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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Treatment of Opioid Dependence and ADHD/ADD with Opioid Maintenance and Central Stimulants

Olof Blix, Arne Dalteg and Peter Nilsson

Addiction Medicine Unit, Department of Psychiatry, Ryhov County Hospital, Jönköping, Sweden, EU

Summary

Since January 2005 Medically Assisted Rehabilitation of opiate addicts (MAR) is a regular treatment supported by the National Board of Health and Welfare in Sweden. Treatment facilities are now open in most parts of Sweden. At the addiction medicine unit in Jönköping, high dose buprenorphine has been used since 1999, and methadone was added in 2005, when the previously separate regulations for the use of those two substances were merged in the present regulations. ADHD and ADD, together with OCD, are relatively common disorders among drug addicts. Since 2004 we have diagnosed over 150 patients with these disorders at the addiction medicine unit. By November 2007, treatment with long-acting methylphenidate or modafinil had been initiated in 85 subjects. Of those 85, 12 had also met the criteria for opioid substitution. This paper will discuss our experiences with the combined treatment with opioids and central stimulants, as administered to these drug addicts. In this naturalistic study, all 12 subjects (1 female), mean age 38 (range 20 to 51) were evaluated before starting Central Stimulant (CS) treatment with clinical interviews, self-assessments and formal computerized tests (EuroCog). The ambition is to follow each patient’s development through the use of drug tests, interviews (subjects and relatives/significant others), and a retest to evaluate the outcome of the combined treatment.

Key Words: Opioid Dependence - ADHD - Stimulants - Opioid Maintenance

1. Introduction

Medically Assisted Rehabilitation (MAR) of opiate addiction was introduced in a research setting in Sweden in 1966 by Professor Gunne [11, 12], following pioneering studies by Drs. Dole and Nyswander [8]. MAR was long restricted and limited, both as to the number of patients in treatment, and to the clinics that were allowed to provide treatment, by the Department of Health and Welfare. In 1999 high dose buprenorphine (Subutex®) was registered as a pharmacological specialty in Sweden without such restrictions and with considerably fewer regulations. On 1 January 2005, the regulations for the use of methadone and Subutex were merged into a common regulation for MAR, which lifted limitations on the number of treatment providers as well as the number of patients in treatment for methadone. From that date on, only specialists in psychiatry working in addiction treatment facilities have been entitled to prescribe methadone and high dose buprenorphine (HDB). At that time, close to 840 patients were receiving methadone in the existing 6 MAR clinics, and over 1,300 were receiving HDB prescriptions. In January 2008, close to 60 clinics were providing treatment with either one or both compounds to 3,000 patients. The Buprenorphine + Naloxone combination (Suboxone®) was registered in Sweden in 2007, and was recently recommended as first choice when HDB treatment was under review by the Medical Products Agency in Sweden.

Attention-deficit hyperactivity disorder (ADHD) has been recognized for a long time in children, and it is a commonly co-occurring mental disorder among patients with substance use disorders. During the last few decades, it has been established that, in 30-60% of children that have the disorder, it persists into adulthood, though the hyperactivity diminishes, and the attention disorder becomes the major problem for the patient (ADD). In
a 2008 study it was shown that 86.7% of adult ADHD patients had other psychiatric disorders, such as antisocial personality disorder, affective disorders, and abuse of alcohol or drugs. The latter accounted for half of the patients [22].

Treatment of ADHD includes both pharmacological and non-pharmacological strategies. Central stimulants, such as dexamphetamine and methylphenidate (MPH), are recommended as first choice. In a 10-year follow up study, Biederman et al. showed that there is no increased risk for later drug abuse in children and adolescents who received such treatment compared to those who did not [6]. In an earlier meta-analysis, Wilens et al. revealed a protective effect [24]. Current research provides data indicating that stimulant treatment is effective in adults, too [10], but more data are required to confirm long-term efficacy.

Treatment of ADHD patients with the problem of current drug abuse is often regarded as a contraindication for stimulant prescription, but there are some studies on methadone-maintained patients that have failed to show any change in side abuse when stimulant treatment was added to methadone maintenance [17].

In Sweden it became possible in 1997 to prescribe CS drugs to adults with ADHD through licensing. An increasing number of adult patients have been assessed for ADHD from the end of the 1990s. Levin et al. showed a prevalence of 15-24% of ADHD in various substance abuse samples [17]. ADHD is usually accompanied by other psychiatric disorders. In a sample of prisoners, Dalteg et al. (1999) found that ADHD was linked to specific personality characteristics and deviant alcohol reactions [7].

2. Methods

2.1 Treatment organization

The addiction treatment unit at the Ryhov County Hospital was established in 1969 (the in patient detox unit [DU]). In 1973 a rehabilitation unit was added, which later on developed into a day care centre, and around 1990 formed the present outpatient clinic (OPC). The latter has since then developed treatment for alcohol and/or drug-addicted patients with concomitant psychiatric disorders, and/or in need of MAR. The catchment area for the OPC comprises 165,000 inhabitants. The DU has the whole county as its catchment area (330,000 inhabitants). The OPC also serves the whole county in assessing applicants for MAR. The clinic administers methadone treatment throughout the county, whereas HDP is dealt with locally.

The authors represent a multidisciplinary team at the OPC - Olof Blix, MD, Arne Dalteg, psychologist and Peter Nilsson, psychiatric nurse.

2.2 Aims of the study

The main aim of the present study has been to determine whether adult patients with comorbid opioid dependence and ADHD/ADD can be treated with, and benefit from, combined MAR and CS treatment. For other psychiatric comorbidities in methadone treatment, it has been shown by, among others, Ball & Ross [4], that the results of treatment with methadone plus psychiatric treatment and social support improve patients' lives in several ways.

The present study is naturalistic, i.e. none of the originally included patients were excluded, even if some data are missing, and some existing data were collected retrospectively.

2.3 Sample

Patients fulfilling criteria for MAR and ADHD/ADD have been included. Most of them were in MAR treatment when assessed for ADHD, but two individuals were started simultaneously on both treatments; a third was first started on CS-treatment, after which MAR was added. The baseline characteristics of patients were compared with the situation 3 months after starting methadone for ADHD/ADD. The abuse situation 3 months before and after central stimulant treatment was added to opioid maintenance was studied primarily through supervised urine tests whenever these were available.

In Sweden the general inclusion criteria applied for MAR treatment are:

1. A verified history of at least 2 years of dominant opioid addiction according to ICD-10.
2. Abuse of other substances that pose a risk of dangerous interactions with MAR must be manageable or be dealt with before a patient can be included in MAR.
3. The regular treatment service (through the social service system) should be judged to be insufficient as a standalone therapy.
4. A plan for social treatment (vocational, economic, housing, non-medical treatments) should be integrated into a treatment plan.
5. Patient participation must be voluntary.

