD 9 and DSM IV Systems of Diagnosis conceptualize diseases as syndromes, which are aggregates of symptoms. If we look at all patients who might qualify for a given diagnosis, they would not all share common features of the disorder as a requisite to receive that diagnosis. It may very well be that certain pharmacological agents may be particularly effective in controlling certain symptoms perhaps present in some members, but not all in other members in a given diagnostic class. Some individuals with a given diagnosis may simply not have that targeted symptom. Any research study that merely analysed outcome globally on all members in a given diagnostic category can miss a positive effect in a significant subset of those patients with a given symptom sensitive to positive change from a pharmacological agent. An examination of the diagnostic criteria for Borderline Personality Disorder is instructive.

The DSM IV Diagnostic Criteria are:

301.83 Borderline Personality Disorder

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

(1) frantic efforts to avoid real or imagined abandonment. Note: Do not include suicidal or self-mutilating behaviour covered in Criterion 5

(2) a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation

(3) identity disturbance: markedly and persistently unstable self-image or
sense of self

(4) impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). Note: Do not include suicidal or self-mutilating behaviour covered in Criterion 5

(5) recurrent suicidal behaviour, gestures, or threats, or self-mutilating behaviour

(6) affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days)

(7) chronic feelings of emptiness

(8) inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights)

(9) transient, stress-related paranoid ideation or severe dissociative symptoms

In order to receive a diagnosis of Borderline Personality Disorder one must meet five of nine criteria. This implies that there are thousands of permutations which could lead to a diagnosis of Borderline Personality Disorder. In a given study of BPD subjects having any given symptoms or set of symptoms may be over-represented or under-represented compared with other studies dependent on numerous factors. For example, subjects recruited from inpatient units may have an over representation of BPD patients who suffer from suicidal acts, self-mutilating behaviour or paranoid ideation, as these symptoms may be largely responsible for the patient being confined in hospital. Conversely, subjects recruited from a university-based student infirmary may set up a particularly strong bias against these symptoms, as a subject with BPD who suffered from these particular symptoms would be less likely to be enrolled as an active university student.

The testing of novel agents or the treatment of BPD may, therefore, be greatly influenced by the recruitment issues related to the cohort under investigation. There have been several studies supporting the use of Opioid Receptor Antagonists in treating Self-Injurious Behaviour. Self-Injurious Behaviour in BPD is distinguished from repetitive suicidal or parasuicidal behaviour in that the patient in question clearly reports that the intention of his or her activity is not to die; it is usually described as a method of reducing stress, self-calming or breaking a state of terror. Common behaviours include superficial cutting, burning, skin picking and head banging. Such descriptions, on what are, at first sight, phenomenological grounds seem to sum up cognitive states that are likely to be mediated at least in part by an endogenous opioid system.

So, if a clinician has a patient with Borderline Personality Disorder who displays Self-Injurious Behaviour in such a form that this symptom is of particular clinical significance, any intervention which aids in its control or elimination may be of great clinical benefit. This would be true regardless of whether other features of BPD in the given patient showed or did not show improvement. The lack of overall
global improvement in a patient, or the lack of improvement in most patients within a given diagnostic category, does not necessarily negate the potential strong benefit a given medication might bring or a particular patient might enjoy. Such may be the case in using the Opioid Receptor Antagonists in Self-Injurious Behaviour, when found as part of BPD or of other conditions, such as Autism or Mental Retardation.

It has been hypothesized that ORAs can block the euphorogenic or rewarding aspects of Self-Injurious Behaviours, which, over time, will lead to their extinction. Behaviours whose overall effect might have been pain-relieving may be experienced more as pain-engendering. The euphoria of a given act, now blocked, only leaves a residue of pain, anxiety or angst. Hopefully, psychotherapy and other interventions will then aid the patient to more adaptive patterns of behaviour.

Similar hypothesizing can be extended to other conditions such as Obsessive-compulsive Disorder. Obsessions are intrusive thoughts or emotional states that are experienced as intrusive and irrational, and that cause anxiety, discomfort or angst. Compulsions are behaviours or thoughts that neutralized, block or “break through” the obsessions or the state of discomfort they cause. Compulsions are often “done” in a stereotypic or ritualistic manner. Certain compulsions, when primarily associated with pleasure in and of themselves, may be referred to as “impulsive”; this is true of compulsive gambling, shopping or sexual activities.

ORAs have been employed as adjunctive medications for treating OCD. The mechanism of their benefit is unclear. One provocative hypothesis, which recapitulates on the above discussion related to Self-Injurious Behaviour, is that ORAs may interfere with the “euphorogenic” effect of compulsive/impulsive activities. In some forms of OCD, obsessions may be of primary clinical importance, whereas in other forms compulsions/impulses may be of primary clinical importance. As discussed above, there may be targeted subsets for which ORAs hold promise, even if they are not indicated globally for all patients who would qualify for a diagnosis of OCD under our current diagnostic systems. An obvious area for targeted research is that marked by “impulsivity”, a tendency that can lead to severe occupational, familial or social disability, such as that associated with compulsive/impulsive gambling, shopping or sexual activities.

There appears to be wide distribution of opioid receptors through the areas of the central nervous system involved in such functions as perception, mood and behaviours. In addition, the endogenous opioid system interacts directly or indirectly with all other major neurotransmitter systems known to be involved with the major neuropsychiatric diseases discussed above [1].

We need to humbly bear in mind that our current systems of classification are arbitrary; they do not constitute the only way to conceptualize manifest psychiatric disease. Our current systems of classification emphasize syndromes which are aggregates of symptoms, yet there may be symptoms which cut across many different disease categories that are more sensitive to treatment with given agents than the larger syndromes [2].
At present, data support trials of ORAs in selected subsets of patients suffering from a variety of neuropsychiatric conditions. Clinical trials focused on specific symptoms associated with particular distress or disability for a given patient may be more fruitful than those that investigate traditionally conceptualized syndromes or diseases.

References

Haematic concentrations versus oral doses of methadone. Comparative assessment of two reference systems during substitute therapy in opiate addiction

Scarlata Salvatore¹, Marcello Chiarotti², Nadia Fucci² and Nadia De Giovanni²

Summary
Therapeutic failures in MMP patients may be due to an inadequate oppioidergic replacement effect of the drug on specific receptors for endogenous opiates. Even with oral doses considered adequate in the current literature, haematic levels may be low, due to genetic or induced over-metabolization of the drug; in addition, even when haematic levels are high, the results may be poor, due to acquired receptor tolerance. 61 heroin addicts on MMP doses agreed on between therapist and patient have been evaluated with Europasi at the beginning and at the end of observational and therapeutic periods ranging between 12 and 57 months. Addicts who showed a positive development revealed haematic levels (non-oral ones) higher than non-responder patients, and some of the former reached haematic levels higher than those reported in current literature. Estimates of the haematic concentration of methadone may be useful, even if availed of “una tantum” during the treatment period.

