Heroin Addiction and Related Clinical Problems

the official journal of

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 vision
EUROPAD exists to improve the lives of opiate misusers and their families and to reduce the impact of illicit drug use on society as a whole. The Association works to develop opiate addiction treatment in Europe but also aims to make a major contribution to the knowledge of, and attitudes to, addiction treatment worldwide.

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Say “Yes” to Methadone and Buprenorphine in Russian Federation

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Summary

The medical community has determined that narcotic addiction is a chronic and relapsing medical disorder, which is effectively treated with medications. The success rate of patients, who are treated with medications, such as methadone and buprenorphine, when combined with other needed treatment services, improves the health of the patient. Methadone and buprenorphine are the most exhaustively studied medications for the treatment of any disease. More than 40 years of research and clinical practice have repeatedly demonstrated its efficacy in millions of patients throughout the world. An objective observer might argue that it is irresponsible not to use such medications to treat narcotic addiction in an age of HIV infection, hepatitis-C and other developing co-morbidities.

Key Words: Methadone treatment - Buprenorphine treatment - Medically Assisted Rehabilitation - Heroin Addiction

Introduction

Opiate addiction is a devastating problem with enormous costs to individuals, families and society. There have been numerous discussions over the past several decades trying to determine whether addiction is a medical disorder or a moral problem. A recent publication by the United States Department of Health and Human Services-Substance Abuse and Mental Health Services Administration (SAMHSA), “Medication Assisted Treatment for Opiate Addiction in Opioid Treatment Programs,” (2005) underscored the fact that: “Studies have supported the view that opioid addiction is a medical disorder...”

This paper is a comeback to the publication in Russian Federation of a paper titled “Say No to Methadone in Russia (see appendix A). For further informations, please, contact AATOD\EUROPAD e-mail <Mark.Parrino@aatod.org><aucns@libero.it>
that can be treated effectively with medications administered under conditions consistent with their pharmacological efficacy, when treatment includes comprehensive services, such as psychosocial counseling, treatment for co-occurring disorders, medical services, vocational rehabilitation services, and case management services.”

Dr. Vincent Dole, the co-developer of methadone maintenance treatment, described the medical basis of methadone maintenance treatment in a journal article, “Implications of methadone maintenance treatment for theories of narcotic addiction.”

The treatment is corrective, normalizing neurological and endocrinologic processes in patients whose endogenous ligand-receptor function has been deranged by long-term use of powerful narcotic drugs. Why some persons who are exposed to narcotics are more susceptible than others to this derangement and whether long-term addicts can recover normal function without maintenance therapy are questions for the future. At present, the most that can be said is that there seems to be a specific neurological basis for the compulsive use of heroin by addicts and that methadone taken in optimal doses can correct the disorder.”

**Methadone: Pharmacology and Mechanisms of Action**

Methadone is among the most thoroughly studied drugs in modern medicine. Methadone has been extensively used for more than four decades in treating millions of people in more than 30 countries throughout the world. These counties include Australia, Italy, Ireland, United Kingdom, Netherlands, France, Spain, Sweden, Norway, New Zealand, China, Switzerland, Poland, Croatia, Bosnia Herzegovina, Slovenia, Slovak Republic, Bulgaria, Greece, Mexico, Canada, Finland, Belgium, Germany, Bermuda, United States, Czech Republic, Israel and Thailand to cite a few. Researchers determined in 1964 that continuous and daily maintenance doses of oral methadone allowed opiate-addicted patients to function more normally in recovery, which was described in a U.S. publication about methadone associated mortality in February, 2004 (DHHS Publication No. (SMA) 04-3904)

Methadone is safely stored in the liver and, secondarily, in other body tissues. It has also been established that methadone has a half-life averaging from 24-36 hours at a steady state. Through many years of clinical trials and extensive experience throughout the world, methadone has been shown to have a favorable safety profile, when used as indicated. The U.S. Report of February, 2004 (Methadone Associated Mortality: Report of a National Assessment) also indicated that: “Few serious adverse reactions and no cumulative organ damage have been associated with daily administration of appropriate doses over more than 20 years in some patients. Mortality from all causes is many-fold lower in methadone-treated patients than in untreated opioid addicts. Studies consistently have shown that the risk of communicable diseases (such as HIV and hepatitis-C) is significantly reduced by participation in methadone maintenance therapy”

Buprenorphine, which has been used more recently in treating chronic opiate addiction, has also been found to be extremely effective in producing similar
rates of treatment retention and abstinence from illicit opioids as compared to equally therapeutic doses of methadone. It has also been determined that the long-term use of methadone and buprenorphine therapy is associated with few side-effects. The medical community has recognized that opiate addiction is a chronic medical disorder that can be treated effectively with a combination of medication assisted treatment and psychosocial services.

The Use of Scientifically Proven Medications to Treat Chronic Narcotic Addiction

The conceptualization of methadone treatment by addiction treatment pioneers was also based on a pharmacological premise: finding a candidate drug which had an affinity with the abused substance, but which was radically different. In such a way, the medication would interact with the neuroreceptors without narcotizing the brain.

In an article written in 1993 by one of the authors (Mark W. Parrino) the early rationale for methadone maintenance treatment was summarized. “Drs. Vincent Dole, Marie Nyswander and Mary Jeanne Kreek pioneered the use of methadone maintenance against the backdrop of rampant heroin addiction and the social turbulence of the 1960s. It was a time of increasing heroin addiction, resulting in the spread of contagious serum hepatitis and increasing overdoses in emergency rooms. An effective pharmacologic intervention had to meet stringent conditions to successfully treat narcotic addiction, as underscored by Dole, Nyswander and Kreek. ‘It must eliminate the euphoric appeal of heroin and the abstinence symptoms that draw addicts back to drug use; it must be sufficiently free from toxic dysphoric effects that patients will continue with treatment; it must be orally effective, long-acting, medically safe, and compatible with normal performance at work and at school with responsible behaviour in society.’” (19).

The original idea was to increase the level of tolerance to a medication so that heroin addicts would be unable to experience the euphoric and sedative effects of illicit heroin any longer. Later on, it was evident that, beyond blockade, high tolerance levels also meant high levels of an anti-craving action: addicts were held back from taking heroin also because they were able to choose whether to use heroin or not (12-17, 19). Eventually, they found themselves breaking the addiction cycle and realizing a newfound freedom of choice.

Pilot programs first confirmed such a hypothesis and paved the way for other and larger programs to start. Through time, it was also clear that methadone (or other agonists) were not primarily effective as detoxification instruments, but as means of providing continued maintenance treatment (20). Studies repeatedly found that patient retention in maintenance treatment was, in itself, a successful outcome, allowing the patient to stabilize both medically and in terms of improved social functioning.

The anti-craving principle was later extended to other forms of addiction, and proved useful (10, 34, 41, 44, 68).

Most untreated opiate addicts, as long as they were able to survive, typically switched
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over to alcohol, prescribed drugs, anxiolytics, cocaine or other substances. This was a means of replacing one drug for another, sometimes with dire consequences to health. Physicians have at times made errors in judgment when prescribing addictive drugs to drive addicts away from their original substance, as it was for the cocaine case (42, 43, 49).

Methadone and buprenorphine are not substitute drugs, but depending on what country you are in and what science you are referencing, methadone and buprenorphine are viewed as replacement pharmacotherapies, although the term replacement has fallen out of scientific acceptance (see Table 1) in favour of using the terms medication-assisted treatment. The effectiveness in treating opiate withdrawal has little to do, on clinical grounds, with the reason they are employed in the treatment of drug addiction. In fact, they are employed as maintenance regimes, which itself indicates how their effectiveness cannot be linked to their narcotic action. Any narcotic action is lost through time, as for heroin itself. Otherwise, drug-seeking behaviour does not extinguish, but is reinforced and sustained in an endless pattern. No craving towards methadone is present in abstinent drug addicts under treatment at therapeutic dosage levels.

The most likely phenomenon for heroin addicts in long-term treatment with low dose methadone is not the request to increase their methadone dosages, but the attempt to lower it in order to use and feel the effects of illicit heroin. Higher methadone doses are also therapeutically driven, responding to individual patient needs.

The most recent publication concerning Medication-Assisted Treatment for Opioid Addiction (1) discusses the issue of appropriate maintenance doses in considerable detail. “Strong evidence supports the use of daily methadone doses in the range of 80mg or more for most patients (61), but considerable variability exists in patient responses. Some do well on dosages below 80-120mg per day and others require significantly higher dosages (36). Buprenorphine dosage should be determined in a manner similar to that used for methadone. The recommended dosage of buprenorphine to begin stabilization is 12-16mg per day for most patients, with increases provided thereafter as applicable (28-32). As reviewed by Johnson and colleagues, if patients continue to show evidence of opioid abuse or withdrawal, the dosage should be increased, using the same types of guidelines as for methadone.”

The word “opiates” indicates a pharmacological class of substances, mainly sharing the acute effects in non-narcotic-tolerant individuals, and the same receptor sites of action. Nevertheless, opiates can be radically different in a repeated administration model: some display strong abuse liability and addictive properties, some others do not. Methadone belongs to the second type (18, 34).

Methadone was successfully employed in the treatment of heroin addiction due to its radical dissimilarities with heroin, although receptor sites were the same.