2.4 Assessment

Current drug history and other important parameters were assessed through the Swedish version of Euro ASI, and through the collection of records from our own and other clinics, the social service system, the Criminal Justice System and the Police, all with written consent from the applicant. In addition, urine specimens taken in MAR during the 3 months preceding the initiation of CS treatment were analysed for benzodiazepines, opiates, cannabis, amphetamines and cocaine; the per-
centres usually have a plan for their social rehabilitation, and a
pharmacological treatment is started. Simultaneously are normally admitted to the DU before patients starting with MAR and CS as abuse. To confirm this, urine tests taken in connection with MAR are used. Patients starting with MAR and CS for ADHD/ADD are normally required to attend from one to three times a week. Supervised u-tests are normally taken once or twice weekly. The focus of the initial months in treatment is to establish a good treatment relationship with the patient. Positive u-tests do not automatically warrant drastic changes to the treatment plan; the difference they make is to provide an incentive to discuss further improvements in treatment.

When the questionnaire for dose titration is administered, we also ask a relative or significant other to give his/her view of the patient’s functioning, if possible. Quite often, those near-the-patient persons take notice of changes before the patient himself/herself becomes aware of them, and they can reassure the patient about his/her improvements.

Blood pressure and heart rate, as well as weight, are measured before the onset of CS medication. Retesting is performed at a minimum frequency of once a year, but when pathological answers are shown, more often, and, when needed, further investigations will be carried out to make possible the treatment of somatic disorders.

One particular problem with this patient group is the difficulty they have in keeping appointments; this, in itself, is a symptom of ADHD. Patients often call the counsellor after the agreed time, to ask what the time of the appointment is. Last-minute attendance is a common pattern for some patients. This problem is best handled with some flexibility and a smile.

2.5 Clinical realization

Once a diagnosis of ADHD/ADD has been confirmed, the patient with his counsellor is scheduled for an appointment with the psychologist and the prescribing psychiatrist. Family member(s) or significant others and, if relevant, the patient’s social worker are invited to participate. The focus is on explaining the meaning of the findings, and to form a treatment plan. This plan, besides the added pharmacological treatment (usually a CS such as MPH), includes social rehabilitation, ADL function and any needs for assistance. When previous vocational experience is missing, special attention must be dedicated to vocational rehabilitation or habilitation.

A prerequisite for initiating CS treatment is that the patient must be free of abuse. Ongoing MAR is not regarded as abuse. To confirm this, urine tests taken in connection with MAR are used. Patients starting with MAR and CS simultaneously are normally admitted to the DU before the pharmacological treatment is started.

Patients who have already been included in MAR usually have a plan for their social rehabilitation, and a social counsellor, in addition to his/her medical counsellor at the clinic. The treatment plan might have to be renewed to address the specific problems that are related to the added treatment, and it is important to include all supporting staff to achieve as comprehensive a treatment as possible. Informative contacts with employers or teachers, when these are involved, are often helpful.

Patients already in MAR are normally required to attend from one to three times a week. Supervised u-tests are normally taken once or twice weekly. The focus of the initial months in treatment is to establish a good treatment relationship with the patient. Positive u-tests do not automatically warrant drastic changes to the treatment plan; the difference they make is to provide an incentive to discuss further improvements in treatment.

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2.6 Statistical considerations

To generalize from a 12-subject sample in a naturalistic study like this is difficult. The results have therefore been interpreted mainly on a descriptive level, even if, on a statistical level, we have tentatively used the Paired-Samples T-test [20].

3. Results

3.1 Subjects

Only one of the 12 patients included was female (8%), compared to the general sex ratio of 20% females in the unit. One patient had impaired eyesight. Three (24%)
were born prematurely. Nine (72%) of them were brought up by their biological parents, one in a foster home and two in other types of institution. All had experienced great difficulty in ordinary schools. They did not keep up with the teaching, showed concentration and learning difficulties, had been bullied and, besides all these problems, they did not bother about school and played truant. Only 33% of the patients had completed senior high school. One of these is a skilled worker. None had started academic studies and none were considered suitable for the military training that is compulsory at around the age of 20; all of them made their living by benefiting from different social welfare systems and engaging in crime at the start of the treatment. They were evaluated for ADHD at a mean age of 38 (range 20 to 51).

Half of the patients have so far been IQ-tested (WAIS-III); their mean general intelligence was 87 (range 60 to 118). The results were slightly higher on the verbal than on the performance side.

The onset of criminality and drug-taking occurred early in the teenage period (12-16 years). There was a tendency for the onset of drug abuse to precede the onset of criminality. Four patients (32%) had displayed deviant alcohol/drug reactions, and at least 3 (25%) were obviously alcohol-dependent, while only 2 (13%) were teetotallers. Almost all had tested positively for benzodiazepines, cannabis, central stimulants, opiates, hallucinogens and ecstasy, while a minority had previously abused solvents. Three (25%) still had an ongoing benzodiazepine abuse, 4 were also cannabis abusers, whereas only two displayed amphetamine abuse. HCV-antibodies were recorded for 10 (83%) of the patients.

Half of the patients so far have also been re-evaluated on their neuropsychiatric symptoms.

### 3.2 Personality traits

The patients were extremely under-socialized; this indicates and confirms their serious social problems and also points to personality disorders (psychopathic and/or schizoid traits). They have high levels of somatic anxiety (physical/autonomic manifestations of anxiety and diffuse discomfort, without any identifiable cognitive correlates) and signs and symptoms of increased muscular tension, to such a degree that they have obviously been suffering from these difficulties for a long time and are in need of physiotherapy. They are easily wearied psychologically, find it difficult to make decisions (psychasthenia), and show a high level of hostility (table 1).

### 3.3 Personality syndromes

The most pronounced personality syndrome among the subjects can be recognized in the extreme forms taken by their acting-out behaviours. All had a conduct disorder or were pre-psychopathic as children (before age 15) and all have been living antisocial lives as adults. They also have a history of anxiety-related syndromes (OCD and social phobia), together with proximity-inhibitional difficulties (e.g. schizotypical - peculiar/strange or magic thoughts, paranoid) (table 2).

All except one (the female) fulfilled the DSM-IV criteria for both childhood and adult ADHD (predominantly Hyperactivity/Impulsivity and “inattention”). They described a chronic course of ADHD symptoms from child- to adulthood. More than half (58%) of the patients were also “short tempered”. Four (33%) patients fulfilled the criteria for Asperger’s syndrome/autistic-like behaviour.

Considered as a whole, the sample is severely impaired in terms of academic achievement, employment, criminality and psychiatric comorbidity.

### 3.4 Global Assessment of Functioning

The mean GAF scores of the subjects during the previous year was 45 and during recent weeks 50. This indicates serious to very serious symptoms, such as suicidal and strange thoughts. They did not care about friends and relatives, and were unable to bring fulfilment to their everyday lives. Most of them needed initial inpatient treatment.

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**Table 1. Personality traits (KSP) in T-values (Mean T= 50± 10).**

<table>
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<th>Max</th>
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<td>91</td>
<td>78</td>
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<tr>
<td>Psychic anxiety</td>
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<td>82</td>
<td>63</td>
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<tr>
<td>Muscular tension</td>
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<td>Social desirability</td>
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3.5 Medication

Half the patients were stabilized on Methadone, at an average daily dose of 107 mg, range 60-130. The other half had prescriptions for HDB (High Dose Buprenorphine), with an average daily dose of 20 mg, and a range of 16-32 mg.