Key words: Substitutive Therapy - Methadone Haematic Concentration - Clinical Consequences

Two objectives are pursued by pharmacological replacement treatment for opiate addiction: first, in the short term, interruption, or at least the reduction of drug abuse, or of high-risk or antisocial behaviour; second, in the long term, retention on treatment to avoid or lessen relapses and achieve reintegration in social, family and working environments.

Data-processing from systematic researches [6] suggests that a daily dose of between 70 and 120 mg of hydrochloride methadone, with a broader range extending above or below, is sufficient for individual patients, at particular moments, as the
appropriate therapeutic regime.
Therapeutic results vary very widely between patients, and, over time, the same patient may present different results with the same dose.

Pharmacokinetic studies [13;8;9;1;14] in normal volunteers, in cancer or postsurgical patients or in opiate addicts indicate highly variable characteristics for the drug: 1) its elimination half-life may vary between 13 and 58 hours; 2) the volume of apparent distribution may vary between 2.1 and 5.6 L/kg and its bioavailability between 65 and 90%.

The administration of increasing doses of methadone C 14 [1] has made evident a proportional increase in the elimination of the product itself and of its primary inactive catabolite (2 ethylidene-dimethyl-phenyl-pyrrolidine), but the relationship between the two substances changes considerably, shifting progressively in favour of the latter, so indicating increased metabolization due to enzymatic induction or the progressive mobilization of deposit substances.

Variations in the free fraction (the active fraction subject to metabolism) are produced by variations in the haematocrit, in the alpha-acid glycoprotein or in albumin, which are the three principal vectors [12].

Variations in urinary pH must modify excretion of the drug, considering that the clearance function is a logarithmically inverse function of urinary reaction [3].

The clinical importance of these variations has not yet been assessed, as the prevalence of the metabolized part compared with the part excreted through the kidneys is unknown. What has become clear is the pertinence of the involvement of cytochrome p 450 in the variability of intrahepatic metabolization (with a reduction of as much as 22 hours with regard to the normal 52-hour half-life of the drug) [8].

Numerous addictive substances used by patients (alcohol, benzodiazepines, barbiturates, tobacco, and other forms of smoking) and those used in therapy (rifampicin, amitriptyline, ritonavir, cimetidine and theophylline), as well as those used in foodstuffs (furancumarine and bergamottine) [8] drastically modify the metabolization and the concentration of the drug in the plasma.

Above all, the drug currently used in therapy is offered in racemic form (d and l methadone in equal quantities, 50:50), while it is almost exclusively the levogyral form that is biologically active, and differences in the clearance media, in the affinity and the average half-life of the two forms have been stressed [8;11].

As the effect of a drug is considered directly proportional to its concentration in specific receptors and, therefore, indirectly proportional to its haematic concentration, numerous tests have been carried out to determine a specific therapeutic range for its concentration in the blood.

The data obtained, however, have not been at all univocal. Even if the haematic concentration of the drug grows in direct proportion to the dose administered, with an average coefficient of 3.5 in ng/over mg/die of the dose, there are large variations in the ratio between different patients and, over time, in the same patient [8].

Horns [11], Loimer [17] and Torrens [20] have not found any correlation between
the haematic concentration of the drug, and either subjective symptomatology, or the objectivity of abstinence or hyper-treatment, or the therapeutic results as perceived in the persistence of the abuse of opiates over a period of a few months.

Dole [7] established a dose of between 100 and 1000 ng/ml as the effective therapeutic range for the treatment.

Bell [4] suggested a haematic level of 100 ng/ml or above as being capable of solving withdrawal symptomatology without increasing the oral dose of methadone.

Holmstradt [10], in a group of MMP patients with a follow-up period of up to 43 months and a preestablished daily dose of about 60 mg/die, reported that the best results, in terms of social, family and work integration and of the reduction of abuse, were found in patients who had the highest haematic levels.

Loimer [17] noticed subjective and objective symptoms of abstinence even with a high methadone level in plasma, but he focused on an inverse statistical correlation between the haematic concentration of methadone and objective withdrawal symptomatology, which was more evident than in the case of oral doses.

Wolf [21] found a positive correlation between dose per kilo of weight and drug concentration in the plasma; data outside this range improve our understanding of some clinical cases (diversion of dose or enzymatic interference).

By using a methadonemic curve, on the other hand, instead of the oral dose curve, Kell [16] obtained a decrease from 10 to 3% of positivity in urinary control for drug abuse substances. Divergencies as sharp as these in the results reported in the literature prompt us to radically reconsider the question of the usefulness of relying on methadone dose values.

At present therapy is carried out by modifying doses in line with clinical attendance and the frequency of relapses.

The delay in therapeutic responses in term of dose adjustment makes therapy difficult to apply; it also suffers from the impact of ideological and emotional interference between therapist and patient, so that the seriousness of many cases is underestimated.

We have tried to clarify the terms of the problem further by examining a group of MMP patients on a constant dose, where a more reliable correlation might be found between the course of the illness (tendency towards changes in the frequency of relapses, behaviour likely to increase the risk of infections, syringe swapping, and promiscuous sexual relationship, as well as reintegration in the social, family and working context) and methadonemic concentration or, alternatively, the oral doses taken.

Materials and methods

From a population consisting of drug addicts and those utilizing a public service, which show an overall rise from 320 to 812 during the period under review, 196 addicts taken opiates or other substances were chosen. Their addiction had lasted for at least two years, on the basis of the standards set down by the DSM III-R, and had been on stable
MMP for at least 6 months, maintaining that dose for the whole period of observation. They were asked to allow a blood sample for the calculation of the proper methadonemic value to be taken in order to assess the progress of the illness. No changes in the therapy were carried out after this value had been calculated.

The oral doses were agreed upon by the therapist and the patient, avoiding withdrawal conditions as far as possible. Only 76 of the patients contacted participated in the trial, and only 61 respected the conditions that had been laid down.

The gravity of addiction was estimated at enrolment by applying the Europasi [19] interview, and summing the therapist’s and patient’s scores for medical, work, alcohol, drug, family and psychic problems. Each index had a range between 0.1 and 0.9, while the range for scores was between 0.7 and 6.3.