In the field of psychiatry, we often face the issue of treating anxiety disorders. It is rather common to handle the changing of incorrectly prescribed medications with therapeutic ones: anxious subjects are mostly prescribed benzodiazepines as first-line treatments, and we systematically replace them for other medications (e.g. SSRIs,
### Table 1. Comparison chart of heroin dependence and agonist therapies

<table>
<thead>
<tr>
<th>Topic</th>
<th>Heroin</th>
<th>Methadone</th>
<th>Buprenorphine$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset of action</strong></td>
<td>A few seconds</td>
<td>30 minutes</td>
<td>30 to 40 minutes</td>
</tr>
<tr>
<td><strong>Duration of action</strong></td>
<td>4 to 6 hours</td>
<td>24 to 36 hours</td>
<td>About 24-48 hours</td>
</tr>
<tr>
<td><strong>Route of administration</strong></td>
<td>Injection, snorting,</td>
<td>Oral</td>
<td>Sublingual</td>
</tr>
<tr>
<td></td>
<td>smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Frequency of administration</strong></td>
<td>Several times a day</td>
<td>Daily$^2$ or more</td>
<td>Every day or every</td>
</tr>
<tr>
<td></td>
<td>as needed</td>
<td>frequently as</td>
<td>other day</td>
</tr>
<tr>
<td><strong>Effective dose</strong></td>
<td>Ever increasing</td>
<td>Blocking dose$^3$,</td>
<td>2 to 32 mg$^4$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>usually 80 to</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td></td>
</tr>
<tr>
<td><strong>Tolerance</strong></td>
<td>Increasing tolerance</td>
<td>Tolerance is</td>
<td>Tolerance is</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stable</td>
<td>stable</td>
</tr>
<tr>
<td><strong>Euphoric effects</strong></td>
<td>Euphoria for up 2 hours</td>
<td>No euphoria when</td>
<td>No euphoria when</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stabilized</td>
<td>stabilized</td>
</tr>
<tr>
<td><strong>Overdose potential</strong></td>
<td>High$^5$ and increased</td>
<td>Rare$^6$, potential if mixed with other depressants</td>
<td>Very rare$^5, 6$</td>
</tr>
<tr>
<td><strong>Overall safety</strong></td>
<td>Potentially lethal</td>
<td>Very safe$^7$ – Possibly associated with rare cardiac irregularities – Treatment choice in pregnancy</td>
<td>Overall good profile – Suboxone injection will cause serious withdrawal symptoms in dependent persons – not recommended for use in pregnancy or breast feeding – Caution with liver disease – Currently under study</td>
</tr>
<tr>
<td><strong>Withdrawal</strong></td>
<td>Within 3 to 4 hours</td>
<td>Within 24 to 36</td>
<td>Within 36 to 48</td>
</tr>
<tr>
<td></td>
<td>after last dose</td>
<td>hours after last</td>
<td>hours after last</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dose</td>
<td>dose</td>
</tr>
<tr>
<td><strong>Craving</strong></td>
<td>Recurring cravings</td>
<td>Eliminated with</td>
<td>Craving may not be totally eliminated due to ceiling effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>adequate dose</td>
<td></td>
</tr>
<tr>
<td><strong>Pregnancy and nursing</strong></td>
<td>Heroin dependence poses</td>
<td>Safe during</td>
<td>Not indicated, however study underway</td>
</tr>
<tr>
<td></td>
<td>grave risks for mother</td>
<td>pregnancy$^8$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and fetus</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Experience of pain and emotions</strong></td>
<td>Blunted</td>
<td>Normal pain and full range of emotions</td>
<td>Normal pain, but opioid analgesics may not be effective. May need to switch to methadone. Full range of emotions</td>
</tr>
<tr>
<td><strong>Mood</strong></td>
<td>Constant mood swings</td>
<td>Normal$^9$</td>
<td>Normal$^7$</td>
</tr>
</tbody>
</table>

$^1$ Buprenorphine is a partial agonist at the opioid receptors.

$^2$ Buprenorphine can be administered as a long-acting injectable.

$^3$ Methadone can be administered as a long-acting injectable.

$^4$ Buprenorphine is available in a subcutaneous formulation.

$^5$ Methadone is available in a subcutaneous formulation.

$^6$ Buprenorphine is available in a buccal formulation.

$^7$ Methadone is available in a buccal formulation.

$^8$ Buprenorphine is available in a subcutaneous formulation.

$^9$ Methadone is available in a subcutaneous formulation.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Heroin</th>
<th>Methadone</th>
<th>Buprenorphine¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical reaction time and intellectual functioning</strong></td>
<td>Impaired</td>
<td>Reaction time normal. Intellectual functioning unimpaired on stable dose¹⁰</td>
<td>Reaction time presumed to be normal like methadone. FDA cautions driving and operating heavy machinery in the beginning of treatment</td>
</tr>
<tr>
<td><strong>HIV &amp; hepatitis C transmission</strong></td>
<td>High rate with needle use and unprotected sex</td>
<td>Reduced/eliminated¹¹</td>
<td>Reduced/eliminated¹¹</td>
</tr>
<tr>
<td><strong>Immune system for HIV positive persons</strong></td>
<td>Rapid progression to AIDS</td>
<td>Progression slowed with methadone¹¹</td>
<td>Progression presumed same as methadone. Data not available for buprenorphine</td>
</tr>
<tr>
<td><strong>Immune/ endocrine system functioning</strong></td>
<td>Impaired</td>
<td>Normalized during treatment¹²</td>
<td>Presumed normalized during treatment. Data not available</td>
</tr>
<tr>
<td><strong>Stress response</strong></td>
<td>Suppressed</td>
<td>Normalized during treatment</td>
<td>Normalized during treatment</td>
</tr>
<tr>
<td><strong>Criminal activity</strong></td>
<td>High level</td>
<td>Reduced/eliminated</td>
<td>Reduced/eliminated</td>
</tr>
<tr>
<td><strong>Personal relationships</strong></td>
<td>Disrupted</td>
<td>Potential for restoration, improvement with counselling</td>
<td>Potential for restoration, improvement with counselling</td>
</tr>
<tr>
<td><strong>Employment</strong></td>
<td>Deteriorating performance, loss of employment</td>
<td>Full functioning</td>
<td>Full functioning¹³</td>
</tr>
<tr>
<td><strong>Community impact</strong></td>
<td>Destructive impact, high crime, high death rate, transmission of diseases</td>
<td>Contributes to public safety, low mortality, increased health</td>
<td>Contributes to public safety, low mortality, increased health</td>
</tr>
</tbody>
</table>

1. Two forms of buprenorphine: Subutex® (pure buprenorphine) used for withdrawal and at treatment induction and Suboxone® (buprenorphine with naloxone) used after initial treatment phase for longer-term maintenance to address addiction. Suboxone® is recommended for all prescription and all out-of-clinic doses.
2. Rapid metabolizers and pregnant women may require dosing twice per day.
3. The dose at which heroin is ineffective and overdose potential practically eliminated.
4. The highest doses are equivalent to about 50 mg of methadone. A ceiling or limit exists for buprenorphine’s therapeutic effects.
5. Overdose potential is increased if mixed with other depressant drugs such as alcohol or benzodiazepines (anti-anxiety medications).
6. Overdose is rare with opioid-tolerant individuals in opioid treatment.
7. No serious side effects have been found in opioid-tolerant patients who have been in treatment for over 20 years. Long-term studies show no liver toxicity. Patients with hepatitis C and AIDS can be treated safely with methadone although changes in dose may be necessary.
8. Neonate who shows signs of withdrawal can be treated successfully with paregoric or tincture of opium. HIV-positive/AIDS mothers should not nurse. Mothers with hepatitis C can nurse with caution.
9. Mood remains normal if no other psychiatric or emotional conditions exist.
10. Methadone patients over the last 30 years have worked in all types of jobs and professions, including work with complicated machinery and computers, and professional work requiring advanced degrees.
11. In conjunction with proper education/counselling, these medications stop the use of heroin, but not injection of other drugs nor unsafe sexual practices.
12. Appears to improve immune response when compared to heroin.
13. FDA label warning cautions against heavy machinery use or driving during initial phase of treatment.

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Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Treatment
www.samhsa.gov

The use of new medications is employed to achieve the best therapeutic results. Prescribing a scientifically proven and effective medication to treat a chronic disease cannot be considered a problem by the medical community. Maintenance on methadone is not due to the patients insisting on continuing their methadone dosages but is based on a long-term therapeutic strategy to control a chronic and relapsing disorder. Through time, addicts seem to be able to maintain their balance despite methadone dose reduction, which suggests a neurological stabilization in the long-term. Dropouts from methadone programs, who discontinued methadone against medical advice, have been found to relapse to previous heroin addiction 80% of the time (3).

**Utilising heroin as a Public Policy Initiative**

Controlled heroin administration is a surrogate and has been used with mixed results to reduce drug-related crime in high-density areas. Heroin “maintenance” is not treatment. It is not possible for the brain to be “maintained” on heroin due to the destabilizing effects of the short-term narcotic. Heroin “maintenance” appears to be intended to reduce drug-related crime. The original concept was to engage the hardcore narcotic addicts, who were not interested in participating in methadone maintenance programs, with the intent to improve the likelihood that they would seek such care at
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some future point. Heroin treated addicts do not resemble methadone treated patients at all. On the other hand, they are still chronically intoxicated and dysfunctional (5, 6, 8, 11, 21-23, 25, 33, 35, 37-40, 45-47, 51-54, 58, 60).

Diversion of Methadone

In Europe, diversion of methadone from take-home programs to the street is the main channel of the methadone black market. Interestingly, no methadone drug smuggling has occurred; and no primary demand for methadone has developed on the black market. In other words, if methadone is used outside of treatment setting, users are heroin addicts electively and resort to the use of methadone as a second choice. When heroin is available, addicts will crave it, showing no interest in the use of methadone. On the contrary, addicts tend to ask for low-doses in order to avoid narcotic blockade.

In our opinion, methadone diversion in Italy is mostly due to the lack of availability of methadone treatment and the spontaneous tendency of addicts to resort to anti-withdrawal drugs in the absence of heroin. Certainly scientific studies should support this claim. The situation is different in the United States. In effect, 280,000 Americans are gaining access to methadone as an analgesic on an annual basis, not an anti-narcotics medication in the methadone treatment setting. At the time of this writing, approximately 240,000 patients are enrolled in methadone treatment programmes in the United States. We have information, indicating that many non-narcotic tolerant individuals appear to be abusing methadone, having nothing to do with the methadone treatment programmes, and dying as a result. The previously cited publication, “Methadone Associated Mortality: Report of a National Assessment,” published by the United States Department of Health and Human Services, indicated the following. “The data confirmed a correlation between increased methadone distribution through pharmacy channels and the rise in methadone-associated mortality. This supports the hypothesis that the growing use of oral methadone prescribed and dispensed for the outpatient management of chronic pain, explains the dramatic increases in methadone consumption and the growing availability of the drug for diversion for abuse.”

A fair amount of methadone gets onto the black market through pain management entities and some methadone treatment programs as well (4, 7, 9, 26, 56, 57).

The fact that the majority of methadone-associated mortalities are not related to the experiences of patients being treated with methadone in the drug treatment setting underscores the value of a regulated system of care.

Multiple Drug Abuse

Some addicts may resort to methadone and use it with other substances. Obviously, the risk does not come from the mixture of methadone and street narcotics, since methadone will blockade them. Otherwise, the combination of methadone and alcohol or benzodiazepines is dangerous and often favoured by the trend to prescribe
benzodiazepines for narcotic detoxification.

Methadone related deaths are mostly due to the lack of narcotic tolerance (untreated individuals or recently detoxified) and the mixture with synergistic compounds (lower dose treated individuals or incautious polydrug treatments) \(^{(2, 27, 50, 55, 56, 59, 64-67)}\).

Addiction is a drug-induced disease. Therefore, addiction treatment, in responding to a long-term and chronic narcotic-addicted person does not consist in cleansing the body from a drug. Addiction treatment aims at behavioural and neurological normalisation. Introducing a chemical medication in a person’s body is the most common method of treating a disease, so it is not surprising that a mental disorder may be treated through pharmacotherapy \(^{(48, 62, 63)}\). No exchange from one narcotic to another is to be made. Methadone treatment means to exchange disease for health.