One of the patients (with 16 mg HDB) was medicated with Modafinil (200 mg daily) and the only female patient took HDB 16 mg and MPH Capsules 30+30+20mg. The remaining 10 patients had MPH Oros, with an average dose of 72 mg per day. Half of them were taking MPH once daily, and the others twice daily (8.00 and 14.00).

3.6 The clinic’s follow-up questionnaire

The clinical follow-up showed that the subjects’ irritation/aggressiveness had decreased; their ability to organize their daily living had improved, as had their ability to relax, for example by reading books and/or watching TV, as well as in planning their daily activities in advance. Sleep and inner tensions were somewhat better. Appetite and craving for drugs were unchanged. Very few side-effects were reported. One subject experienced increased tics and involuntary movements.

3.7 Neuropsychological tests and re-tests

The results of the EURO COG re-test after 3 months did not display any major changes.

3.8 Basic neuropsychological functions

Subjects’ reaction abilities were initially mostly within normal range with the exceptions of two-choice visual (Right/Left), where subjects seemed more hypo-reactive. There were no significant changes at re-test (table 3).

All subjects were right handed. Motor speed and co-ordination on the simple dexterity tests were initially within a normal range. There were indications (p<.10 - p<.05) of a decreased motor speed and co-ordination at the re-test (table 4).

Their perceptive and continuous performance, with attention on a certain feature (the letter K) of the environment, while ignoring distractors, were initially below

<table>
<thead>
<tr>
<th>Test/variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Re-test</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audi</td>
<td>10</td>
<td>163</td>
<td>373</td>
<td>240</td>
<td>6</td>
<td>171</td>
<td>373</td>
<td>257</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Visu</td>
<td>10</td>
<td>165</td>
<td>326</td>
<td>232</td>
<td>6</td>
<td>175</td>
<td>339</td>
<td>243</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>2-choice Left</td>
<td>10</td>
<td>236</td>
<td>492</td>
<td>329</td>
<td>6</td>
<td>271</td>
<td>457</td>
<td>328</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>2-choice Right</td>
<td>10</td>
<td>235</td>
<td>439</td>
<td>328</td>
<td>6</td>
<td>225</td>
<td>491</td>
<td>350</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>L/R error</td>
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<td>.0</td>
<td>.5</td>
<td>.27</td>
<td>6</td>
<td>.0</td>
<td>.75</td>
<td>.25</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Inhib</td>
<td>10</td>
<td>275</td>
<td>681</td>
<td>442</td>
<td>6</td>
<td>328</td>
<td>2000</td>
<td>784</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Failed inhib</td>
<td>10</td>
<td>.0</td>
<td>.23</td>
<td>.14</td>
<td>6</td>
<td>.0</td>
<td>.46</td>
<td>.13</td>
<td>n.s</td>
<td></td>
</tr>
</tbody>
</table>
average range, especially within the more difficult version - 'letters as distractors' - indicating, for instance, a high level of dyslectic subjects. Signal detection ability (d-prim) increased significantly (p<.05) over time within the simpler version - 'squares as distractors' (table 5).

### 3.9 Specific aptitudes functions

The visual-spatial competence (Maze-tests) i.e. visual search, visual ability and general intelligence were initially within a normal range and did not change significantly over time. The R/L-quotes indicated these subjects’ general preferences to see solutions on the left side of the screen. This might indicate that the right half of the brain is more active among abusers (table 6).

### 3.10 Learning and memory functions

The learning ability (AL), Short-Term/working memory (STM) and Long-Term memory (LTM) were initially within a normal range. No significant changes were observed at re-test except an indication (p<.10) of worsened Long-Term memory (table 7).

### 3.11 Changes in abuse patterns

All patients took urine tests 2-3 times per week. The results of those tests showed a tendency to reduced or unchanged abuse of all kinds of drugs, except for amphetamines, where a marginal increase was noted, even if from a very low level. Overall, the percentage of negative urine tests increased by 19%, from 66.2 to 79% (Figure 1).

### 4. Discussion

The aim of this study was to find out if treatment that combines opioids and stimulants in a comprehensive setting was feasible for this multi-problem group, and if it could improve the functioning of those otherwise often overlooked individuals. Our results so far indicate that it does, and that it makes a difference not only in reducing the abuse of opioids, which the MAR treatment is well...

---

**Table 4. Finger Tapping. Test and re-test results. Min. max and mean values.**

<table>
<thead>
<tr>
<th>Test/Variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Re-test N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right index finger</td>
<td>10</td>
<td>4.9</td>
<td>8.1</td>
<td>6.3</td>
<td>6</td>
<td>4.0</td>
<td>7.6</td>
<td>5.8</td>
<td>n.s</td>
</tr>
<tr>
<td>Left index finger</td>
<td>10</td>
<td>4.6</td>
<td>7.0</td>
<td>6.0</td>
<td>6</td>
<td>4.4</td>
<td>7.2</td>
<td>5.3</td>
<td>n.s</td>
</tr>
<tr>
<td>Alt R</td>
<td>10</td>
<td>1.4</td>
<td>4.5</td>
<td>3.7</td>
<td>6</td>
<td>1.6</td>
<td>4.4</td>
<td>3.0</td>
<td>&gt;.10</td>
</tr>
<tr>
<td>Alt L</td>
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<td>1.5</td>
<td>4.5</td>
<td>3.2</td>
<td>6</td>
<td>1.6</td>
<td>4.3</td>
<td>2.8</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>Alt R/L index finger</td>
<td>10</td>
<td>3.1</td>
<td>4.6</td>
<td>3.9</td>
<td>6</td>
<td>1.7</td>
<td>4.5</td>
<td>3.3</td>
<td>n.s</td>
</tr>
</tbody>
</table>

**Table 5 Selective perception (K-test 'letters' & 'squares' as distractors). Test and re-test.**

<table>
<thead>
<tr>
<th>Test/Variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Re-test N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Corr.rsps</td>
<td>10</td>
<td>43</td>
<td>86</td>
<td>72</td>
<td>5</td>
<td>69</td>
<td>95</td>
<td>80</td>
<td>n.s</td>
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<tr>
<td>Err.rsps</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td>3.7</td>
<td>5</td>
<td>0</td>
<td>7</td>
<td>3.0</td>
<td>n.s</td>
</tr>
<tr>
<td>D-prim</td>
<td>10</td>
<td>2.5</td>
<td>4.6</td>
<td>3.6</td>
<td>5</td>
<td>3.4</td>
<td>4.6</td>
<td>4.0</td>
<td>n.s</td>
</tr>
<tr>
<td>Raptime corr</td>
<td>10</td>
<td>1480</td>
<td>5979</td>
<td>2213</td>
<td>5</td>
<td>1616</td>
<td>4972</td>
<td>2395</td>
<td>n.s</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test/Variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Re-test N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corr.rsps</td>
<td>10</td>
<td>87</td>
<td>141</td>
<td>116</td>
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<td>119</td>
<td>143</td>
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<td>n.s</td>
</tr>
<tr>
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<td>1</td>
<td>10</td>
<td>4.6</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>3.6</td>
<td>n.s</td>
</tr>
<tr>
<td>D-prim</td>
<td>10</td>
<td>2.8</td>
<td>4.7</td>
<td>3.7</td>
<td>5</td>
<td>3.7</td>
<td>4.8</td>
<td>4.0</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>Raptime corr</td>
<td>10</td>
<td>655</td>
<td>1321</td>
<td>874</td>
<td>5</td>
<td>634</td>
<td>868</td>
<td>759</td>
<td>n.s</td>
</tr>
</tbody>
</table>
### Table 6 Maze-tests (with target info & no target info). Test and re-test.