The interview was repeated by the same therapist at the end of the treatment period, in the case of patients who wished to interrupt or change therapy, and at the end of the observation period for those who completed the therapy.

Differences between the first and the second results were evaluated and divided into three outcome classes, according to whether the score was greater than, equal to, or less than before:

- Class A: Worse situation
- Class B: Unchanged situation
- Class C: Improved situation

The patients were visited weekly, and urine samples were taken at random more or less three-monthly, when samples had been collected, they were analysed for opiates, ecognina, barbiturates and amphetamines.

The percentage of positivity for addictive substances and the frequency of urine sampling helped to determine the therapist’s score along the drug-problem gravity axis.

After the minimum fixed observation period, patients who wished, or who had to change their oral dose permanently, were assessed on the basis of their outcome and then registered as new patients.

**Detection of methadone value in serum**

Once the observation period had elapsed, a sample of venous blood was taken between the administration of one dose and the next. Separated serum was frozen until it could be examined. Quantitative analysis was performed in RIA using coat a count methadone solidphase I 125 radioimmunoassay from DPC (Diagnostic Products Corporation), 700 West 96th Street, Los Angeles, California.

For each of the three groups the following were evaluated: average age, duration of addiction, time of retention on treatment, oral dose and methadonemic level, and the ratio between rate in ng/ml and oral daily dose in mg/die.

**Results**

Group A, with a worse situation, comprised 8 patients (13% of all patients who completed the study); they showed a very small increase in ASI.

Group B, with an unchanged situation, comprised 21 patients (33% of the patients
Group C, with an improved situation, comprised 33 patients (54% of the patients completing the study); their ASI value fell from 2.8 to 2.3.

Significant differences were found:
- On the duration of addiction: group A reported a period of 14.9 years, against 10.4 in group B (+43%) and 9.7 in group C (+52%).
- On the oral daily dose of methadone: 55 mg in group A, against 76 in group B (-28%) and 77 mg in group C (-29%).
- Mean methadonemic level: 313 ng/ml in group A, against 260 in group B (+20%) and 661 in group C (-53%); in group C methadonemia varied from 17 to 4000 ng/ml.

Ratio between methadonemia in ng/ml and oral dose (mg/ml):
- Group A: 5.70
- Group B: 3.24 = 43.70% of A
- Group C: 8.64 = 151% of A

Discussion

The rationale which inspires methadone treatment is the constant saturation of the receptors for endogenous opiates, so as to give physiological tone and opioidergic reactivity at three rising levels:
1) Resolution of the withdrawal crisis;
2) Inhibition of the gratification response to the abuse of opiates;
3) Attenuation of the craving for opiates.

As therapy progresses, conspicuous individual differences in the capacity to modify drug metabolism are elicited, as widely demonstrated by studies on pharmacokinetics, followed by conspicuous diversity in the methadonemic concentrations deriving from the same oral dose.

In any case, some patients treated in “open” studies, with doses agreed upon between therapist and patient, developed very high haematic concentrations, up to ten times the average values; those levels would certainly have been lethal in patients who had not become tolerant. This induces us to think that the highest tolerance level and the greatest diversity develop in line with receptor sensitivity.

In clinical practice there is no opportunity to correlate anomalous therapeutic responses with either of the two mechanisms, so it may be worth determining the methadonemic level in the blood, even if only once.

Low haematic values of methadone caused by genetic disparity or pharmacokinetically induced by other drugs may require the removal of the interfering factors, the fractionating of doses, or the choice of levo-acetyl-methadolo with a longer half-life.

Disappointing therapeutic responses even in the presence of high haematic levels, due to high receptor tolerance, may call for a further increase in the dose, with an expectation of attenuation in the stressors that induced the relapse.

Most observers agree that it is not possible to determine a therapeutic haematic concentration within constant or precise limits. A reduction of high levels, significant
<table>
<thead>
<tr>
<th></th>
<th>n. of patients</th>
<th>% of total patients</th>
<th>Duration of addiction</th>
<th>Average oral dose</th>
<th>Average ematic rate</th>
<th>ratio ematic/oral</th>
<th>Initial ASI</th>
<th>Final ASI</th>
<th>Retention time (months)</th>
<th>Overall age</th>
</tr>
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<td>Group A &quot;pejorative evolution&quot;</td>
<td>8</td>
<td>13</td>
<td>14.9</td>
<td>55</td>
<td>313</td>
<td>5.22</td>
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<td>4.2</td>
<td>46</td>
<td>40</td>
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<td>Group B &quot;invariated situation&quot;</td>
<td>21</td>
<td>33</td>
<td>10.4</td>
<td>76</td>
<td>260</td>
<td>3.67</td>
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<td>47</td>
<td>37.7</td>
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<tr>
<td>Group C &quot;improved situation&quot;</td>
<td>32</td>
<td>54</td>
<td>9.7</td>
<td>77</td>
<td>661 min 17 max 4000</td>
<td>8.61</td>
<td>2.8</td>
<td>2.3</td>
<td>48</td>
<td>35.4</td>
</tr>
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S Scarlata: Haematic concentration versus oral dose of methadone. Comparative assessment of two reference systems during substitutive therapy in opiate addiction

enough to be noted clinically, may still keep values well above the usual ones; low haematic levels may maintain a good behavioural equilibrium in the mild phases of the illness.

Our data match those of Holmstradt: long-term improvement in the illness comes about in the presence of high methadonemic level rather than high oral doses. Methadonemia only marks an intermediate point in the cascade which proceeds from the daily oral dose to the methadonemic level, on to concentration on receptor unity, to the affinity of receptors, and to behavioural response, but it does make a useful contribution to management of the therapy.

Above all, it may prove to be a useful instrument in the therapeutic relationship: high oral doses are adversative [5;2;15] or are almost always refused by patients because of their resistance to therapy or fear of long-term dependence on it. The relationship between therapist and patient is a useful instrument, because high levels can produce a negative reaction from the patient, due to therapeutic resistance or fear of long-term dependence on therapy.

To shift the terms of the problem from subjective cenaesthesiaic sensations to objective laboratory data may help to convince patients that they should accept adequate oral doses.