To date, no short-term and drug-free regimen has proved as consistently effective for the treatment of the long-term and chronic narcotic addict. To be dependent on a maintenance treatment is just another way of saying that ill people owe their well-being to an ongoing treatment, which is available, safe and effective.

Some diseases can count on effective short-term approaches. Others can be controlled more or less brilliantly by maintenance treatments, such as diabetes or self-immune disorders. Some others can just benefit from palliative treatment. Narcotic addiction is best treated by maintenance regimens. Dependence on effective medications should be regarded as a guarantee for continued health and a therapeutic opportunity for people who are otherwise destined to die or worsen due to a chronic relapsing disease.

Addiction spreads because of the addictive property of certain substances. In large populations the risk is amplified by the availability of addictive substances and the lack of effective treatment programmes. Any country, which does not provide access to medication-assisted treatment combining methadone or buprenorphine with appropriate ancillary medical and psychosocial services, is destined to see the development of a major narcotic epidemic. Western and Eastern countries may support or be characterized by different lifestyles and cultural imperatives. However, the disease is the same regardless of geography.

The fear of using dangerous drugs is justified but does not apply to the safe and effective use of medications to treat narcotic addiction, including methadone and buprenorphine. The conceptual rejection of an exhaustively studied treatment does not make for an effective health policy. Eastern countries have the opportunity to avoid repeating the same mistakes, which were made by Western nations in treating chronic opiate addiction.

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Appendix A

MEMORANDUM

SAY NO TO METHADONE PROGRAMS IN RUSSIAN FEDERATION
(Use of methadone cannot be considered treatment)

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Foreign emissaries have been increasingly raised the issue of introducing substitute therapy in the form of methadone programs for treatment of patients with heroin drug addiction.

Substitution therapy has had more than a century long history, starting with attempts to treat morphine addiction with cocaine, a medicine then considered to have no side effects. In 1898, German scientist-researcher Desser synthesized new chemical substance – acetyl morphine chloride of heroin from morphine. Heroin prevailed over morphine in its analgesic effect and it began to be used to treat morphine addicts. It was soon discovered that heroin use led to addiction even more rapidly than morphine, and heroin, and other forms of substitution therapy, were abandoned.

Methadone was synthesized in Germany during World War II and was started to be used as a substitute treatment in patients with heroin addiction.

In January-March 1961 in New York, a new Single Convention on Narcotic Drugs was accepted. Experience of protocols and conventions used previously was analyzed, beginning from those adopted by the League of Nations. The convention stated that any non-medical drug use was unacceptable, as well as illegal drug circulation and the vicious system of “narcotic allowance”. The convention recommended restrictions of methadone for use as a medical treatment similar to heroin. However, defenders of methadone asserted that there was not enough experience of its use and that there were some data that methadone could be effective means against such dangerous type of addiction as heroin addiction and they did not support prohibition of methadone, but insisted on its inclusion in Schedule 1 of strict control.
8 years later a report of the Commission on Narcotic Drugs under the auspices of the World Health Organization was announced at the 23rd session of the United Nations. Based on the results of scientific research, the report emphasized the danger of substitution treatment and expressed doubts about the wisdom of changing one drug for another in addiction treatment. Though there was some negative attitude to giving methadone to patients with heroin addiction, many countries continued substitute methadone therapy use in treatment of patients with heroin addiction.

The UN Commission on Narcotic Drugs has repeatedly discussed question of methadone use. It was claimed that methadone use could not be regarded as treatment of heroin addiction, since this was just to change one drug for another. At the same time, proponents of methadone use emphasized that methadone was supposed to treat only the most severe forms of heroin addiction. The control for provision of methadone to drug addicts instead of heroin enables to normalize its intake, and then slowly decrease its dose until giving it up completely.

By the end of the 1970s of the last century, practical experience had demonstrated that use of methadone as substitution therapy for heroin addicts led to quick creation of a new group of addicts, now with methadone addiction.[The whole issue of calling methadone patients addicts is outrageous and completely uninformed].

The CND started getting data about severe complications of methadone use, based on long practical experience and multiple scientific researches. While symptoms of heroin withdrawal lasted from five to seven days in duration, methadone withdrawal continued for as long as forty. Characteristic features of methadone addiction, not observed in heroin addiction, included body mass increase, development of edema in arms and legs, cardiomyopathy, hepatitis, hepatic cirrhosis, changes in respiratory system with apnea, sleep problems, and nightmares [there is no scientific basis to these statements].

As noted by American scientists Kpeinbor and Baden, a serious problem, especially in young drug addicts who used methadone, was lethal comas provoked by occasional overdoses. During a conference held in Washington it was pointed out that the number of mortal cases due to methadone use exceeded the number of those due to heroin.

On the seminar in Helsinki, sponsored by the United Nations, several examples were given that in the first two weeks of methadone program in Lithuania, which was initiated by social movement “Drug addicts and their parents for methadone”, two drug addicts died due to methadone overdose.

On the 66th session of INCB Nations in May 1999, while discussing the Swiss “experiment” on giving drug substances to drug addicts, the INCB member from Germany O. Schreder said that in some German regions they started to be more careful with the Swiss “experiment”, because serious complications had often been noted and mortality due to methadone use had doubled. In the newspaper “Frankfurter Allgemeine Zeitung” of May 4, 1999 it was suggested to use methadone more carefully and increase control over its use, because 100 patients with drug addiction died due to methadone in Germany in 1997, and 240 in 1998.

It was repeatedly mentioned that most patients on methadone program systemically or
periodically used heroin. As the American scientist Dops observed, “methadone treatment exchanges one drug for another, but does not promote giving up drugs entirely.”

[The authors omit the need to stabilize a patient on a therapeutic and blockade dose of methadone. If that is achieved, heroin is either dramatically reduced or eliminated, which is based on scientifically replicable studies].

Doctor M. Cochman in the article “Problem of drug addiction in the Netherlands”, published by the Erasm University (Rotterdam, the Netherlands), contradicts the commonly held opinion among specialists and officials that the methadone programs in Netherlands have been successful. The author declares, “…methadone maintenance programs were introduced into practice without big success in 1972. The programs were based on the illusion that drug addicts would be motivated to pursue further treatment if they had contacts with specialist professionals. However, the population of drug addicts continued to grow, as did street crimes. That is why Dutch drug policy has changed, and since 1978 methadone was started to be used more as a method to decrease crime, rather than method of drug addiction treatment. This proved to be an illusion as well.”

In many countries, numerous cases were revealed when methadone programs enrolled occasional drug users without drug addiction who then became addicted. This fact is confirmed in two reports from England that warned against danger of making occasional drug users into patients with methadone addiction. The reports of INCB repeatedly emphasized that the increase in methadone addiction was observed in all countries with methadone programs. That is how methadone, as well as the other narcotic substances, became a source of new type of severe drug addiction and illegal circulation.

Thus, Switzerland, the Netherlands, Belgium and Australia have recently started offering other types of drugs to treat patients with heroin addiction, particularly heroin. On the CND session in 1994, a representative of Switzerland declared officially that the government of his country was planning a new experiment – to give heroin to patients with heroin addiction. Explaining the decision, the Swiss representative noted that the government thought it was necessary to change switch to heroin, because methadone use did not give the expected effect. Shortly thereafter, the Australian government announced their shift from methadone to “heroin prescription”. The Embassy of Australia in the Russian Federation, in its letter number 18 dated 15 August 1995, supported position of its government, noting that “The practice of giving methadone loses its effectiveness. Because methadone does not give desirable effect, drug addicts give it up”.

Despite the fact that those declarations met sharp criticism and became subject of special discussion of International Narcotics Control Board, the CND confronted an increasing return to so-called “drug allowance” – a controlled system of giving special drugs to drug addicts, including methadone or heroin.

At the same time, even when the Single Convention on Narcotic Drugs was prepared in 1961, it was demonstrated that “narcotic allowance” was ineffective and even harmful in the treatment of drug addicts based on the analysis of its use. It was emphasized
then that the use of “narcotic allowance” practically stops the search for new effective methods of drug addiction treatment, because giving drugs to drug addicts is much easier than socializing them into a life without drugs. Because of that, in resolution 2 of the UN Diplomatic Conference on the adoption of the 1961 Single Drug Convention, the system of “narcotic allowance” was criticized as follows: “The conference … declares, that one of the most effective methods of drug addicts treatment is treatment in a health institution, in an atmosphere free of drugs.” Use of methadone was allowed only as an exceptional and temporary measure for severe form of heroin addiction.

However, the search for new evidence to defend methadone use, which has been proven ineffective, is still going on. This is explained, as we already noted, by the fact that it is much easier to give methadone, than to organize the course of patient’s treatment. Producers of this rather expensive narcotic substance, who are trying to prevent closing of this program and, thus, of the methadone production, play an important role in advancing these arguments [Methadone is an incredibly inexpensive medicine, especially when compared to most medications on the market, which treat chronic illnesses of any kind].

In the USSR, after the scientific discussion of foreign data about effectiveness of methadone programs and considering pharmacological characteristics of methadone effects on humans, methadone (phenadone) was excluded from the list of approved medicines and its use was prohibited (order of Ministry of Health of USSR, 15 April 1977, #336). In the orders of the Ministry of Health of USSR, the system of “narcotic allowance” was negatively evaluated. The order from the Ministry of Health of Russia dated 14 August 1995 #239, titled “About additional measures on control of narcotic drugs, dangerous substances and poisons,” answered the attempt to return to “narcotic allowance” and introduce methadone into medical practice and stated: “To reassert the order, established before, that prohibits use of drugs in therapeutic purposes in drug addiction treatment, including giving of narcotic substances (“narcotic allowance”) to drug addicts in any form (giving prescriptions, giving in the hospital, outpatients department and others)”.

Thus there have been several periods in the history of substitution therapy when it has been under well-founded criticism: Methadone, just as heroin, was included into the List I of the Single Convention on Narcotic Drugs of 1961 - Nowadays lobbyists of methadone producers and methadone programs do not attract attention to the problem of treating drug addiction, but try to represent methadone as a panacea for “saving” from AIDS. This information appeared on the Internet, and there are voices that favor drug legalization and that call to use economical and political sanctions penalties against those countries that resist spread of methadone and expansion of substitution treatment programs. [AATOD and EUROPAD do not favor drug legalization and most responsible methadone treatment providers and their respective organizations, would not either].

At the same time parenteral drug use is not the only, and nowadays, is not the primary
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way of HIV transmission. Only a low percentage of heroin addicts are HIV-positive, and this is definitely not justification enough to introduce the program of drug supply for all drug addicts.