<table>
<thead>
<tr>
<th>Test/Variable</th>
<th>Target info</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Re-test</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxrows</td>
<td></td>
<td>10</td>
<td>8</td>
<td>15</td>
<td>12</td>
<td>5</td>
<td>9</td>
<td>18</td>
<td>15</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>% corr</td>
<td></td>
<td>10</td>
<td>.49</td>
<td>.93</td>
<td>.70</td>
<td>5</td>
<td>.40</td>
<td>.79</td>
<td>.58</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Process speed</td>
<td></td>
<td>10</td>
<td>1.15</td>
<td>10.1</td>
<td>3.9</td>
<td>5</td>
<td>2.06</td>
<td>11.4</td>
<td>7.0</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Inspec speed</td>
<td></td>
<td>10</td>
<td>1.65</td>
<td>59.8</td>
<td>17.2</td>
<td>5</td>
<td>7.0</td>
<td>58.4</td>
<td>33.5</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Check time</td>
<td></td>
<td>10</td>
<td>.56</td>
<td>1.4</td>
<td>.95</td>
<td>5</td>
<td>.44</td>
<td>1.4</td>
<td>.82</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>R/L quotient</td>
<td></td>
<td>10</td>
<td>.21</td>
<td>.56</td>
<td>.38</td>
<td>5</td>
<td>.25</td>
<td>.55</td>
<td>.39</td>
<td>n.s</td>
<td></td>
</tr>
<tr>
<td>Rubouts</td>
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<td>10</td>
<td>.01</td>
<td>.74</td>
<td>.22</td>
<td>5</td>
<td>.01</td>
<td>.36</td>
<td>.09</td>
<td>n.s</td>
<td></td>
</tr>
</tbody>
</table>

### Table 7. Associative Learning (AL). Short-Term Memory (STM-Digit span) and Long-Term Memory (LTM). Test an re-test results

<table>
<thead>
<tr>
<th>Test Variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Re-test</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL Correct rsps</td>
<td>10</td>
<td>35</td>
<td>62</td>
<td>.464</td>
<td>6</td>
<td>35</td>
<td>54</td>
<td></td>
<td>47.2</td>
<td>n.s</td>
</tr>
<tr>
<td>Error rsps</td>
<td>10</td>
<td>0</td>
<td>2</td>
<td>.8</td>
<td>6</td>
<td>0</td>
<td>2</td>
<td></td>
<td>0.5</td>
<td>n.s</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>STM</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max forward</td>
<td>10</td>
<td>5</td>
<td>7</td>
<td>6.2</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td></td>
<td>5.7</td>
<td>n.s</td>
</tr>
<tr>
<td>Max backward</td>
<td>10</td>
<td>3</td>
<td>6</td>
<td>4.6</td>
<td>6</td>
<td>4</td>
<td>7</td>
<td></td>
<td>5.8</td>
<td>n.s</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Variable</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>LTM</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct rsps</td>
<td>10</td>
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<td>47</td>
<td>13.0</td>
<td>6</td>
<td>1.0</td>
<td>23</td>
<td></td>
<td>10.5</td>
<td>n.s</td>
</tr>
<tr>
<td>Error rsps</td>
<td>10</td>
<td>17</td>
<td>71</td>
<td>41.1</td>
<td>6</td>
<td>11</td>
<td>71</td>
<td></td>
<td>42.3</td>
<td>n.s</td>
</tr>
<tr>
<td>Remembered</td>
<td>10</td>
<td>0</td>
<td>7</td>
<td>2.1</td>
<td>6</td>
<td>0.0</td>
<td>2</td>
<td></td>
<td>.05</td>
<td>&gt;.10</td>
</tr>
</tbody>
</table>
known to do, but also some of the bothering symptoms of ADHD/ADD. The group studied was too small to generalize from, but the results are encouraging, and warrant further investigations.

From a neuropsychological point of view, there were few significant changes at re-test in this small sample. However, indications of a decreased motor speed and co-ordination were observed, together with an increased capability in perceptive signal detection. Contrary to expectations, there were no indications of more of “think before you leap” and fewer executive errors. It is noteworthy that the subjects’ right hemisphere seems to be more active than the left one. When considering these subjects’ learning and memory functions, there were no indications of any improvements. It is even possible that the MAR treatment alone can contribute to the reduction of ADHD/ADD symptoms, as mesolimbic dopamine levels are affected by µ-opioid receptor stimulation. However, the role of dopamine and its receptors in the rewarding of drug effects and the role in treating ADHD calls for further studies [14].

Previous studies have not shown any significant effects on craving or drug abuse behaviour [17], but the changes noted in our group as early as 3 months after treatment started indicates that it can reduce the abuse of benzodiazepines, cannabis and even opioids. The number of patients continuing with cannabis was reduced to one person on 6 months, whereas 3 patients were occasionally using cannabis before the added treatment. Figure 1 only gives the total percentage of positive u-tests in the group. It might be interpreted as a result of the decreased inner tension and anxiety that these patients attribute to the added CS treatment when they answer the clinic’s questionnaire.

On the other hand, amphetamine use turned out to have increased marginally in our sample. This can be interpreted in terms of some patients’ continuing habit of self-medication, but could also indicate that even a ‘mild’ CS such as MPH can trigger a latent amphetamine craving.

Our general impression, though, is that those patients who occasionally took amphetamines were doing so to test if they could achieve a better level of functioning. Many of them, after an increase in MPH, discovered that the lower level was better overall; as a result, they not only cut out their amphetamine intake, but also asked for a cut in MPH dosage. So far we have noticed this tendency among our approximately 50 non-MAR ADHD/ADD-patients who were treated with CS medication and were addicted to drugs other than opioids.

5. Conclusions

All in all, the addition of this new tool in treating our addicted patients has been an inspiring experience in our everyday work. Our feeling is that we are at the beginning of a new era of addiction treatment, where the basics from MAR are being translated into a similar, but at the same time different method of helping a patient group that has been overlooked for too long, while suffering
considerably from our previous lack of understanding of their problems.

Role of funding source

This study was supported by internal funds.

Contributors

The authors contributed equally to this work.

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present study.