References


Received October, 20, 2000 - Accepted March, 15, 2001
Therapeutic effects of paroxetine on the cocaine abuse in heroin addicts

Vincenzo Manna

Summary
During the last few years, cocaine abuse has been detected in increasing numbers of heroin addicts taking part in a methadone maintenance programme. Paroxetine, a serotoninergic reuptake blocker, was administered, 20 mg p.o. a day, to 12 outpatients, cocaine abusers with heroin addiction, during a methadone maintenance treatment, to evaluate the possible anti-craving and therapeutic effects of the prescribed drug on cocaine use. Four patients discontinued paroxetine treatment after a few days. Eight patients received paroxetine for at least eight weeks. Cocaine abuse was detected by weekly toxicology screening. After eight weeks of treatment, three patients had completely stopped using cocaine, and four had considerably reduced their consumption. One patient reported no change. So, paroxetine, as suggested for other serotonin reuptake inhibitor drugs, may be considered a safe, effective therapeutic agent in treating of cocaine abuse in heroin addicts.

Key words: Paroxetine - Cocaine - Heroin Addicts - Methadone Maintenance - Craving - Depression - Addiction

Introduction
During the last few years, the consumption of cocaine appears to be growing among heroin addicts taking part in a methadone maintenance programme [10]. Cocaine use is associated with fatal arrhythmias, depression, psychosis and increased criminal activity [5]. In addition, there are risks of a progression in injecting behaviour, in users who...
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consume cocaine together with heroin in a “speed ball”. Thus, the development of feasible alternatives to the current pharmacological interventions that aim to reduce cocaine use are highly desirable. The avoidance of unpleasant withdrawal symptoms, such as depressed mood, craving for the drug, disorders of the sleep-wake rhythm, can be considered the most important factor in the perpetuation of cocaine consumption. Cocaine interferes with the noradrenergic, dopaminergic and serotoninergic systems. There is evidence of long-term neurobiological and neurophysiological changes to noradrenergic, dopaminergic and serotoninergic neuronal pathways in animal models of chronic cocaine consumption [13]. Although it is not correct to extrapolate the type or degree of such changes from experiments on animals to humans, it is highly probable that effects of this kind can occur in the human brain [8]. Chronic cocaine abuse appears to lead to a fall in the central serotoninergic activity, so the effects of drugs that increase the functional levels of the brain’s serotoninergic systems call for clinical evaluation [1].

Serotonin has been implicated in the mediation of a variety of behaviours and mood states such as depression, obsessive-compulsive disorder, panic attacks, anxiety, appetite, aggression, suicide and alcoholism, as well as in addictive behaviours [3]. Moreover, drug abuse is strongly associated with depressive illness and antisocial personality; some reports gave evidence of a fall in the brain’s serotoninergic activity in these patients [11].

A number of psychopharmacological agents have been reported as effective in reducing cocaine use and craving, including SSRI antidepressants, dopamine agonists, psycho-stimulants, lithium, carbamazepine and others [5]. In particular, fluoxetine has been reported to be effective in the treatment of cocaine abuse in heroin addicts [12]. In vivo studies confirmed that the co-administration of fluoxetine with methadone did not significantly modify the plasma levels of methadone in addicts [7]. SSRI vary widely in their interaction with cytochrome P450 (CYP) isozymes in the liver. [14] Most information is available on the inhibition of CYP2D6 by the SSRI drugs, with decreasing potency: paroxetine, norfluoxetine, fluoxetine, sertraline, citalopram, fluvoxamine and demethylsertraline [2]. Methadone, which is widely used in the treatment of opioid dependence is mainly metabolized by cytochrome P450 3A4 (CYP3A4) [6]. There is evidence that paroxetine is a specific substrate of CYP2D6 [2].

On the basis of these metabolic and clinical considerations we have used paroxetine, a highly specific serotonin reuptake inhibitor that is known to be effective, relatively safe and generally well tolerated. Paroxetine was administered in the management of craving and withdrawal from cocaine in twelve heroin addicts, taking part in a methadone maintenance programme. Twelve outpatients were recruited at the Drug Dependence Department (SER.T.-AUSL FG/3) at Foggia in Italy. This is the central base for the community drugs team responsible for the city of Foggia and the health service and social security districts of its province. Referrals to the drug centre service (SER.T.) can be made by any medical or health service agency, or by individual patients. Every case, at initial assessment, but also during treatment, is reviewed at a multidisciplinary team meeting, where any clinical activity is discussed and planned. From 1st
January 2000, heroin addicts who were also cocaine users, and were taking part in a methadone maintenance programme, were assessed once they expressed a wish to achieve abstinence from cocaine. The initial proposal was a two-week treatment with paroxetine 20 mg. p.o. daily. In addition, counselling or other forms of psychotherapy or social support were continued, offered or re-proposed. The monitoring of cocaine use was carried out at one-week intervals, and drug use was registered by self-report and urine toxicology screenings based on the enzyme-multiplied immunoassay technique (EMIT) [9].

Case Reports

Twelve patients were recruited, 10 male and 2 female, of mean age 27 yrs. 3 mths. (range 19-43 years). Mean duration of heroin addiction was 5 yrs. 9 mths. (range 3-12 yrs.). All patients had been on a methadone maintenance programme, for at least three consecutive months, before initiating the paroxetine trial. Methadone dosages varied from 60 to 80 mg/day. In particular, methadone 60 mg/day/p.o. were administered to five patients, while methadone 80 mg./day/p.o. was administered to the other seven patients. Four patients discontinued paroxetine treatment within the first two weeks of initiation because it showed no lack of any acute therapeutic effect. The remaining eight patients received paroxetine for at least eight weeks. These patients can be divided into those who achieved a period of cocaine abstinence, those whose use was reduced and those whose use of cocaine was unaffected.

Abstinent Group

After eight weeks of paroxetine treatment, there were three patients who had attained cocaine abstinence. They reported markedly decreased cocaine craving. Two patients stopped using cocaine, during the fourth week of treatment, and one during the sixth week. Two patients received paroxetine for longer than the standard eight weeks of treatment because their clinically evident depression showed improvement. They were abstinent for two more months while continuing on paroxetine. One non-depressed patient, who stopped using cocaine after the fourth week of treatment and whose paroxetine treatment was discontinued after the standard eight-week period, was abstinent for three more months, before reporting a single lapse, during a period of considerable stress.

Reduced Use

Four patients achieved a reduction in use: the first from using cocaine three times daily to once weekly; the second reported a 60% reduction in the frequency and quantity of cocaine intake; the third and the fourth, after having used it every day, used cocaine only once a week.

No Change

One case reported no change in cocaine daily consumption. None of the
patients reported an increase in cocaine use during the period of paroxetine treatment.