Thus, tactics of introduction of “narcotic allowance” and a shift to substitution therapy in the Russian Federation is not a viable approach for the treatment of heroin addiction. Recently observed attempts to legalize methadone programs and introduce them into drug treatment system are not based on therapeutic motives, but rather on economical purposes. The cost of realizing these purely profit-minded aims is lives and health of drug addicts.

The INCB reports of 1999 (paragraphs 450, 451, 452) and in 2000 (paragraphs 443, 446, 460), expressed concern with tendencies, observed in several European countries, toward renewal of methadone and heroin “allowance” under the slogan of “reduction of danger from use.” Almost a century long experience of substitution treatment with narcotic substances has shown that methadone use in heroin addicts’ treatment would not lead to decrease of incidence and prevalence of drug addiction, but rather to its high increase, since it causes methadone addiction as well.

That is why it was rather surprising to see a position paper by WHO, UNODC, and UNAIDS, published in spring 2004, which was practically contrary to all previously held researches and admitted conventions and decisions of the United Nations.

Currently the Government of the Russian Federation in its order dated 30 June 1998 number 681 approved the List of narcotic medicines and psychotropic substances, where methadone (phenadone) was included into the List 1 of narcotic drugs whose circulation is prohibited on the territory of the Russian Federation. Because the Federal Law of the Russian Federation of 8 January 1997 #3-FZ “About Narcotic Drugs and Psychotropic Substances” prohibits treatment of drug addiction with narcotic substances (article 31.6), methadone cannot be used on the territory of Russian Federation in health care practice.

We appeal to all health specialists of Russia to estimate reasonably and correctly the declarations of foreign and local representatives who lobby for methadone programs as an alternative treatment of heroin addiction. Inclusion of a patient with drug addiction into methadone program is not his treatment. In this case, one drug is simply exchanged for another. The resulting drug (methadone) addiction is more severe than that caused by heroin, with development of severe social and medical complications for the patient and for society in general. Methadone programs do not play a role in the treatment of drug addiction, and do not solve HIV-transmission problem [An enormous amount of research and scientific information has definitely indicated that methadone maintenance programs, when effectively managed, very definitely reduce HIV infection]. Lobbying of methadone programs is connected only with financial interests of methadone producers. The lives of sick patients are set on stake.

The effective way to solve the problem of drug addiction treatment is an intensive search for and introduction of new methods and means that focus on complete cessation of drugs use by patients with addiction, their socialization into a new life style free from drugs, but not on exchanging from one drug to another.
Knowledge and attitudes of drug treatment professionals towards HIV prevention and care activities in the Russian Federation

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Summary

Illicit drug use and HIV has spread rapidly in Russia, with 75% of HIV cases attributed to heroin and opiate IDU. The integration of drug treatment and HIV services would ensure access to HIV prevention and treatment for IDUs, but so far this has not happened. A series of interviews and focus groups reveals the attitudes of drug treatment specialists to the risks run by their patients, together with those specialists’ knowledge of the issues involved; these data make clear the opportunities that exist to integrate HIV services. We recommend better training in HIV issues such as principles of HIV counselling, harm reduction and substitution treatment. Measures to ensure access to HIV information and care within drug treatment settings and better research on these issues are an important priority.

Key Words: IDUs – heroin – opiate - HIV prevention – drug treatment professionals

Background

HIV epidemic among injecting drug users

In the past decade, following a period of socio-political change and economic instability, both illicit heroin and opiate use and HIV have spread rapidly in the Russian Federation. By the end of 2003, 343,000 drug-dependent individuals were officially
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registered (241,0 per 100,000 population) (as attested by the Ministry of Health in 2004)\textsubscript{19}, whereas experts suggest that the real number of drug-dependent people in Russia is 10 times that figure \textsuperscript{18}. As of June, 2004, the cumulative number of officially registered HIV infections totalled 284,000, but experts estimate that the true number of people living with HIV/AIDS (PLWHA) in the country is 2-5 times that number, or between 800,000 and 1.5 million (UNAIDS, 2004). Injecting drug users (IDUs) constitute 75\% of all HIV cases with known routes of transmission \textsuperscript{20}. Injecting drug use and needle sharing is an important factor in the transmission of HIV in Russia. The results of sentinel surveillance studies on the prevalence of HIV among IDUs vary significantly in different regions of Russia: from 0\% in a sample of 543 participants in a needle exchange project (NEP) in Pskov \textsuperscript{24} to 64.5\% in a sample of 152 drug users in Irkutsk \textsuperscript{25}. Studies in the world and in Russia have shown that levels of HIV prevalence may increase rapidly and explosively during periods as short as one year from the introduction of HIV into an IDU community. For example, in Togliatti, region of Samara, a study carried out in May 2001 on 426 IDUs recruited by communities found an HIV antibody prevalence of 56\%. 41\% of IDUs who had reported a negative antibody test result in 2000 and 2001 tested antibody positive by the time of the survey, suggesting high rates of incidence as well as a recent explosive spread \textsuperscript{22}.

In cities, where this epidemic started several years ago, individuals are rapidly realizing their need for HIV treatment, but this is hard to obtain because of the high costs of effective combination therapy and the lack of training among medical professionals. Drug users are especially vulnerable in terms of access to HIV treatment, as they are commonly considered a marginal and undesirable group within society. Russian experts estimate that up to 56,000 people, most of them IDUs, were in need of antiretroviral treatment (ART) by 2003, and this figure will reach half a million by 2010, yet by 2003 only 2000 PLWHA (3.6\% of those in need) had received it nationwide \textsuperscript{25}.

Risk reduction

A high level of HIV prevalence and explosive spread of HIV in Russian cities is mostly connected with the absence of adequate access to harm reduction services for IDUs, including information on needle exchange, drug treatment and risk reduction. Studies in Russia \textsuperscript{4,21,22}, as elsewhere in the world \textsuperscript{3,14,16}, have associated needle exchange interventions with lower risks of HIV among IDUs. A network of NEPs has been operating in Russia since 1998, but most reviews have found that the coverage of these programmes is inadequate. For example, a review by Burrows \textsuperscript{2} estimated that the average coverage of urban populations of IDUs by 48 NEPs that participated in the study was less than 1\%. Other authors have given higher estimates of coverage. For example, in a review by Rhodes et al., 2004, these authors estimate that in 2001-2 an average NEP reached 14-16\% of an estimated city population of IDUs with percentage coverage estimates varying considerably from city to city, the highest being 80\% in Belgorod and 79\% in Pskov \textsuperscript{22}. With most NEPs, however, inadequate amounts of funding and organizational capacity make it impossible to ensure that a high proportion of IDUs is reached by prevention initiatives.
Access to drug treatment is also very limited throughout the Federation. Substitution treatment programmes that were found to be effective in reducing risks of HIV among HIV-negative patients \(^{12}\) besides improving participation in ARV treatment among HIV-positive individuals \(^{15,17}\) worldwide — programmes that have been recommended as a component of effective HIV prevention and treatment by leading international agencies \(^{28}\) — are unavailable in the Russian Federation as a result of legal constraints. According to the Federal Law on Drugs (1998) any treatment of drug-dependent patients with narcotic substances included in Lists 1 (methadone) and 2 (buprenorphine) are outlawed. Moreover, any discussion, even in scientific publications, of substitution treatment is liable to be considered an offence, because “propaganda of narcotics, psychotropic means or precursors” is punishable under article 6.13 of Administrative Code of the Russian Federation. While substitution treatment is developing rapidly in other former Soviet Union countries, with pilot methadone programmes started in Kirgyzstan (2002) and Moldova (2004), and methadone being registered in Georgia, Belarus, Ukraine, Kazakhstan and Azerbaijan \(^{23}\), no progress is being made in Russia. This greatly impedes efforts in HIV prevention, as well as provision of ARV treatment for HIV-positive drug users.

Attitudes of professionals

Drug treatment professionals act as an important first point of contact for drug users entering into HIV prevention and treatment programmes \(^{9,10,11}\). Experience elsewhere in the world demonstrates that the integration of drug treatment and HIV services is an optimum solution for ensuring that most drug users have access to HIV prevention and treatment services, and that drug users with HIV have access to drug treatment \(^{29,13}\). In the Russian Federation this integration have not taken place. The process has been complicated by the inherited post-soviet structure of the public health service, based on a centralized, vertical model where horizontal links between different services (for example, drug treatment and infectious disease treatment) are difficult to set up and maintain. Hence, doctors working on drug treatment are not trained in HIV issues or other health problems related to heroin use, and are therefore not qualified to provide information or referrals to drug users who come to visit their offices.

Apart from being an important entry point into the broader medical service system for heroin users with related complications or risks of complications (such as HIV and hepatitis), the medical community could become an important actor in advocating progressive drug treatment and integrated HIV prevention and care strategies. In many countries all over the world, the medical community, along with affected groups of populations, has been a driving force in advocating more effective and humane treatment. Not much research is being done in Russia among medical professionals to determine their knowledge and attitudes on treatment efficacy, and the constraints they encounter on a daily basis, as well as ways of optimizing services.
Aims of the study

The aim of our study has been to investigate the knowledge and attitudes of medical professionals at a drug treatment clinic in Moscow, Russian Federation, towards the related complications or health risks of their patients, especially HIV, together with opportunities to integrate HIV prevention and care services into heroin treatment. We also discuss doctors’ perception of their work with HIV-positive patients, as well as their attitudes to harm reduction programmes.

Methods

A series of structured interviews and focus-groups was carried out in two in-patient departments of the Clinic of the National Research Centre on Addictions in 2001. The interviews were carried out with physicians, researchers and medical nurses, and with patients and their relatives. Due to the limited scope of this study, we will concentrate on the findings among the first two groups: physicians and medical nurses. In all, 50 physicians and researchers, and 41 medical nurses, took part in the interviews. The interview design varied between these two groups, with some questions overlapping. It was focused on gaining information about professionals’ knowledge about HIV and related issues, their experience and attitudes regarding the provision of HIV-related information to HIV-positive and HIV-negative patients, their expectations of the results of drug treatment in general and their views on areas where knowledge about, and training on, HIV is insufficient.

Three focus-group discussions were carried out. The first included 11 people: Deputy Head Doctor, 3 heads of departments, 7 physicians specializing in addictions. We investigated the feasibility and difficulty of providing HIV prevention/care information and services (on drug-related risks, safer sexual behaviour; HIV pre- and post-testing counselling) as part of clinics’ service package. The second focus group included 9 people: 1 head of department, 5 physicians specializing in addictions and 3 researchers. The main focus of discussion was attitudes to harm reduction programmes. The third focus group included 6 nurses at the Department for HIV-infected Addicts of Addiction Hospital No 17.