References


Received June 17, 2008 - Accepted October 1, 2008
Pre-Conference Sessions

Sunday, April 26, 2009

EUROPEAN OPIATE ADDICTION TREATMENT ASSOCIATION (EUROPAD) - HEROIN ADDICTION AND RELATED CLINICAL PROBLEMS

TIME: 1:00 PM - 5:00 PM

Chairmen: Icro Maremmani, MD
Pisa, Italy, EU
Marc Reisinger, MD
Brussels, Belgium, EU

1:00 PM Efficacy of Opioid Agonist Therapy on Psychopathological Symptoms: Methadone vs Buprenorphine
Icro Maremmani (Pisa, Italy, EU)

1:20 PM Repressive Strategy Against Liberal Strategy in Treating Heroin Addicts in Russia
Vladimir Mendelevich (Kazan, Russia)

1:40 PM Economic Evaluation of Interventions To Treat Opiate Dependence: A Review of the Evidence
Christopher M. Doran (Sydney, Australia)

2:00 PM The European Experience Delivering Buprenorphine and Methadone. Comparison Between France and Portugal (regulations, clinical experience, practice)
Pascal Courty (Clermont-Ferrand, France, EU), Luis Patricio (Lisbon, Portugal, EU) and Didier Touzeau (Paris, France, EU)

2:20 PM Foundamental Principles and Rules in Treating Heroin Addicts at "Fondation Phenix" in Geneve, Switzerland
Michel Bourquin and Jean-Marie Rossier (Geneve, Switzerland)

2:40 PM Screening and Treatment of Viral Hepatitis B and C in Inmates With and Without Opioid Agonist Therapy. Results of Four French National Surveys (2000-2005)
Andre-Jean Remy (Perpignan, France, EU)

3:00 PM What Treatment is Good Treatment? Clinician's Reflections on Patient Perspectives
Alexander Kantchelov, Tsvetana Stoykova, Orlin Todorov and Alexander Belchev (Sofia, Bulgaria, EU)

3:20 PM Heroin Addiction and Mortality
Barbara Lovrecic and Mercedes Lovrecic (Lubiana, Slovenia, EU)

3:40 PM Opioid Maintenance Therapy (OMT) and Cardiac Arrhythmia. Mortality Assessment in a Norwegian National Registry Study
Thomas Clausen, Katinka Anchersen & Helge Waal (Oslo, Norway)

4:00 PM Treating Heroin Addicts in Jail
Andrej Kastelic (Lubiana, Slovenia, EU)

4:20 PM Opiates and Alcohol. Important Clinical Connections
Albrecht Ulmer (Stuttgart, Germany, EU)

4:40 PM Discussion

5:00 PM End of Forum

In collaboration with EUROPAD-Italia and Italian Society of Addiction Medicine (SITD)
Dihydrocodeine for the Treatment of Alcohol Dependence

Albrecht Ulmer, Markus Müller and Bernhard Frietsch

HIV- and Addiction-Disease-Practice, Stuttgart, Germany, EU

Summary

Objective: In most cases, alcohol dependence shows a profile similar to that of many chronic diseases, but no effective basic treatment comparable to that adopted with the other illnesses has been established up to now. In particular, patients with repeated relapses, despite a broad range of therapeutic approaches, and patients who are unable to attain what is essentially a state of abstinence from alcohol, continued to need a basic medication. Methods: Convinced by a few specialized colleagues who reported successful treatments of alcohol addicts with Dihydrocodeine (DHC) and by a first own patient of ours who showed a complete reduction of his severe alcohol craving when given Codeine-based pain medication, we went on to treat as many as 77 (M/F: 55/22) heavily alcohol-addicted patients with DHC, beginning in 1997. Right from the start, the data were documented meticulously. We present a retrospective analysis of this documentation here. Results: The patients had a history of a total of 1060 medically assisted detoxifications and specialized therapies. The 4 year-retention rate was 26.1%, including 6.5% of treatments that had a successful outcome. In our 12-step scale on clinical impressions, we noticed a significant improvement from a mean of 3.5 to 6.7. The demand for medically assisted detoxifications in patients who had at most 2 years left was reduced by 63%. Mean GGT improved from 201.1 U/l at baseline to 57 U/l after 4 years. The MCV value also showed a significant improvement. Mean GGT of patients with additional chronic hepatitis C improved from 198.3 U/l at baseline to 86.4 U/l after 1 year. Conclusions: Our data are preliminary, and these are practice-generated results, which are far from reflecting the whole potential of this new approach. Between 10 and 20% of these patients recorded no good effects from DHC. In around half of the patients the treatment was abandoned for several reasons, in some cases because of the anxiety caused by the pioneering nature of this non-established therapy: a treatment with partly overcautious dosages. But in about 25% of the patients, DHC was an almost perfect medication, sometimes even crucially better than all previous approaches, even in absolutely desperate cases. A lot of regular studies are needed, comparing different substances, settings, dosages and clarifying the cause and pathomechanism of the effects. This should be done because it seems that we are standing at a gateway leading into immense new opportunities. In the long run the breakthrough will be a question of the right mixture of scientific investigation, well-structured implementation with sufficient control, but also, and this may be most important factor, enough trust in our patients and the prescribing doctors. On a long-term basis there will be no success without a structure that supports and reassures, but also represents, this trust.

Key Words: Dihydrocodeine - Alcohol Dependence

1. Background

Basic treatments have been developed for most diseases with a chronic or polyleptic character, e.g. asthma, hypertension, diabetes, rheumatic disease, migraine, especially if they are associated with too many or too severe exacerbations. Dependence on alcohol shows a similar profile in most cases, but, to date, no effective basic treatment has been established. The need is extremely evident, mainly for patients with no working abstinence and repeated relapses, despite all the therapeutic approaches implemented, and for patients who are unable to achieve an urgently needed abstinence from alcohol.

Basic treatment means basic medication. In alcohol dependence, the aim of that medication should be a reduction of craving, relapses and alcohol-related problems. The first hope was to achieve this by using substances without any potential addiction-inducing capacity. The practical relevance of such substances remained limited. The number of prescriptions of the most prescribed substance in Germany, Acamprosate, is so low (0.7 Mio DDD 2006, [21]) that it does not reach 1% [11] of these addicted patients or 5% of the appropriate patients [12], and most of those who take it report no effect. The effect of the opioid antagonist Naltrexone does not seem crucially stronger, though the substance is more frequently prescribed in...
the Scandinavian countries. The role of Disulfiram has remained absolutely marginal for decades.

The failure of the antagonistic or addiction-avoiding substances probably offers a crucial hint about how to treat patients. Why are addictive substances used? If we ask patients themselves, they answer: ‘As tranquilizers, to blot out bad things in the brain, sometimes to overcome displeasing self-consciousness’. This implies that they have unpleasant, inhibiting perceptions, in some cases uninterruptedly, in others sporadically. They describe it as a grave handicap, which is often hard or impossible to bear. No wonder, then, that the craving repeatedly turns out to be stronger than willpower.

From this point of view, it is clear enough that what many of them need is an agonist that is strong enough to bring some of the positive effects of alcohol. This is not as easy as in the case of opiate addicts, where we know the opiate receptors. Heroin, for instance, can be replaced by other substances acting at the opiate receptors, like Methadone, Codeine, Morphine and Buprenorphine.

For alcohol, too, a replacement is needed, because it is too toxic and too hard to control. But nothing is known about alcohol receptors. What kinds of agonists are able to give some of the positive effects of alcohol without the associated dangers? In this case, too, we get important hints from our patients. Some try a switch to or a completion with benzodiazepines; this is very questionable, because of a more dominant, negative impact on psychic resilience and, in most cases, no good therapeutic control over the real dosage is possible.