**Side-Effects**
Slight side-effects were reported by four patients, as follows:
- nausea (n=1), constipation (n=1), tremor (n=2), sweating (n=1), diarrhoea (n=1)

**Discussion**
The high rate of early dropouts, which occurred in this clinical study, is a common phenomenon, well-known to those working in this field of medical activity. There are evident difficulties in assessing the level of illicit drug use. The very large variability in the purity and concentration of illicit drug preparations also reduces the reliability of self-reporting. Reliance on urinalysis is of limited value in confirming real quantities of cocaine intake. Some cocaine users seems to overstate their use at the initial interview in order to maximize their chance of receiving prescriptions for large doses, and this may induce an apparent trend towards decreased cocaine use. However, in previous studies by us that aimed to reduce injecting behaviour, self-reporting was verified as a reliable way of assessing illicit drug use [9]. Four patients reported side-effects of slight intensity and duration. These effects were transitory and not severe, so that paroxetine treatment did not have to be discontinued.

**Conclusion**
Of the eight outpatients, heroin addicts who were also cocaine abusers and were being treated on a methadone maintenance programme, received paroxetine 20 mg /day/ p.o. for eight weeks; only one subject failed to report a reduction in cocaine use. This result appears consistent with reports in the literature about the effectiveness of other SSRI drugs on this difficult group of patients [5; 12]. Paroxetine proved to be an effective, well-tolerated, relatively safe drug in treating of cocaine abuse in heroin addicts. A longer-term prescription of paroxetine could help prevent relapses into cocaine use, especially in patients with evident depressive disorders.

**References**

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Heroin Addiction and Related Clinical Problems
Methadone regulations in USA: Comments, proposal to adopt new regulations and proposed rule

Robert G. Newman

Summary
The current regulatory process governing methadone treatment of addiction is associated with one problem that overshadows all others: it effectively limits the prescribing of methadone to “programmes” that, collectively, can accommodate no more than 15-20% of all who need and could benefit from this medication. As a consequence, lives are lost (literally as well as figuratively), and there are staggering costs to the general community. The proposed new Rule does nothing about this problem. To the contrary: it exacerbates it, and by implicitly endorsing the status quo reduces the prospects for future change. In addition to raising further the barriers to expanding methadone availability, the Rule would complicate rather than streamline the bureaucratic process that governs treatment, do nothing to enhance quality of care of the lucky few who do gain access to methadone, and raise costs for Government, providers and patients.

Key words: Methadone Regulations, Policy Initiatives

Barriers to treatment
As long as methadone prescribing is limited to “opioid treatment programmes,” and the general medical community is legally excluded from this field of treatment, methadone treatment capacity will never be expanded. The first barrier is the cost associated with “programmes,” which currently exceeds a half-billion dollars (well over $100 million comes directly from the patients themselves). Were an additional billion dollars to be allocated annually for methadone programmes (hardly a likely prospect!), approximately half of all heroin addicts in America would still be left without access.

The second, and equally formidable, barrier is the “not-in-my-backyard” phenomenon that for years has caused virtually every proposed new facility in the nation to be challenged — usually successfully. It is naive in the extreme to believe that the fierce,
almost universal community opposition to “clinics” will be overcome by the initiatives incorporated in the new requirements or by any other means. In fact, the unparalleled constraints the Rule continues to impose seem to reflect — and will surely reinforce — the very same prejudices against the patients and the providers of methadone treatment that are prevalent among the public at large.

The bureaucratic process

Although it is claimed that “the new system would increase significantly the direct participation of the medical community in the oversight of addiction treatment” (p. 39810), no clue is given as to how this will be achieved. What is clear is that the new “accreditation agency” layer that is proposed will be incremental, adding to the extraordinary bureaucracy that already exists. Specifically, the Department of Health and Human Services will continue to promulgate “Federal opioid treatment standards as enforceable regulatory requirements that treatment programmes must follow as a condition of certification” (p. 39819). Among the areas these requirements will address are the medications that may be used, the “dosage form limitations,” the criteria for take-home privileges, staffing patterns and responsibilities, criteria for admission, and “required services” (p. 39810).

The hurdles facing providers seeking to be qualified to prescribe methadone can only be described as Kafkaesque. According to the proposal, applicants must first be “accredited” by one of a number of agencies specially approved by the Substance Abuse and Mental Health Services Administration (SAMHSA) for this purpose. However, accreditation (even though based on standards and regulations that SAMHSA itself shall establish!) does not obviate the need for “certification,” and “...there are circumstances in which SAMHSA could deny certification to an accredited programme” (p. 39817). In addition, the Federal Drug Enforcement Administration (DEA) will continue to exercise independent approval authority over every applicant and provider, and while it appears that SAMHSA will not require separate State approval, DEA will (p. 39818)! In any event, it is explicitly noted that there is no intent to restrict State governments from imposing their own distinct regulatory procedures and requirements. And once approved, each program “must agree to allow SAMHSA, DEA officials, relevant State officials, and authorized accreditation bodies access to conduct surveys and inspections (including unannounced inspections) and full access to patient records” (p. 39818).

The responsibilities imposed by the Rule on methadone providers go far beyond the clinical management of opiate dependence. They include, for example, “reducing or eliminating associated criminal activities, reducing behaviours contributing to the spread of infectious diseases, and improving quality of life ...” One of the most extraordinary demands is that providers describe “a comprehensive diversion monitoring program that assigns specific responsibility to medical and administrative staff for carrying out diversion control measures and functions” (p. 39820). On the surface, each of these requirements may seem reasonable (although perhaps overly ambitious) as an objective of a comprehensive medical service; as a yardstick against which to measure the qualifications of potential providers and the success of medical care, however, they are
unprecedented and inappropriate. Consider, for example, demanding that physicians develop plans for monitoring possible sharing or selling of needles and syringes by diabetics, or barbiturates by epileptics, or Ritalin by hyperactive teenagers, or Viagra, Prozac, narcotics prescribed for analgesia, etc. Imagine requiring that venereal disease treatment services demonstrate a “plan for reducing or eliminating” unsafe sexual practices, or that a cardiac clinic serving a predominantly indigent population be held accountable for the proportion of its patients that becomes employed. Again, these are all laudable goals, but it would be ludicrous to suggest (and catastrophic to insist) that they be applied as criteria to grant or deny physicians the right to treat patients who need help. And yet, that is precisely the policy and practice the Rule imposes on methadone treatment.

Notwithstanding the statement that “…the proposed definition of a ‘certified opioid treatment programme’ includes individual practitioners, such as private physicians” (p. 39816), no practitioner would or could comply with these requirements. The conclusion, therefore, is inescapable: this Rule ensures that there will continue to be exclusive reliance on “programmes” for methadone treatment, thus precluding any narrowing of the gap between demand for and availability of this medication.