Results

Perception of the drug treatment process and its outcomes by physicians

Among 50 interviewed physicians, 73% shared quite optimistic views on treatment outcomes. Of these, 23% believed that it is possible to achieve long-term remission, and 21% expected “a positive result” (without further specification). Despite the generally optimistic views of this group, only 8% of them expected complete abstinence as the result of drug treatment. 23% of the physicians expressed a pessimistic or alarmed
prognosis. Of these, 6% indicated that they had no hope whatsoever of positive results from addiction treatment. Six per cent of respondents from this group expressed concern about possible complications in their patients, such as viral hepatitis and HIV. Two per cent of physicians were not at all concerned about the outcomes of treatment and indicated that for them the only motivation for providing services was financial reward.

According to 64% of doctors, the treatment of drug addicts is hard, demanding, exhausting work; for them, the treatment of drug-dependent patients resembles the treatment of mental disease patients, which requires great psycho-emotional effort. Another 15% of doctors view their work as a collaborative effort with a patient — for them treating addiction means helping patients find a substitution for drugs in life and overcoming their problems together with their doctor and with relatives; ten per cent of respondents didn’t have any emotional attitude to their work and viewed drug treatment as a routine professional activity, while only 6% of the doctors thought of their profession as an interesting, creative and rewarding activity.

**Providing risk reduction information**

Our respondents expressed very varied feelings about the possibility and necessity of discussing risky behaviour and patterns of drug use with their patients.

Half of the physicians considered that any discussion about ‘safer drug use’ with patients was absolutely impossible and unacceptable. Their reasoning was that, firstly, they believed that any substance use is dangerous and there is no such thing as “safe” or “safer” drug use, and, secondly, they viewed such consultations as undermining patients’ motivation for complete abstinence. Another half (54%) of the doctors considered such discussions very important and even mandatory, especially in view of the importance of preventing blood-borne infections. There were also some professionals who believed that such discussions with patients were very difficult, and could only be used as a desperate measure (46%).

Focus-group discussions revealed that, unlike discussions on safer drug use, those on patients’ sexual behaviour were a natural and integral part of the treatment process for many doctors. These discussions allowed specialists to discuss safer forms of behaviour, but also to achieve a better understanding of their patients’ personality. Nevertheless, a minority of physicians believed that such discussions were undesirable and difficult for them; they feel awkward entering into discussions with patients on their sexual behaviour. All focus group participants did, however, express a desire to undertake some professional training in this area.

Discussions about pre-test HIV counselling (although formally voluntary by law, HIV testing is usually provided to all patients on initiating drug treatment at entrance as part of in-patient facilities) revealed that pre-test counselling was not always provided to patients. In some situations doctors found it difficult to provide such counselling to drug-dependent individuals suffering from a withdrawal syndrome. Some doctors expressed the opinion that such counselling should be provided not immediately before testing, but after a period when acute withdrawal syndrome is overcome but before the results are communicated to the patient.
All focus-group participants realized that providing HIV-related information should, ideally, be an important part of their jobs and admitted the need for better professional training in this area.

**Attitudes to harm reduction programmes**

A majority of focus-group 2 participants agreed that, in spite of the existing legislative barriers in Russia, harm reduction programmes are necessary and important in preventing parenteral infections and helpful in re-socializing drug users. Many considered harm reduction to be an important alternative in the variety of drug services and thought its development should be encouraged. Four doctors thought that the expansion of NEPs was urgently necessary and very useful, especially in preventing blood-borne infections, and that there should be as many of them as possible, even stating that “it would be best if the State could offer these services to drug users now”. Three doctors were less emotional about these programmes, but believed that they would do no harm. Meanwhile, two physicians expressed concern about the level of management as well as the general effectiveness of harm reduction programmes in the Russian Federation. They also shared the opinion that such intervention may encourage drug use and the spread of drugs. They also thought that the endorsement of such activities was a step towards drug legalization and symbolized unacceptable indulgence towards street drug abusers.

As to substitution treatment programmes, the general level of acceptance and approval was much lower than in relation to NEPs. Some participants believed that such programmes were inefficient and dangerous, as they could lead to a leakage of opiates to the street. A minority of physicians considered that substitution therapy could be applied in Russia, but only to certain patients.

**Experience of work with HIV-positive patients**

The interviews with 50 physicians and researchers at the Clinic indicated that practically all of them had, at one point, had an experience of treating an HIV-positive drug user: 76% of the doctors had had between 1 and 10 patients, while 24% had had over 10 patients.

While the overwhelming majority of physicians (87%) believed that they were familiar with some of the clinical symptoms of HIV infection, all of them recognized the need for additional knowledge. While 82% considered that they needed such knowledge for their professional activity, the other 18% thought it would be useful not only for professional activity, but for private life, too.

Drug treatment of HIV-positive patients was not considered essentially different from the treatment of other addicts by 42% of these doctors. Thirty-one per cent thought that treating HIV-positive patients was more challenging, due to the persistent emotional tension and higher anxiety of patients. Some doctors (4%) also shared the opinion that it would be preferable to involve an infectionist and a psychologist in the treatment process.

For 21% of physicians, informing patients about the positive results of their HIV-
testing was a very difficult psychological task, and they would prefer this job to be done by doctors who had well-established relationships with their patients, while 17% believed that any specialist (not necessarily a physician) with a good psychological training could inform patients about the positive results of HIV-testing. The need for a special training was recognised by 47% of the doctors interviewed. Some physicians (4%) shared a concern that informing patients about their HIV-positive status was not always appropriate in drug treatment clinics, because of the complicated physical and psychological state of patients who have just started drug treatment.

In identifying the specific features of treatments for HIV-infected drug addicts, 29% of the physicians mentioned: modified sensitivity and tolerance to drug treatment medicines; the accompanying somatic pathology; reduced immunity; and special needs arising during therapy for drug addiction. They believed that an atypical abstinence syndrome development, a more difficult recovery process and frequent relapses were observed with greater frequency in HIV-positive patients.

Some doctors reported that, in the process of treating HIV-positive patients, they often encountered the psychology of a doomed, psychopathic person, who had “lost a sense of life”, and was therefore difficult to motivate in seeking withdraw from drugs, and recovery, while four per cent of these physicians actually considered all efforts dedicated to the drug treatment of such patients to be futile. Eleven per cent of respondents admitted that they avoided treating such patients. At the same time another group of physicians reported that, for some patients, awareness of their HIV-positive status stimulated their motivation to withdraw from drugs, so they tried to reinforce this motivation in their patients.

Interviews with medical nurses revealed that 85% of them were afraid of getting HIV from the patients. This is despite the fact that all the nurses reported using means of universal precaution and maintaining an anti-epidemic health care regime. Even so, 17% reported that they do not always keep to that regime. Among nurses, 88% felt the need to obtain additional knowledge on the prevention, clinical picture and treatment of HIV.

Some respondents stated that they would prefer HIV tests to be performed on patients before they enter a clinic, so that those found to be HIV-positive would not be admitted. More than half of the nurses interviewed (68%) considered that HIV-positive patients must be isolated from other patients. Although there were no open conflicts with HIV-positive patients, 68% of the nurses interviewed spoke about the need for psychological support and for after-work relaxation when they had such patients. An overwhelming majority of the nurses interviewed believed that social privileges for professionals working with HIV-positive patients should be increased (e.g. rises in salary, bonuses, longer vacations and permission to take vacations 3 or 4 times a year, and the lowering of retirement age to 50 compared with 55 years as the standard retirement age). The nurses mentioned some things that would be helpful to them in their work: the provision of up-to-date information about HIV prevention, diagnostics
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and treatment to staff and patients; staffing the clinic with qualified psychologists; and providing staff with special clothes and modern, non-toxic means of disinfection.

A separate focus group was carried out with nurses, working in the Department’s unit for HIV-infected addicts. All the staff in the unit are highly aware of the importance of keeping to the anti-epidemic health care regime, but, in spite of all the preventive and health care measures, they are still afraid of being infected. Some nurses feel that, because patients who overcome psychological stress lose their ‘sense of life’, it is difficult to ask them to keep to the health care regime and its norms of behaviour. The psychological situation in the unit is quite difficult because, as was reported, the patients who enter the unit are often aggressive. It is therefore important for staff to avoid situations of conflict with such patients. Once a month, the Head of the unit provides training on conflict management and communication skills to the staff as well as on precautionary measures.

As a result, nurses working in the unit believe that they would benefit if additional psychological support was provided for staff, such as psychotherapeutic sessions and a space where they could relax and take a break. They also think that it is important to increase the number of nurses working in the unit and improve the social package for those who have direct contact with HIV-positive patients.

Conclusions and recommendations

Approaches to drug treatment has been slowly progressing in the Russian Federation, but the indicators of the effectiveness of its drug services are still oriented towards goals of complete abstinence. Medical professionals have very low expectations about the positive outcomes of such treatment, and this influences their relationships with patients, their attitude to work and their satisfaction with its progress. It seems that the introduction of a wider spectrum of treatment modalities would change this situation. The HIV prevention and harm reduction approach provides a unique opportunity to reshape service provision and introduce various goals besides complete abstinence. Any positive change in patients’ lives, such as success in reducing drug-related harm, accepting risk reduction strategies, or controlling and managing their drug use could be viewed as treatment successes on a wider scale. Such outcomes could serve as a foundation for an alternative set of effectiveness indicators in drug treatment, and their introduction would allow doctors to view their routine tasks as more rewarding, to establish more healthy and productive relationships with patients and assist them in the long process of solving various problems related to the use of illicit drugs.

In the meantime, we notice that doctors and medical nurses in drug treatment lack an understanding of risk reduction strategies, and that they are not familiar with methodological approaches to risk reduction counselling. This is especially worrisome in the light of the HIV epidemic in Russia. It is clear that, for some drug users, contacts with drug treatment specialists may be the only — or at least one important — source of information — on HIV prevention and treatment. At least, not all doctors and nurses in
the drug clinic feel that they are capable or well-trained enough to provide information on risk reduction and on HIV prevention and treatment to their patients. It is clear that most doctors are highly aware of the problem of HIV and other blood-borne infections, but some still underestimate or doubt the importance and feasibility of such counselling in drug treatment settings. It seems that the development of a comprehensive training programme able to help doctors and nurses appreciate the rationale of risk reduction counselling, and to understand its underlying principles and approaches, is an urgent priority in the Russian Federation.

Many treatment specialists are aware of harm reduction programmes that operate in the Federation, and most of them support the idea, but there is still no real cooperation in terms of service provision. Ideally, harm reduction initiatives should be closely linked to drug treatment services so that both (as well as their clients and patients) benefit from this cooperation. As noted above, drug treatment would greatly benefit from accepting and providing different modalities of harm reduction strategies: from motivational interviews to needle exchange and expanded out-patient services. Harm reduction programmes would also benefit by being able to refer their clients to effective drug treatment programmes.