Possibly related to this, but clearly showing an improvement, are the first encouraging results obtained with Gamma-Hydroxybutyrate (GHB), a GABA (B) receptor agonist, so far mainly documented in Italian studies [1, 2, 3, 7, 8, 22, 23, 24, 26]. GHB is effective in reducing alcohol intake and in maintaining abstinence, partly better than Naltrexone or Disulfiram. Some results were not much better than with the antagonistic substances, and considering their marginal clinical role, this is only the beginning of a new way forward. Critical experiences due to dangerous or fatal poisoning with GHB have been reported, for instance from Spain [14] and Sweden [20].

Another substance with a similar agonism is Baclofen. In this case too Italians have demonstrated that severely alcohol-dependent patients can be treated very effectively with this agonist [4, 5].

In Germany, Clomethiazole is the standard medication for the treatment and prevention of alcohol withdrawal syndrome. It is also widely used as an agonist substance for long-term treatment, but almost only by non-specialized physicians without a therapeutic concept. A lot of life-threatening emergency events with combined Alcohol-Clomethiazole poisonings led to official declarations that Clomethiazole is obsolete for outpatient treatment [9].

Some alcohol-dependent patients report the good effects of amphetamines, and that they need more alcohol if they have no access to these substances.

What about the opioids? Heroin addicts often report that they stopped drinking too much alcohol when they switched to heroin. This substance acting at the opiate receptors was obviously able to displace alcohol. Did it happen because of a greater potential for exhilaration?

In any case, a connection between alcohol and opiate receptors has been scientifically known for many years. Publications, in particular by Fröhlich and Gianoulakis [13, 15, 16, 17], have proved this clearly. The partial efficacy of treatment with opiate antagonists [28] also demonstrates this connection. Caputo et al., once again an Italian group, published results suggesting a possible effect of short-term Methadone administration in reducing alcohol consumption in a population of non-alcoholic heroin-addicted patients in 2002 [6]. On the other hand, many Methadone maintenance patients have alcohol-related problems, and their physicians are often unsure how to overcome them. In individual cases, raising the dosage of the opioid to very high levels (Methadone for instance, to 400 mg daily) was extremely successful, giving us another hint that opioids can help to overcome alcohol addiction.

For our specific procedure, we have learnt both from colleagues and patients. 2 pioneering German doctors, originally specialized in maintenance treatment for opiate addicts, reported and published their first convincing experiences in treating alcohol-dependent patients with Dihydrocodeine (DHC) [18, 10]. This idea was first made public as early as 1929 [19], but was then forgotten for decades. Our personal scepticism was crucially minimized when one desperate patient, permanently suffering from strong craving and repeated relapses, reported to us in 1997 that the intake of 3 analgesic tablets each containing 30mg Codeine had strongly reduced his craving. Very cautiously, and with his comprehensive written consent, we started to treat him with DHC systematically.

2. Methods

Since then, we have treated 77 (M/F: 55/22) heavily alcohol-addicted patients with DHC. The whole prescribed medication, its dosage, all further relapses, detoxifications, laboratory results and the general impression, were continuously documented right from the start. We now present the retrospective analysis of this documentation.

3. Results

The medical history of these patients was impressive: 922 previous medically assisted detoxifications, 679 of them in a hospital; additionally, 138 therapies in specialized addiction clinics. Mean age of the patients was 46.0 y, mean duration of ostentatious alcohol consumption 22.1 y. In 93.2% the indication was an inability to live with or
without alcohol, in 33.8% there were urgent somatic and in 29.7% urgent social reasons. 15 patients had a history of sporadic or dependent use of opiates, which had been overcome for 9.4 years on average.

DHC has to be normally taken q.i.d.. Starting dosage in most cases was 120 mg (4 x 30mg) daily. The mean dosage was raised to 287 mg daily after 21 months and >2 years (n = 21) had an improvement from 3.5 to 8.1 at the end of the 2 years (Figure 3).

Of 46 patients, included until 12/03, 9 (19.6%) were still on treatment 4 years later. 3 had successfully finished the treatment without further relapses (4 year-retention rate among all patients was 26.1%) (Figure 2).

The actual status of the 77 was: 18 remaining on treatment (23%), 6 had finished with sustained success (8%), 53 were no longer being treated, and had been unsuccessful (69%, including 14 (18%) who left the treatment within the first month). In our 12-step scale on clinical impressions, we noticed a statistically significant improvement from mean 3.5 to 6.7. Patients remaining of all patients fell to 1.13 at month 9 but then rose to 7 after 4 years and reached 100% no relapse level by the 5th year (Figure 5).
Mean GGT of all patients improved from 201.1 U/l at baseline to 79.2 U/l after 1 year (or 216.6 in all patients, including more than one year before, to 79.2 U/l, p=0.05) and to 57 U/l after 4 years (n then only 6, p therefore only 0.093, Figure 6).

There can be no doubt: all the attempts made with agonists, the general success of maintenance therapies for opiate addicts and the widespread ineffectiveness of abstinence-based, or treatments that aim to achieve abstinence, indicate that this chronic disease has to be treated in the same way as other chronic diseases – with effective basic medication. It must be a substance, or a combination of substances, able to give patients at least some of the effects of alcohol, in many cases. The experts have to find out and perform studies on which substance is the best, generally and individually, and what the best setting is for this kind of treatment.

All these substances, in principle, have to face four central problems:
1. Addiction;
2. Danger in case of abuse;
3. The black market;
4. Uncontrolled prescriptions from doctors who have no therapeutic concept.

On item 1: Our patients have a chronic disease with an addiction or a craving for substances that have an addictive potential. One of their central problems is their denial of the addiction and its chronic character, together with the continuing failure of their attempts to escape the addiction. What they need is to finally accept the chronic character of the disease and their addiction. The addiction has then to be treated in the best possible way, with settings and substances that allow the subject to live as well and as free of danger as possible. Of course, there is no universal solution applicable to all patients. The treatment has to be as individually differentiated as in other chronic diseases, especially in mental disorders. Practical experience and evidence from scientific trials have to be animatedly connected. Addiction itself is widely acceptable, if all this can be guaranteed, and in many cases it is much better than an unsuccessful attempt to live without any addiction.

On item 2: The tendency to abuse agonistic substances is always strong; as a result, none of these substances can be considered innocuous. But when they are used regularly, many of these substances are relatively harmless and well tolerated. It is therefore our responsibility to do everything possible to ensure that their use shows a high degree of reliability. This is a central issue for an intelligent infrastructure, as it comprises both the single treatment and the whole logistical network that covers an entire region, with all its regulations and rules. We have experienced very different conditions deriving from the regulations of earlier periods, and are therefore sure that it is possible to find very intelligent solutions that guarantee a satisfactory quality of this treatment without exorbitant bureaucracy, restrictive regulations and dramatic disadvantages for our patients.
The side effects, as well as the acute and the chronic toxicity of each substance, must be taken seriously. Consideration of these factors and their consequences have to be well-balanced. Unduly lax handling and excessively restrictive administration are both able to do a lot of harm, and this is a crucial objection that can be made against any form of use of agonistic medications. But a very reliable and effective middle course is possible. We are able to report this very encouraging experience.