Quality of care

The most surprising aspect of methadone treatment over the past 35 years has been the consistency of the reports of its effectiveness. Significant decline in illicit narcotic use has been noted in every published study from all over the world, in communities with vastly different social, political and economic characteristics, and with respect to patients of varying ethnicity, age and background, using different opiates by different routes of administration. While staffing patterns and policies and procedures have been found to have an impact on the degree of therapeutic success, even these important variables, individually and collectively, have not precluded substantial benefits of methadone treatment for most patients.

The 1990 General Accounting Office (GAO) report [2], to which reference is made in the Federal Register, dramatically illustrates this consistency. The GAO carried out an extensive evaluation of 24 methadone programs located throughout the United States, and reviewed the medical records of 5,600 patients. In the case of every one of these programmes, GAO determined that over 50% of all patients were using no heroin within six months of enrolment (for the five New York programmes, GAO found 95% or more of all patients abstaining from heroin within the same six-month period after starting treatment)! These outcomes are all the more extraordinary since the GAO found that 21 of the 24 programmes prescribed an average daily dose of methadone that was less than optimal (see below), and some of the patients-to-staff ratios were deemed far too high (in the five New York programmes, for example, the average number of patients per counsellor ranged from 42 to 67).

Of course, there always exists an obligation to pursue better results, and in this
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regard it is important to note two practices that are associated with the considerably increased likelihood of persistent and/or recurrent heroin use: the widespread, self-imposed, arbitrary refusal of providers to prescribe adequate doses of methadone, and the practice of urging patients to terminate treatment. As early as 1989 the Director of the National Institute on Drug Abuse observed that 60 mg of methadone per day had been found to be “the lowest effective dose” for most patients. He went on to say, “... in this age of AIDS, a low dose policy is not simply inappropriate — it can be fatal to the IV drug abuser in treatment as well as his or her sexual partners and children” (NIDA Notes, Spring/Summer 1989, p. 3). And yet, a just-published survey of programmes throughout America [1] found over half still provide patients an average dose of less than 60 mg, and urge patients to detoxify from treatment. It is therefore paradoxical that the new Rule refers to the “pressing need to increase the clinical discretion” permitted to methadone prescribers (p. 39820).

Cost

Finally, the question of cost — which, while important, is the least consequential of all the criticisms that can be levelled at the new Rule. The Federal Register predicts that the cost of enforcing methadone regulations would rise more than 100% — from the current $3.9 million per year to $8.3 million (these figures apply only to the Department of Health and Human Services regulations; the costs associated with DEA and State oversight are separate). Of the latter amount, $2.6 million is projected to be the cost of “coming into compliance and assuring an acceptable level of quality” (p. 39828). Since there are approximately 900 approved programmes, this amounts to less than $3,000 per programme — hardly justification for anticipating a significant impact on quality of care!

Alternatives

For the problem of inadequate dosage and pressuring patients to detoxify, there appears to be a simple remedy. For over 25 years every methadone patient in the United States has been required to sign a consent form, for which the precise wording was specified by the Federal government. A new Federal mandate should be promulgated, requiring that every patient for whom a maintenance dosage of 60 mg per day or less is contemplated, or for whom detoxification is considered, must provide informed consent documenting that the physician has explained the significant risk of recidivism and death known to be associated with the recommended regimen. The consent form also should advise patients that if they perceive duress in the presentation of these treatment plans, they are encouraged to contact SAMHSA (which should develop a toll-free number for this purpose). Inevitably, some cynics might worry that even access to a federal ombudsman will not prevent therapeutic abuses. Accordingly, it might be worth considering, in addition, giving patients the number of the local bar association for referral to attorneys qualified in medical malpractice. Either way, in an exceedingly complex field, with so many problems for which there are no easy solutions, this would
appear to be an exception!

Sadly, there is no such readily apparent means of assuring that methadone treatment is available promptly to all who need it. SAMHSA must assess every option that could be implemented easily and quickly, but one suggestion is simply to allow all licensed physicians, in private offices or in institutional medical facilities, to prescribe methadone to those who need it. Before dismissing this idea as frivolous, it should be noted that private practitioners, in conjunction with community-based pharmacies, are the primary source of methadone treatment in many places of the world, including Germany, France, Australia and Ireland. In this hemisphere, British Columbia has authorized approximately 500 general practitioners to prescribe methadone in their offices. In considering this or any other approach, the governmental agencies that are charged with serving the public must ask themselves one fundamental question: Is this alternative likely to be more or less harmful than continuing to condemn heroin addicts, including those who desperately want help, to persistent heroin use, with all the associated risks to themselves and to the community? If this simple and objective assessment of advantages and disadvantages guides the course that government will pursue, there is no doubt that the public — addicts and non-addicts alike — will be well served!

References


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Heroin Addiction and Related Clinical Problems
Articulation of codeine treatment and methadone maintenance programs

Lubomir Okruhlica, D Klempova, K Timulakova

Summary
The Centre for Treatment of Drug Dependencies in Bratislava is implementing a complex integrative model which provides fourteen different programme options for its clients. This paper studies the relationship and interaction between the treatment process in two maintenance programmes: 1) with codeine phosphate (n=74), and 2) with methadone hydrochloride (n=132). There were no differences in the gender composition or working status of the groups, but a significant difference was found in age composition; differences in retention rates and dosages were focused on, too. Codeine substitution had been introduced into our practice prior to the availability of methadone maintenance. It has still not been eliminated, largely due to the fact that it is requested by the patients, but also because of some other aspects considered by the therapist in managing the treatment process. The different characteristics of these two programmes, their possible determinants, as well as practical considerations and the advantages of keeping the two programmes running side by side on a noncompetitive basis are discussed.

Key words: Codeine Maintenance - Methadone Maintenance

Introduction
The Centre for Treatment of Drug Dependencies in Bratislava is implementing a complex integrative model, which provides fourteen different programme options for its clients. Table 1 shows the main programmes designed for illicit drug users, especially users of heroin. At present the system accommodates approximately 600 clients/patients on a weekly basis. There are also about 300 other clients with alcohol-related problems who are treated at our centre.

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Heroin Addiction and Related Clinical Problems

The variety of different programme options within the same system not only allows the therapist to find an option matching the needs of the client, but provides a better range of choice for each patient. The system combines outpatient programmes with the inpatient ones, low-threshold with high-threshold programmes, drug-free with maintenance programmes. This system makes it possible to answer client’s needs as well as their “wants”, and is flexible enough to keep most of them away from the drug scene.

Methods

Aim

The aim of this study has been to describe the role, and compare selected characteristics of two programmes, which use stable doses of the opioids and are run side by side at the Centre for Treatment of Drug Dependencies in Bratislava: 1) the Codeine Maintenance Programme (CMP), and 2) the Methadone Maintenance Treatment Programme (MMTP).