One of the critical factors identified during the interviews was that HIV testing should be performed on all patients on entry to a clinic. It is of absolute importance that such testing should be performed in strict accordance with the Federal Law on HIV (1995), which guarantees volunteer anonymous HIV testing to all citizens in combination with pre- and post-test counselling. The provision of such counselling is a critical factor in preventing and treating HIV, so clear, unified guidelines and protocols for testing and counselling in drug treatment clinics should be introduced, and staff should be trained in their implementation.

HIV testing results should not serve the function of enforcing sanctions on patients, such as their being assigned to a separate unit, or being given different treatment compared with other patients. It has been proven in other countries of the world that there is no need to treat people with HIV separately from other patients. Given that Universal Precaution Measures have been introduced and followed, and staff are given ongoing training in self-protection, there is no danger whatsoever of medical staff contracting HIV. As we observed in the interviews, the separation of HIV-positive patients from others can create an atmosphere of anxiety and constant stress not only in patients, but also in medical personnel. It seems to us that the in-depth training of medical staff and improvements in the psychological climate in the drug treatment facilities, as well as measures to ensure professional support in burn-out prevention and management, could all contribute to upgrading the situation and treatment conditions of HIV-positive drug users, as also the job environment of medical staff, including doctors and nurses.\textsuperscript{1,5,6}

The integration of drug treatment with HIV treatment is a challenging task for the Russian health system in general. In the present situation, HIV treatment and drug treatment are provided by absolutely distinct types of service (specialized AIDS centres and drug treatment centres), which find it difficult to cooperate and interact
productively. Although it is quite apparent that the integration of these services will become inevitable when more drug-dependent individuals come to need ARV treatment, today there is none. At the current stage of development it can at least be recommended that a professional infectious disease doctor (or doctors) and a professional psychologist (or psychologists) should work as part of the team providing drug treatment facilities and a focus for the provision of counselling, care (where necessary, the prevention of opportunistic infections), and ARV treatment to HIV-positive patients.

Substitution treatment seems an undesirable and taboo topic among drug treatment professionals in Russia. Our study makes it clear that many doctors have very little understanding of the rationale of such treatment, and lack truthful information about it. In the light of the emergency brought about by the HIV and AIDS epidemic, whose greatest impact has been on drug users, it seems that Russia should seriously review its current legislation and undertake at least pilot methadone/buprenorphine projects to deliver drug treatment alternatives, but also to ensure that people have access to all means of HIV prevention, and that opiate-dependent PLWHA have access to all means of stabilizing their lives and receiving ARV therapy. Doctors should be among those who actively advocate substitution treatment, but, to achieve that, they also should have reliable sources of information and education about it. The international community of drug treatment specialists could become an important source of information and education for Russian medical specialists, as these programmes have been experimented very successfully in the West. We recommend that a series of training sessions, study tours and informational support for Russian health specialists should be developed at all levels to improve the degree of knowledge and understanding of the importance of such interventions.

Last, but not least: although it was not a primary focus of our study, one important topic to emerge in the interviews and focus groups with specialists was that of the human rights of patients in the drug treatment system. A human rights culture is still absent in the post-soviet countries, and people often lack knowledge about their basic rights and mechanisms of protection. At least one human rights-related issue was noticed in the course of interviews, that is, the right to informed consent to HIV testing, access to health-related information such as HIV counselling and the protection of confidentiality about the diagnosis. We were struck by the ubiquitous lack of protection of patients’ rights in this area, which may be indicative of other violations within the system. This area is greatly under-researched in this country, and we recommend that a further series of studies and initiatives should become a priority in the area of drug treatment. We also recommend that violations of these rights should be routinely monitored and reported to improve the situation of patients’ human rights protection.

References


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A Low Value Voucher Contingency Management Programme with Israeli Methadone-Maintained Patients – A Pilot Evaluation Study

Eli Lawental1,2 and David Eshkol1

Summary

Purpose: This study evaluated, for the first time, the effectiveness of a voucher-based contingency management programme (CMP) with a population of methadone-maintained patients outside the U.S.A. The study reported was carried out at the Haifa Drug Abuse Treatment Centre in Israel. The population studied differed culturally from previously studied groups in the U.S.A. Vouchers were given to patients upon providing a urine test that was negative for illicit drug use. With the accumulation of three consecutive vouchers subjects could redeem one for one take-home dose. After the accumulation of five or more consecutive vouchers subjects were able to redeem two for two consecutive take-home doses. Method: Two groups of subjects were evaluated in this study. In the first group, subjects (n = 35) treated prior to the initiation of the CMP were included. These subjects provided 455 urine samples in the three months prior to the CMP. In the second group, subjects (n = 41) treated after initiation of the CMP were included. A three-month period was allowed for the Centre to adjust to the new CMP. Subjects in the “post” group provided 554 urine samples in the three months following this period. No statistically significant differences were noted between the groups with reference to their pre-treatment characteristics and the length of time subjects stayed in treatment. Results: The post CMP group showed an improvement in providing samples free of illicit substance abuse. An improvement of 36.3% was noted. The post group also had 47.1% more stable-on-methadone subjects. Conclusions: This study supports the claim that such a CMP may be effective in reducing illicit drug abuse in the Israeli methadone-maintained patient population. As the sample of this study is relatively small and no attempt was made to identify a specific group of Israeli patients that may benefit even more from this type or other types of CMP, additional studies are needed.

Key Words: Contingency management - methadone maintenance - opiate abuse treatment - substance abuse treatment - vouchers.
Introduction

Methadone maintenance, as indicated in NIDA’s booklet *Principles of Drug Addiction Treatment* (9), has been a widely accepted opiate abuse treatment modality for nearly 40 years. This type of treatment started in the US and has spread all over the world. In Israel, the treatment of opiate addicts with methadone started in 1977. To date, about 2000 opiate abusers in Israel have been treated with methadone (2, 3). Evidence for its effectiveness in Israel has been reported by Lawental et al. (8). Pharmacological treatment with methadone does not, however, directly address the many additional problems of polydrug abuse, lifestyle and psychiatric difficulties that patients bring to the treatment setting. Psychosocial treatment, psychiatric and psychological services, vocational training, and so on, are frequently offered to meet these additional needs.

As described in the literature, various methodologies of contingency management (CM) have generally been shown to be effective in a variety of drug abuse treatment settings in improving patient treatment retention and relapse prevention, and in limiting the abuse of non-prescribed drugs. Griffith et al. (4) carried out a meta-analysis of CM in outpatient methadone maintenance treatment in 30 separate studies. They report results confirming that contingency management is effective in reducing illicit drug use. Petry (10) has published a literature review and guide to the application of CM procedures in treating substance abuse disorders in clinical settings. High value CM programmes such as Higgins’ community reinforcement approach (5) were not feasible at that time in the Israeli context. Alternatively, low value voucher-based CM has been extensively researched and been shown to be effective (1, 6, 12-15). This fact led the National Institute on Drug Abuse to indicate, in *Principles of Drug Addiction Treatment* (9) that “voucher-based reinforcement therapy in methadone maintenance treatment helps patients achieve and maintain abstinence from illegal drugs. This is done by providing them with a voucher each time they submit a drug-free urine sample”.

The rationale for studying our low cost voucher-based CMP is to determine if such behavioural reinforcement is also effective with patients in countries outside the USA. Vouchers redeemable for a take-home dose of methadone are given for each urinalysis free of illicit drug use. In our literature review through Medline and other available electronic searches, we were unable to find reports of international research using CM in drug abuse treatment. We know of no formalized attempts to evaluate a CMP with methadone maintenance patients in Israel. In spite of the many similarities between the Israeli and American cultures, there are significant demographic differences.

Approximately 50% of our Israeli patients are of North African and Asian origin (of these, half were born in Israel), approximately 20% are from former states of the Soviet Union, approximately 20% are of European and American origin (of these, half were born in Israel), and the remaining 10% are of Arab extraction (Annual Report of the Haifa Drug Treatment Centre (11); Annual Report of the Israel Ministry of Health, Department of Addictions Treatment (7)). It is important to point out another significant difference between the populations: the typical family structure contains many children,
often 5 or more, and is still based on a hierarchy of patriarchal authority.

We are therefore reporting our evaluation of the take-home voucher CMP developed at the Haifa Drug Abuse Treatment Centre. This programme was initiated to assist patients in limiting the abuse of non-prescribed drugs during treatment, and was not initially designed as a rigorous research study. In order to evaluate the effect of this CMP, we compared urinalysis results for a group of subjects who were in treatment prior to initiation of the CMP and a post initiation group. It is important to point out that there were no other changes in the Centre’s activities, treatment approaches or staff during the study period. We believe the evidence of its success with a population that had not been previously investigated justifies our report.

The Treatment Centre serves patients from the Haifa metropolitan area with a population of about one million people. Haifa is the third largest city in Israel. It is estimated that about 10,000 opiate addicts reside in this area. The Centre’s basic philosophy is that drug addiction is a bio-psychosocial problem that must be treated holistically by an interdisciplinary team. The Centre provides the following treatment services:
1. Ambulatory methadone rehabilitation programme – 150 treatment slots.
3. Thirty-day inpatient detoxification programme – 16-bed department.
4. Hostel for post-detoxification patients – after-care programme for patients that completed either the thirty-day detoxification or a T.C. This is a 10-bed unit, where patients can stay for up to half a year.
5. Long-term (12-month) inpatient unit in a T.C. format for women. This too is a 10-bed unit.
6. Treatment for families of substance abusers.

The Centre is also involved in community action, education and research. It is funded by the Israeli Ministry of Health with some additional funds from the Israeli Anti-Drug Authority. Patients make a symbolic payment for using these services.

Methods

Subjects
All subjects (n = 76) were patients treated at the ambulatory rehabilitation unit of the Haifa Drug Abuse Treatment Centre. To be included in the study, subjects had to be enrolled for at least three months to allow enough time to adjust to treatment and reach a stable methadone dose. Two groups were evaluated in this study. The “Pre” group (35 subjects treated prior to initiation of the CMP) consisted of all patients who received methadone as part of their treatment plan and who met the research criteria. The “Post” group (41 subjects treated after initiation of the CMP) consisted of all the patients who received methadone as part of their treatment plan and who met the research criteria. 21 of these subjects were included in both groups.

Subjects were evaluated to detect possible differences between the two groups. All the relevant data recorded on the standardized intake form of the Israeli Ministry
of Health were considered. The length of time in the treatment programme was also recorded for each subject. There were no statistically significant differences between the groups in length of treatment (months in treatment: table 1). Comparison of the groups revealed no statistically significant differences between the groups in any of the variables tested. T tests were computed for six of the variables and Chi Square for eleven. The results of this analysis are presented in two tables, one for the t tested variables and the other for the Chi Square tested variables (Tables 1 and 2).

In both groups methadone doses varied from 20 to 130 mg. 84% of methadone doses were between 50 and 120 mg. Average dose was 64 mg in the Pre group, 69 mg in the Post group.