Good infrastructure of specialized centres and practices, a good level of cooperation well with less specialized physicians, cooperation with all interdisiciplinary partners, as well as with patients’ relatives and other contact people, are all necessary. Financial incentives can help to build this infrastructure. Central details include: support features, specialists, support centres, handouts, quality circles, meetings, training and retraining offers, and control over the quality of support. All this should not be restrictive or frightening, but bring encouragement and a sense of support.

On the plane of individual treatment, a few basic medical rules for addicts are helpful and crucial:
- regular, thorough, empathy-based dialogues before and during therapy,
- an interdisciplinary approach,
- written dosage regulations, along with advice to take doses on schedule and never as needed,
- strict bookkeeping of consumption (my personal recommendation),
- prescription and rationing of the substitutes, counted out for a limited period of time only,
- blood and/or urinary parameters, to be checked as random samples.

This is not the place to explain this in greater detail. A summary is essential: what has been shown is that a much more qualified and humane treatment can be provided by adopting an intelligent regimen of this type, instead of lots of restrictive regulations laden with mistrust. It will never be possible to exclude the danger of fatal abuse one hundred per cent, but we can minimize this risk crucially. We must weigh this residual risk against all the other risks deriving from too much anxiety and avoiding all possible risks, may, on all overall basis, be higher than the real risks arising from abused substances on the black market. What is needed is a cooperative, pragmatic consideration of all aspects.

On item 4: we have to minimize uncontrolled prescriptions from doctors who have no therapeutic concept. For the same reasons. These prescriptions induce and perpetuate individual abuse and give an incentive to the black market. It is no solution to prohibit nearly all prescriptions, by limiting them to only a few physicians or centres. These restrictive concepts are implemented in most countries. They are based on mistrust, while trying to ensure the best possible quality. This is not the place to discuss this thoroughly. But we can point out that we have had a much better experience by applying a much less restrictive system, based on much more trust, support and pragmatic evaluation. We are able to solve this problem in a very satisfactory way, but we have to work on it. It does not happen automatically. And it is clear that new therapeutic concepts are a question of having an appropriate infrastructure both for individual treatment and for whole regions.

DHC has a special history in Germany, touching on all these problems. For many years, it was the most prescribed substitute for opiate addicts, while the prescription of Methadone was strongly restricted until 1998. The prescription of DHC was neither forbidden nor really allowed; it was left unregulated. There was no research, nor coordinated evaluation: the psychiatric experts railed against it, and doctors who prescribed it had to fear major difficulties in case of any bad event. By contrast, addicts said: ‘I need it, it helps me’, and many stories of impressive success were reported in circles of prescribing doctors, mainly GPs. Thus many prescribed it, but many of them partly on the basis of hearsay, without integration in any quality circle, and without regulation, because they were absolutely left alone. As a result, many prescriptions were made out without observing the basic rules of medicine for addicts mentioned above.

Treatment of opiate addicts with DHC became more widespread without rules, standards or controls. More and more deaths occurred, in each case connected with disastrous mismanagement, showing the central importance of proper management and the dangers of using this substance without a responsible structure. The best way to have optimized the situation would have been to install support centres and promote the foundation of quality circles. But there was too much resistance in society. Therefore an opposite course was implemented, against the advice of experienced doctors and despite some good published data [21,29]: DHC was then almost forbidden; it was only allowed in rare emergency cases if no other admitted substitute would be tolerated.
Doctors were forced to switch these patients over from DHC to Methadone. This was an interesting experience, because many patients reported: ‘It’s not the same’. Most patients preferred Methadone, but their doctors recognized increased alcohol-related problems. This was never properly evaluated well, but was a development often reported by practitioners. It should also be mentioned that the new, much more restrictive rules changed our therapeutic relationship with patients in a fundamental way. Crucial components of a good treatment (‘good’ always comprises ‘based on trust’) as well as of projects for the development of a flourishing addiction medicine were lost.

Codeine and DHC remained widely forbidden. They were almost never prescribed any more, and now have an unproven, bad reputation. In other countries without this special history, the development took a quite different direction. In Scotland, for instance, Robertson et al. were able to publish a study in 2006 that compared DHC with Methadone, concluding that these two substances have a similar level of effectiveness and are safe to use in treating opiate addiction [27].

The special nature of events in Germany has given it an inappropriate background for the introduction of DHC as a basic medication for alcohol-dependent patients. For this very reason we have to be especially cautious. Any future attempt would mean starting from scratch.

In addition, we have to deal with several fundamental objections that DHC treatments can only:

- Worsen the situation by making alcohol dependent opiate addicts, too; patients would then have two addictions, which is worse than having only one. We never observed this in any case. Where the effects of DHC were insufficient and there were new relapses with alcohol, we had to take one of two decisions: either to increase the DHC dosage, because it appeared to be the right way to go, or to leave the DHC treatment by tapering the dosage. Both options were easily applicable in most of these cases.

- Worsen the situation, because mixed intoxications with opioids and alcohol are more dangerous than those with alcohol alone. This is a question of having an adequate therapeutic concept and order. In our management of cases, we never saw a really dangerous mixed intoxication.

- Worsen the situation, because opiate addiction is not better than alcohol dependence. This is an old misunderstanding. Switching from alcohol to opiates brings a crucial improvement to the situation of most patients: alcohol is the cause of severe acute and long-term toxicity. Opiates do indeed bring a dangerous acute toxicity in the case of serious overdoses (which were responsible for the cases of death described above), but nearly no long-term toxicity at all. Alcohol is almost uncontrollable. Medically prescribed opiates are perfectly controllable – a crucial difference and improvement.

- Worsen the situation, because the degree of dependence is greater: withdrawal from opioids is more difficult than from alcohol. This objection is based on the illusion that the way to stop an addiction as quickly as possible is by withdrawal. The concept of basic therapies must be long-term, with the aim of achieving sustained stability, and this is normally achievable not by withdrawal but by a very gradual reduction in the dosage of the medication up to abstinence. For some patients, it is certainly better to keep them on adequate medication for the rest of their lives.

All these objections go to show that many questions need to be clarified. Anxiety-based restrictions are a handicap on the implementation of new developments. They are often misunderstood as being able to replace the development of a good infrastructure. Our results provide only a first hint. Ordinary trials for more evaluation and basic knowledge (by comparing different substances, settings, dosages and clearing the cause and path mechanism of the effects) are needed as a first step, then the development of a good standard guaranteed by specialized doctors; in addition to these criteria, there should be no barriers against the inclusion of normal practitioners. Quite the contrary: we need to avoid the outcome that GPs leave this field to a few experts, or that they ever get the feeling of being left alone. Our attention should at last turn to a good and encouraging support system able to ensure a good practical standard; it should not be focused on a lot of rules and discouraging laws.