Description of Programmes

An outpatient detoxification programme with so-called minor opiates, such as Ethylmorphine and Codeine phosphate is the first option for those who request treatment for the opiate dependency syndrome. It is a comprehensive programme with individual counselling, didactotherapy and motivational psychotherapeutic group sessions. It varies from fourteen days to six or even more weeks in its duration. A gradual decrease in the dose of prescribed opiates is the routinely applied treatment strategy. There are four possible options (apart from dropout), which can be chosen after the phase of detoxification treatment:

1. outpatient drug-free
2. inpatient detoxification
3. **maintenance programme**
4. dropout.

It is up to the therapist to advise the patient, but it is up to the patient to choose.

In the case of unsuccessful outpatient detoxification and if the patient has decided for further outpatient pharmacological treatment with an opiate, a **maintenance treatment approach** is provided. As there is a waiting list for the **methadone maintenance treatment programme**, which may last from three weeks to two months or occasionally even longer, the option of the **substitution programme** with Codeine phosphate is given to those who would prefer to be on the MMTP.

The **codeine maintenance programme** may immediately follow an unsuccessfully completed outpatient detoxification programme with the same medication for some of its patients. In principle, **Codeine (Codeine dihydrogenophosphat hemihydricus)** is prescribed in tablets (30 mg each) for a usage which is recommended to be split up into three doses, to be taken every eight hours. This is a variation on the four doses to be taken every six hours during the period of detoxification. The same daily doses of Codeine are generally prescribed until:

1. entry into the **methadone maintenance programme**
2. the resumption of outpatient detoxification, this time very gradually
3. entry into the inpatient detoxification programme, or
4. dropout.

The codeine phosphate programme with stable daily doses was basically designed as an alternative to the outpatient detoxification programme with MMTP during the waiting period for the latter. A patient is still allowed a free choice among the other possibilities which may be chosen in the mean time. A decision in favour of the continuation of the treatment process can be voluntarily made by the individual at any moment. The programme is also comprehensive, with individual and group therapy sessions, which include motivational and supporting techniques. We refer to it as a “cross-road” programme.

The **methadone maintenance treatment programme** is a long-term open-ended treatment, with no upper dose limit, and a maximum of one three-day take-home per week. Extensive urine analysis is applied; a behavioural and comprehensive treatment approach is implemented in this programme. Emphasis is put on the clean urine samples, and on social reintegration, such as that involving work and family. MMTP is free of charge. The inclusion criteria are as follow: 1) opiate dependency syndrome, 2) age above 18 years, 3) two medically documented unsuccessful attempts at detoxification, the patient’s voluntary decision. The exclusion criteria are 1) any form of violence, 2) noncompliance — repeatedly missing the doses, 3) urine samples repeatedly positive for morphine.

**Sample**

This descriptive, cross-sectional analysis was carried out with groups of 74 patients in CMP and 132 patients in MMTP at the end of November 1999.
Gender composition. There were 80% of males and 20% of females in the codeine group vs. 83% of males and 17% of females in the methadone group.

Age. The average age in the codeine group was 23 (SD=4) vs. 26 years (SD=6) in the methadone group.

Unemployment. Forty-nine patients in the codeine group were unemployed (53%), and sixty-six in the methadone group (50%).

Statistical Analysis

We have compared the basic characteristics, doses of active substances and duration of the stay of patients in both programmes: the codeine and the methadone maintenance programme. The variables were compared by chi-square test and t-test using SPSS win software.

Results

The differences in the gender composition of these groups were not statistically significant.

Age differences were statistically significant (p<0.01). The age range was 17-38 years in the codeine group vs. 18-46 years in the methadone group.

Doses. An average dose of codeine was 420 mg (SD=150 mg) in the range: 0-900 (mg). An average dose of methadone was 106 (SD=53 mg) in the range: 10-250 (mg).

Duration of the maintenance treatment (Graph 1). The average duration of treatment in the codeine maintenance group was 13 (SD=21) weeks vs. 61 (SD=32) weeks in the MMTP group. It ranged from 0 to 114 (weeks) in the CMP group and from 2 to 108 (weeks) in the MMTP group. This difference was statistically significant (p < 0.001). The median was 6 in the codeine and 68 in the methadone group, with a mode of 4 and 60 weeks, respectively.

Discussion

Several German studies have shown good results with codeine substitution treatment for patients with an opiate dependency syndrome [1-11]. As was also the case several years earlier in Germany, there was no methadone available for treatment purposes in the Slovak Republic at the beginning of the heroin epidemic in the mid-nineties. Both codeine and ethylmorphine were used for detoxification and, more gradually, for the maintenance treatment of clients, who were unable to achieve a drug-free condition. The latter situation has become increasingly common, as the number of chronic users has increased and the capacity of the newly implemented methadone maintenance treatment programme was limited by a long waiting list. During our study the time spent on the waiting list for MMTP was about three months in Bratislava. Waiting list times were shorter for those who decided to enter an inpatient detoxification programme, which can last up to one month. The patients who decided to switch from an unsuccessful period in the opiate outpatient detoxification programme into either the inpatient detoxification programme or the methadone maintenance treatment programme had to wait several weeks for entry. This period is bridged by their maintenance in CMP on
Graph 1. The number of patients and length of their stay in codeine/methadone maintenance treatment programs

stable doses. The demographic characteristics of our study groups showed that patients in the codeine programme were significantly younger, they had a significantly shorter duration of stay in the programme, and there was a lower proportion of those who were

Graph 2. Self-reported heroin use in methadone and codeine group
employed. In our system for the integrated care of people with heroin dependency, this programme does not have the same status as the methadone maintenance programme. It is only a temporary solution, which is why it is called crossroads programme. Our results confirmed our expectations. Despite this special status assigned to the CMP, our results show that it was a long-term solution for a limited number of patients. However, only one third of all these patients stayed in the programme for over three months, compared with 84% of the patients in the MMTP. Our approach has changed since we have had a higher availability of MMTP; in addition, our self-reporting questionnaire (same as in 6) had demonstrated a much more frequent usage of heroin among patients in the codeine programme vs. those in the MMTP (Graph 2 and 3). We are stricter now about limiting the time spent in the CMP. All patients must enrol on a waiting list for MMTP or inpatient detoxification. Detoxification is ordered for those who do not comply with these instructions.