**Tools**

The background data presented in the subjects section was collected from the Israeli Ministry of Health standardized intake questionnaire contained in each subject’s file. Urine tests from all the subjects were obtained under supervision and sent for analysis to the main drug testing facility at Tel-Hashomer Hospital. All urine samples are routinely tested for methadone, opiates, benzodiazepines, and THC. Levels of use are not reported. Random test samples sent to the Tel-Hashomer laboratory from all treatment programmes in Israel are screened for other illegal drugs of abuse (including cocaine). At the time of the study less than 2% of these samples tested positive for all other drugs of abuse.

A translation from Hebrew to English of the voucher given to subjects who provided clean urine tests is presented in Figure 1.

**Procedure**

The CMP was initiated on 1st July 2005. From that date forward, patients providing clean urine tests received the vouchers described in the Tools section. Urine samples were taken from all patients at least once a week on randomly selected days. Patients received a voucher for each urine sample delivered free of illicit drug use. The case manager checked weekly urinalysis results, completed details on the voucher, and forwarded it to the Director. Vouchers were signed and immediately distributed to individual patient mailboxes at the Centre. Upon the accumulation of three consecutive vouchers subjects were allowed to redeem one for a one take-home dose. With the accumulation of at least five consecutive vouchers, subjects were allowed to redeem two for two consecutive take-home doses. If a subject delivered a urine sample containing illicit drugs the counting of the vouchers was reset to zero.

In order to establish a base line, all the patients who received methadone at the Centre on July 1st and who met the research criteria were included in the ‘Pre’ group. This group had 35 subjects. All urine tests (n = 455, mean per subject = 13) provided by these subjects from April 1st to June 30th were evaluated. After initiation of the CMP on July 1st, we allowed three months for the staff to fully implement the programme as designed and for the system to adjust to the change. In the ‘Post’ group, all subjects who met the research criteria and were still treated at the Centre on December 30th were
Figure 1: The voucher utilized in the study

included. The post group had 41 subjects. All urine tests (n = 554, mean per subject = 13.5) on samples provided by these subjects from October 1st to December 30th were evaluated. As previously stated, this group included 21 subjects who had also been in the ‘pre’ group. It is important to note that during the study period no other changes were made in the Centre’s activities, treatment approaches or staff.

Results

The pre CMP group provided 455 urine samples. From these samples 101 tested positive for illicit drugs other than methadone (22.8%). The post CMP group provided 554 urine samples. From these samples 78 tested positive for illicit drugs other than
methadone (14.1%). The urine tests of the post group showed an improvement of 36.3% in clean urine tests as compared with the pre group. A Chi Square test shows a significant statistical difference between the groups (Chi Square = 11.08, p < 0.01).

In the pre CMP group 18 out of 35 (51.4%) subjects were stable on methadone (i.e., no more than 2 urine tests out of the last 15 tested positive for other illicit drugs than methadone). In the post group 31 out of 41 (75.6%) subjects were stable on methadone. This shows an improvement of 47.1% in number of stable subjects in the post group as compared with the pre group. A Chi Square test shows that this difference is statistically significant (Chi Square = 4.88, p < 0.05).

A major factor in the stabilization of methadone maintenance patients is retention in treatment. In order to isolate this factor we also looked at the group of subjects who received treatment only after initiation of the CMP (n=20). The mean treatment time of this group was 7 months as compared with the a mean of 11.9 months for the pre CMP group and 11.6 months for the total post CMP group. The post CMP only group provided less positive (for illicit drug use) urinalyses than either the pre CMP group or the post CMP group. In addition, the post CMP only group contained more stable-on-methadone patients than the pre CMP group and almost the same percentage of stabilized patients as the entire post CMP group (Tables 1,2,3).

**Discussion and conclusions**

This study evaluated the effectiveness of a voucher based contingency management programme (CMP) with methadone maintained patients at The Haifa Drug Abuse Treatment Centre, Israel. The study compared two groups of subjects. One group included

<p>| Table 1 – Comparing pre and post groups on t-tested variables. |
|----------------------|--------|--------|------|------|
| Variable             | Means       | F      | p    | T    |
|                      | Pre    | Post   |      |      |
| Age                  | 37.9   | 34.2   | 0.91 | 0.34 |
| Years of education   | 9.5    | 10.5   | 1.41 | 0.24 |
| Months worked in the last year | 3.3  | 4.5    | 0.11 | 0.74 |
| Months of jail terms served | 24.3 | 22.9   | 0.08 | 0.78 |
| Number of arrests in the last year | 0.8  | 0.9    | 0.35 | 0.56 |
| Months in treatment  | 11.9   | 11.6   | 0.03 | 0.86 |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>Results</th>
<th>Chi Square</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Pre Male = 28</td>
<td>0.5</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>Female = 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post Male = 30</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female = 11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family status</td>
<td>Pre Married = 11</td>
<td>1.6</td>
<td>0.81</td>
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<td></td>
<td>Divorced = 8</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Widow = 0</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Bachelor = 15</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other = 1</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Post Married = 14</td>
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<tr>
<td></td>
<td>Divorced = 14</td>
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<td></td>
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<tr>
<td></td>
<td>Widow = 1</td>
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<td></td>
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<tr>
<td></td>
<td>Bachelor = 18</td>
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<td></td>
</tr>
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<td></td>
<td>Other = 1</td>
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<td></td>
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<td>Religion</td>
<td>Pre Jewish = 18</td>
<td>2.6</td>
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<td></td>
<td>Muslim = 8</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Christian = 7</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Druze = 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other = 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post Jewish = 26</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Muslim = 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Christian = 7</td>
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</tr>
<tr>
<td></td>
<td>Druze = 0</td>
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</tr>
<tr>
<td></td>
<td>Other = 2</td>
<td></td>
<td></td>
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<tr>
<td>Army Service</td>
<td>Pre Full = 7</td>
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<td>0.72</td>
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<td>Partial = 1</td>
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</tr>
<tr>
<td></td>
<td>None = 20</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Post Full = 11</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Partial = 3</td>
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<td></td>
<td>None = 25</td>
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<td></td>
</tr>
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<td>IV use</td>
<td>Pre Yes = 12</td>
<td>2.1</td>
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<td>No = 12</td>
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<tr>
<td></td>
<td>N/A = 11</td>
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<td></td>
<td>Yes = 23</td>
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<td></td>
<td>No = 11</td>
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</tr>
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<td></td>
<td>N/A = 11</td>
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<td>Previous addiction treatment</td>
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<td>No = 15</td>
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<tr>
<td></td>
<td>Yes = 12</td>
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<tr>
<td></td>
<td>No = 15</td>
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Table 2 – Comparing pre and post groups on Chi Square tested variables.

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<th>Variable</th>
<th>Results</th>
<th>Chi Square</th>
<th>p</th>
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<tr>
<td>Previous psychiatric hospitalization</td>
<td>Pre</td>
<td>Yes = 1</td>
<td>No  = 25</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>Yes = 3</td>
<td>No  = 34</td>
</tr>
<tr>
<td>Previous outpatient psychiatric treatment</td>
<td>Pre</td>
<td>Yes = 2</td>
<td>No  = 25</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>Yes = 5</td>
<td>No  = 33</td>
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<tr>
<td>Criminality</td>
<td>Pre</td>
<td>High = 4</td>
<td>Medium = 7</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>Medium = 9</td>
<td>Light = 9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None = 5</td>
<td>High = 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medium = 7</td>
<td>Light = 12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None = 12</td>
<td></td>
</tr>
<tr>
<td>Profession</td>
<td>Pre</td>
<td>Yes = 14</td>
<td>No  = 14</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>Yes = 21</td>
<td>No  = 17</td>
</tr>
<tr>
<td>Reasons for arrest(s) during the last year, not including drug arrests</td>
<td>Pre</td>
<td>Property = 3</td>
<td>Other = 1</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>Violence = 4</td>
<td>4</td>
</tr>
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<td></td>
<td></td>
<td>Other = 1</td>
<td>1</td>
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<td></td>
<td></td>
<td>Violence = 5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other = 1</td>
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</table>

Table 3 – Comparing the pre CMP and post CMP groups on urine test samples and numbers of subjects stabilized-on-methadone.

<table>
<thead>
<tr>
<th></th>
<th>Pre CMP group (n = 35)</th>
<th>Post CMP group (n = 41)</th>
<th>Subjects in post CMP only (n = 20)</th>
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</thead>
<tbody>
<tr>
<td>Positive urine samples</td>
<td>101 (22.8%)</td>
<td>78 (14.1%)</td>
<td>33 (11.74%)</td>
</tr>
<tr>
<td>Total urine samples</td>
<td>455</td>
<td>554</td>
<td>281</td>
</tr>
<tr>
<td>Number of stable subjects</td>
<td>18 (51.4%)</td>
<td>31 (75.6%)</td>
<td>14 (70%)</td>
</tr>
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</table>
subjects treated at the centre prior to the initiation of the CMP (n=35) and the other group included subjects treated after initiation of the CMP (n=41). There were no other changes in the Centre’s activities, treatment approaches or staff during the study period. No statistically significant differences were noted between the groups on pre-treatment variables. The post CMP group showed statistically significant improvement on both outcome measures. The post group delivered 36.3% fewer urine samples positive for illicit drug use and 47.1% more subjects who succeeded in stabilizing on methadone. As the subjects in the post CMP group only (n=20) showed improvement similar to or better than those subjects enrolled in both the pre CMP and post CMP groups we concluded that length of treatment did not account for the improvements observed.

Reinforcement by non-monetary vouchers given to subjects who submitted urine samples free of illicit drug use, redeemable for take-home doses alone, seems to significantly improve the number of “clean” urine samples of the subjects as well as the number of subjects stabilized on methadone. We therefore conclude that the CMP initiated at the Haifa Centre provided additional cost-effective support for successful treatment with Israeli methadone patients. The significant improvement detected in the post CMP group offers strong support for its use in methadone maintenance programmes outside the US.

The findings of the study should be viewed with caution due to its relatively small sample. In this study no attempt was made to determine if such a CMP might work differently with sub-groups in our patient population. More studies are needed in this direction. It is important to note that we have not compared this particular CMP to other CMPs, for example those providing higher value vouchers, so further studies are needed to determine if other CMPs will produce better results.

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Treatment for hepatitis C in jailhouses is doable and successful: definitive data of first national French study (POPHEC)

André J. Remy¹, Laurent Serraf², Anne Galinier², Valéry Hedouin³, Didier Gosset³, Patricia Wagner⁴ and others POPHEC investigators.