Despite the preference for methadone maintenance treatment therapy, there still remains at least a limited role for codeine maintenance, especially there where it is necessary to fill the therapeutic gap between an unsuccessful attempt at detoxification and further long-term treatment options.

References


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Heroin Addiction and Related Clinical Problems
The differences between inpatients and outpatients with illegal drug use: Prevalence of comorbid mental disorders

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Summary
The aim of the survey was to compare clinical and sociodemographic differences between patients with substance abuse or dependence and mental illness who, over a three-month period, sought psychiatric help in a hospital (UPH) or a methadone clinic (CPTIDD).

On average, patients were 26 years old, with almost 7 years of drug dependence. The most frequent diagnoses among CPTIDD patients were depression and anxiety disorders, and, among UPH patients, schizophrenia and bipolar affective disorders. In UPH patients dependence on, or abuse of, heroin were equally common, while all CPTIDD patients were dependent on heroin and other illegal drugs.

Key words: SAMI patients - Psychiatric comorbidity - Inpatients Vs Outpatients comparison

Introduction
Drug abuse or dependence and psychiatric comorbidity have recently generated extensive research and clinical interests. There are several combinations of mental disorders and substance dependence [6]. Clients sometimes seek help over substance abuse or dependence, and sometimes over a mental disorder, and the comorbid condition might go unrecognised, especially when there is no close collaboration between mental health services and services for illegal drug treatment programmes [3].

The increasing incidence and prevalence of comorbidity, unfavourable outcome and special needs call for a modified approach [5].

In Slovenia there has been an enormous increase in the use of illegal drugs over the last 10 years. Drugs have become cheaper and more accessible, and the market...
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offers a variety of drugs and drug mixtures. It has recently become clear that younger patients with mental disorders abuse illegal drugs and alcohol. In our country this is the first survey that has been made with the aim of pointing out the problems of sub-populations of patients with drug-related problems and comorbid mental illness, who need special attention and a specific approach.

The survey was drawn up to verify the interplay of mental disorders in addictive behaviour, and to find out the clinical and sociodemographic differences between comorbid patients (substance abuse and mental illness (SAMI)) who had sought help in two different settings (psychiatric hospital or outpatient methadone clinic) within a three-month period.

Subjects and methods

All SAMI inpatients from University Psychiatric Hospital (UPH) in Ljubljana and SAMI outpatients from the Centre for Prevention and Treatment of Illegal Drug Dependence, Koper, Slovenia (CPTIDD) who sought psychiatric help within a three-month period (November 1st 1999 - January 30th 2000) were included.

Characteristics of heroin and other substance abuse and dependence were investigated with the Rating Scale for Drug Addiction (RSDA) [7]. RSDA was translated into the Slovenian language. RSDA is a complex instrument and covers the following areas: physical condition, mental state, socio-environmental conditions, substance abuse and substance abuse clinical status.

Diagnoses were made according to ICD-10 criteria [12].

T tests and chi-square tests were used.

Results

In the observational period 23 (15 males, females) outpatients from (CPTIDD) and 18 (1 males, 8 females) patients who were admitted to UPH were identified as SAMI patients.

The diagnoses were deferred in both groups. In UPH most patients — 13 — had schizophrenia, 3 had bipolar disorder and 2 acute and transient psychoses. In UPH 9 patients were addicted, and 9 abused heroin. In CPTIDD most patients — 17 — had a depressive episode, 5 an anxiety disorder and one psychosis. All patients from CPTIDD were addicted to heroin. None were HIV-positive or had AIDS.

Tables 1 and 2 summarize patients’ sociodemographic and clinical characteristics.

Discussion

In our survey in two different settings, a large number of SAMI patients was identified. Like other studies [8], our survey supports the view that psychiatric treatment-seeking individuals represent the heterogeneous population.

A majority of those seeking help at UPH received a diagnosis of serious mental illness — principally schizophrenia, secondarily bipolar disorder. In the case of CPTIDD
patients, a clear majority had a depressive episode, and several others an anxiety disorder. We found sharp differences in diagnostic structure, but those differences were not significant when age, age at first use and age of continuous drug use were compared.

Only two SAMI inpatients had a prescription of methadone before being admitted to UPH. They underwent detoxification and received psychopharmacotherapy for their mental illness, while they had supportive psychotherapy and counselling for their substance use disorders.

SAMI patients are a new problem at UPH, where there are still no integrated treatment programmes. The application of integrated mental health and substance use treatment has given promising results [1], and, despite the scepticism of mental health professionals, we must expect an increasing need for those programmes in our country in the near future. In psychosocial treatment approaches for schizophrenia and other severe mental illnesses, several different interventions have been indicated, including assertive integrated mental health and substance misuse treatment for “dually diagnosed” patients [9]. Comorbidity has been mentioned for the first time in the new Slovenian National Guidelines for the treatment of schizophrenia.

Half of the SAMI patients from the group who sought help at UPH were addicted to heroin and abused many other substances as well. The other half abused heroin, probably due to self-medication. We can say that those patients are in danger; in future all of them may develop addiction, or have a serious mental illness with delusions, hallucinations, mood symptoms and sleeping problems. Most of them have had legal problems and they show aggressive behaviour. Legal problems in SAMI patients are not always the result of criminal activity. In many cases disorganised and violent behaviour gives rise to legal problems [2].

In CPTIDD all the patients were addicted to heroin and abused other psychotropic substances as well. All those patients were given a prescription for methadone and addi-
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Psychotropic medication was used in order to tailor treatment to their special needs [11].

Physical problems were similarly distributed in both groups. Alcohol, cannabinoids, LSD, and cocaine use were more frequent in CPTIDD patients. Patients with affective disorders in one study more frequently abused alcohol, stimulants, and cocaine than did those with schizophrenia [4].

Due to sharp differences in diagnostic structure and the small size of the sample, some statistical analyses were possible. Patients in UPH sought help or were admitted to hospital after a shorter period of dependence. Severity of psychotic illness acted as a protective factor.

Table 2. Sociodemographic and clinical characteristics of UPH and CPTIDD group of patients

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<td>Organic disease</td>
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<td>Memory</td>
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Conclusions

In our survey we identified a large number of SAMI patients seeking psychiatric help in hospital and in methadone outpatients’ program. On average, those patients were 26 years old, with almost 7 years of drug dependence or abuse, with serious consequences in terms of mental illness and drug-related behaviour. In the near future we can expect increasing numbers of SAMI patients. In every setting, therefore, patients must be carefully diagnosed, and the abuse of substances must be managed to prevent developing addiction or, at least, when addiction is already present, diminish the impact of its consequences [10].
References


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INFORMATION FOR CONTRIBUTORS

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