Summary

Background: A French survey of 85 jailhouses in 2000 yielded disappointing results on the diagnosis and treatment of hepatitis C (HCV) in inmates: serology was available for 2/3 of the patients, but only 36% had undergone liver biopsies (LB) and only 4% had been treated. LB access was identified as an obstacle to therapy. This prospective study (POPHEC) was designed to increase treatment access in this population. Methods: 37 medical units in French jailhouses participated. Patients were all to be treated with a combination of pegylated interferon alpha 2b and ribavirin. LBs were optional. Biochemical, virological and clinical data were collected. Therapy and data collection continued for patients who were transferred. In cases where final data were unavailable, patients were classified as non-responders. Results: As of 1st June 2004, 200 patients were analysed: 94% were male, mean age 37 years, contamination route IVDU in 78%, transfusion in 3%. The genotype was 1a, 1b, 3a and 4 in 28%, 11%, 36% and 7%, respectively; 12% were also infected with HIV; 37% were treated with methadone or buprenorphine. The average viral load was 1227689 IU/mL; 33% had LB before treatment, with a mean Metavir score of A1.8 F1.73. The mean treatment duration ranged between 4 months in patients with early termination due to non-medical reasons and 7 months for patients who completed therapy; 95 patients (47.5%) experienced a complete sustained response). Conclusion: treatment for HCV in jailhouses is feasible and successful; the limitations placed on indications for LBs, as recommended by the 2002 French consensus conference, apply specifically to the inmate population and facilitate access to HCV therapy, besides helping initiatives such as POPHEC

Key Words: Hepatitis C - Treatment - Jail - Heroin Addiction - Methadone - Buprenorphine

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A first national French survey of hepatitis C diagnosis and therapy in 85 jailhouses in 2000 yielded disappointing results on the diagnosis and treatment of hepatitis C virus (HCV) in 48,000 inmates (half of the jailhouse population): 97% of medical units take care of chronic viral hepatitis C, but serology was only available to 71% of the patients. The incidence of hepatitis C was 6.3% in inmates, with a range of 0-20% in different prisons. Only 36% of patients had undergone liver biopsies (LB), which are a precondition for treatment. A 5-week mean delay was observed before LB, the range being 3 days to 4 months. In the 85 jailhouses, 153 patients had been treated, so that only 4% of inmates had experienced positive serology C. In our survey, LB access was identified as an obstacle to HCV antiviral therapy. We decided to organize a POPHEC STUDY (a French acronym meaning the initial study of treatment for hepatitis C in jailhouses) comprising 37 medical units in French jailhouses, starting in March 2001.

This prospective study was designed to increase treatment access for this population. LBs were optional, even if doctors wanted them. Patients were all to be treated with a combination of pegylated interferon alpha 2b (1.5 mg per kg per week) and ribavirin (800 to 1200 mg per day as a function of weight). The duration of treatment was 24 weeks for HCV genotypes 2 and 3 and 48 weeks for HCV genotypes 1 and 4. Biochemical, virological and clinical data were collected from all patients. Therapy and data collection continued for patients who were transferred. The general quality of life index was to be assessed before, during and after treatment. In cases where final data were unavailable, patients were classified as non-responders. Altogether, 217 patients were included in the study. As of 1st June 2004, 200 patients had been analysed, 6 months after the completion of antiviral treatment. Participants were 94% male and 6% female. The mean age was 37 years, with a range of 18-51 years. The contamination route was that of intravenous drug use in 78% of cases and transfusion in 3%. Other types of contamination were rare, and the route was unknown in 11% of patients. The HCV genotype was identified as 1a, 1b, 3a, 2 and 4 in 28%, 11%, 36%, 3% and 7%, respectively; in 15% data were unavailable. Twelve per cent of patients were also infected with HIV. None of the patients were also infected with the hepatitis B virus. Thirty-seven per cent of patients were treated for drug substitution with methadone (12%) or buprenorphine (25%). Before treatment, the average viral load of HCV was 1227689 IU/mL. A total of 33% had LB before treatment, with a mean histological Metavir score of A1.8 F1.73 and a Knodell score of 8.0. Of the first 100 patients included in the study, 36% had LB and in the second group (patients 101 to 200), only 30% had LB. Analysis was carried out by applying the guidelines set at the French consensus conference held in February 2002. The mean antiviral treatment duration varied between 2 groups of patients: it was 7 months for patients completing therapy and 4 months for patients who had an early termination for medical or non-medical reasons (patients transferred without hepatology care, adverse effects or voluntary end of treatment). No serious adverse effects were found. No final virological data were available for 61 patients, and 24 patients were non-responders. So it could be said that 95 patients (47.5% of all the cases included in the study) experienced a virologically
complete sustained response. The medical factors contributing to sustained response were similar to those in general studies of HCV treatment: genotypes 2 and 3, complete treatment and no HIV infection.

In conclusion, treatment for HCV in jailhouses is feasible and successful; the limitations placed on indications for LBs, as recommended by the 2002 French consensus conference, apply specifically to the inmate population and facilitate access to HCV therapy, besides helping initiatives such as POPHEC, in which hepatologists and general practitioners participate.

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Is heroin addiction related to a dysfunctional processing of reward and hedonism in the brain? Insights from neuroimaging studies

Chantal Martin-Soelch

Summary

The functioning of reward in drug addicts is a major issue both in terms of pathophysiology and in a rehabilitative view. We used a PET imaging device to assess the hedonic functioning of methadone maintained heroin addicts, compared to control subjects, by two modalities: 1) the elicitation of interest by anticipated monetary reward; 2) the neuroimaging correlates of visually elicited pleasure. In heroin addicts fewer brain regions showed activated during tasks implying known monetary reward in comparison to tasks without any reward. On the other hand, the processing of subjectively pleasant videoclips resorted to different brain pathways in heroin addicts. Heroin addicts seem to show a lower level of anticipatory sensitivity to monetary reward, whereas the topography of pleasure-feeling seems to be different from normal subjects’. Such results show a different reward-seeking and reward-feeling status of methadone maintained heroin addicts, although it is to be clarified whether such a status was also fore-running heroin use, or developed as a correlate of addiction.

Key Words: Reward - Heroin Addiction - Methadone Maintenance - PET

Introduction

A large body of empirical evidence indicates that the reinforcing properties of psychoactive drugs are mediated by the mesostriatal and meso-corticolimbic dopamine system. Studies have shown that most psychoactive drugs, including heroin, cocaine, nicotine and alcohol, increase the dopaminergic transmission within this system, especially in the ventral striatum. This system, in its turn, is involved in the processing of reward information (1).
Reward has an important motivational function and is also involved in learning. It can elicit approach and consummatory behaviour. Obtaining reward is associated with pleasant feelings, which give a positive motivational value to the goal-object. The neural bases of reward processes have been investigated with various experimental approaches, including brain lesions, psychopharmacology, electrical self-stimulation, single neuron recording and neuroimaging. Most of these studies indicated that dopamine neurons were involved in the processing of reward information. Furthermore, specific regions of the mesolimbic dopamine system, like the midbrain, the striatum and the orbitofrontal cortex have been shown to be involved in several aspects of reward processing, suggesting that these regions belong to a cortico-subcortical loop that mediates motivational processes. It is not clear, however, whether dopamine is involved in the mediation of the pleasant feelings associated with rewards or is, rather, involved in learning processes.

Because drugs of abuse and rewards are associated with similar neural processes, it can be hypothesized that drug addiction is a dopamine-dependent disorder in which the positive reinforcing value of the drug is mediated through the activation of the mesolimbic dopamine system. On the other hand, the possible role of dopamine in processing pleasant feelings suggests that drug addiction could be related to a dysfunctional processing of hedonic information. We will present here the results of two PET (Positron Emission Tomography) studies that have investigated the neural processing of reward and of pleasant information in heroin addicts.

**Reward processing in heroin addiction**

It is well known that drugs have a rewarding value, but very little is known about the processing of natural rewards in the addicted brain. We have used PET to investigate activation related to the processing of monetary reward in a group of former heroin addicts on methadone maintenance and in a group of healthy controls. The subjects performed a visuo-spatial recognition task during PET acquisition under three different feedback conditions: feedback comprised no reinforcement, a non-monetary reinforcement, or a monetary reward. The tasks were exactly identical except for the reinforcer used. Under the condition involving no reinforcement, the subjects received a nonsense feedback for every response. Under the reinforcement condition, no reinforcement appeared if the response was wrong. As to monetary reward, the subjects were instructed before the scans that they would receive the sum shown at the end of the session. The maximum which could be won was 320 Swiss Francs (approximately 210 Euros). The subjects were thoroughly instructed before the scans, and they performed the task once under all three conditions during a training phase.

Our results showed that fewer regions were activated in response to reward in the brains of dependent subjects. Typical reward-related regions were activated by monetary reward, but not by non-monetary reinforcement, in contrast to the healthy subjects. These results corroborated previous findings obtained in a smoker group showing a similar
C. Martin-Soelch: Is heroin addiction related to a dysfunctional processing of reward and hedonism in the brain? Insights from neuroimaging studies

pattern of activation as that of the heroin addicts in response to reward. Taken together, these results show that there is a common pattern of reward-related activation in the two forms of dependence. This pattern could indicate that non-monetary reinforcement has insufficient motivational value to activate reward-related regions, suggesting that specific reward regions require more stimulation in addicts’ brains (3).

The processing of hedonic information in heroin addiction

In a second study, we investigated the processing of hedonic information in a group of healthy control subjects and a group of former heroin addicts on methadone maintenance. The cerebral blood flow was measured with PET, while the subjects were shown pleasant and neutral film clips. Our results showed that the presentation of pleasant film clips was associated with activation in the striatum and in other typical reward regions in the heroin addicts, but not in the control subjects. These results suggest that hedonic information is processed in a different way in the brain of heroin addicts.

Conclusion

In conclusion, we were able to show at a neural level that there is a dysfunctional processing of reward information in heroin addicts. Furthermore, the reward-related brain activation was similar in two major forms of dependence (heroin addiction and tobacco dependence) and differed noticeably from the activation observed in healthy subjects. Thus, typical reward-related regions were activated only by the highest rewards in dependent subjects. Furthermore, the passive viewing of pleasant information was associated with the activation of typical reward regions in the brain in heroin addicts, but not in healthy control subjects. These findings could indicate that the brains of dependent subjects interpret and react to motivational and emotional stimuli in a different way from the brains of healthy, non-addicted, subjects.

References

4. MARTIN-SOELCH C., MAGYAR S., KUNIG G., MISSIMIER J., SCHULTZ W.,


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<td>SP-CME Pre-conference Workshop - Buprenorphine educational meeting</td>
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<td>Symposium 1 - Heroin Addiction and Related Clinical Problems</td>
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<td>Symposium 7 - Psychosocial Aspects of Heroin Addiction</td>
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<td>Chairman: P. Quigley (Dublin, Ireland)</td>
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INFORMATION FOR CONTRIBUTORS

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