Our treatments cannot yet represent an optimized standard. The setting and the whole logistical framework have not been developed yet. Patients realize that many other experts react sceptically. Any explanation that includes reservations makes them anxious. 10 - 20% of the patients had no good effect from DHC. Lastly, our dosage was cautious, possibly too cautious for several for our patients. Due to the extremely pioneering character of the treatment, we avoided giving higher dosages, for fear of inducing a double addiction in the long run. In reality, we did not observe this development in any single case. The predominant improvement in most cases and the almost perfect result in a quarter of our patients showed that there is now a new way to improve the situation, even in absolutely desperate cases.

Our results, meanwhile, covering more than 10 years, indicate long-term perspectives. There can be no question about it: the all-or-none law is no longer valid in the treatment of alcohol dependency. It’s always a lucky situation to achieve a doubt-free, stable abstinence from alcohol. But, then again, it’s absolutely expedient to treat all the patients who are desperate because of recurrent relapses despite all interventions, including ours. Some of the patients reported that the DHC-based therapy was a much better solution for them than all the previous
abstinence-based therapies, and they were sorry they had not had this opportunity much earlier.

A few patients were suffering from a concomitant attention deficit disorder. For a short time, they were simultaneously being treated by our psychiatrists with methyl-amphetamines, and some of them showed a second crucial improvement. This experience is still at too early a stage for a regular publication, but the first impression is very clear: another helpful way forward is now available.

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Contributors

The authors contributed equally to this work.

Conflict of Interest

The authors have no relevant conflict of interest to report in relation to the present study.

References


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Use and Abuse of High-Dose Buprenorphine (HDB) Obtained Without a Prescription: a French Survey

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Summary

Objectives: To gain information on the profile of patients using High-Dose Buprenorphine in France without a medical prescription.
Methods: This was a naturalistic survey on 27 survey sites (n=298) comprising three different groups: people who had always obtained their HDB without a prescription, people who had obtained HDB both with and without a prescription over the previous month and an intermediary group who had previously obtained it on prescription, but not over the course of the previous month.
Results: In terms of treatment and supervision objectives, significant differences were found between the group of patients who were under the supervision of a doctor and those who continued to obtain HDB without any prescription. Discussion: Medical supervision is a central factor in treatment. Conclusion: Treatment education for patients, medical training for prescribers, and pharmaceutical form appear to be means that need to be developed simultaneously to optimize the treatment.

Key Words: High-Dose Buprenorphine; Misuse

1. Introduction

High-Dose Buprenorphine (HDB) is considered safer to use than methadone, but it also brings with it the benefit of a more flexible prescription framework, as it is well suited to local GP practices; this makes it accessible to more people in France.

Moreover, restrictions on patients are minimized: it is dispensed via a pharmacy and not daily, and no urine checks are needed. Any doctor may prescribe it.

According to the circular of March 31 1995 of the DGS [5], the main objectives of substitution treatments may appear general: basically, beyond the sphere of HDB treatment itself, prevention factors and harm reduction are important, too.

Substitution treatments should contribute towards raising the levels of social integration of patients suffering from major opiate dependence.

Annexe 1 of circular DGS/DH No. 96/239 of April 3rd 1996 [6] sets out the objectives of HDB substitution treatment and provides recommendations for its prescription, which should optimize inclusion in a treatment programme and the medical supervision of any disease associated with opiate dependence.

These circulars view substitution as a phase, the final objective being, ideally, that each user should build him- or herself a dependency-free life, which should include becoming independent of the treatment itself.

During the ANAES consensus conference (2004, www.has.fr), the “clearly positive” impact of opiate substitute treatment was described: broad access to treatment (over 100,000 patients), a reduction in the number of deaths due to heroin overdoses (3,500 lives saved), improved social integration for 50% of patients, 3 times fewer infringements of the drugs law between 1995 and 2003, and cost savings. But even substitution treatments have their limits: heterogeneous access to treatment, misuse of the medication (the injection and snorting of Buprenorphine, death due to methadone overdose and Buprenorphine-Benzodiazepine boosting, a black market for treatments, continuation of black-market use, little impact on hepatitis C virus contamination, and continuing stigma associated with dependency.

HDB is registered on list I. Previously available on...
production of a prescription in the form of a counterfoil book for a 28-day supply, it is now dispensed on production of an authorized prescription (“ordonnance sécurisée”), which is prescribed and dispensed subject to the current regulations on addictive substances.

Subsequently, several legal restrictions have been applied in this area: in particular, Decree 20/09/1999 [10], whose main aim was to deal with the issue of certain Buprenorphine-based medicines, was introduced in the context of certain derivative uses; it restricts dispensing, which was initially unlimited, to a maximum period of 7 days, with the possibility of an extension to 28 days if that is specifically authorized by the consultant.

In France, according to SIAMOIS/InVS data and OFDT estimates [13], in 2003 the policy of HDB substitution applied to 84,500 people, according to a high estimate, and 71,800 patients according to a low estimate. Additionally, health-insurance data (OFDT estimate) provide an estimated figure of 79,000 for those who received an HDB prescription in the second half of 2002; those data allow the identification of several HDB-user population:

- Patients registered on a treatment programme under medical supervision (estimated at 52,000)
- Patients receiving prescriptions for substitute products in an irregular manner, the “substitution intermittents” (estimated at a minimum of 22,000)
- People responsible for significant resale activity (an estimated 5,000 “-traffickers”).
- A fourth group comprising the “non-prescription” consumers, who are difficult to quantify but are estimated by the “low-threshold” structures to be in the region of 4,000.

However, according to the TREND 2005 report, [1] among people familiar with treatment mechanisms, substitution treatments increasingly seem to be part of a medical programme that is supervised by a doctor. That was true of 94% of these patients in 2005.

The misuse of HDB (i.e. with the aim of getting high, or regulating the effects of other TREND5 products) would seem to be worsening in the front line structures, since, even though the number of HDB users for the previous month remained stable (44% in 2006, 43% in 2003), the percentage of users exclusively misusing HDB rose to 28% in 2006, compared to 11% in 2003.

In parallel, the percentage of users stating that they mix therapeutic use (i.e. with the aim of getting off heroin TREND) and abuse is on a downward trend (34% in 2003, 23% in 2006) [2, 3]. In addition, it seems that there is a diversification in the profiles of people who abuse HDB.

A projection performed on a regular evolution of the 2003 data leads to an estimate of 96,500 HDB users at the end of 2006. In the French context, with the widespread use of HDB and derivatives as mentioned in various reports, it seemed to us to be important to find out more about the section of the population that continues to obtain this molecule without any prescription.

Our aim was to ascertain the actual use of a variety of medicines containing High-Dose Buprenorphine, in other words, the specific manner in which they are obtained and used by those ‘on the margins of treatment’, who may see a doctor regularly or occasionally, but who obtain it in parallel through means other than a pharmacy purchase.

2. Materials and methods

As the objective of the study was to collect information on the use of HDB by people who obtain it without a prescription, exclusively or otherwise, the type of study selected as being most appropriate was a naturalistic one.

2.1 Inclusion criteria

The inclusion criterion adopted was the use over the preceding month of HDB obtained by a means other than prescription.

2.2 Recruitment of the participants

The recruitment of subjects was carried out at 27 survey sites, distributed over 22 zones, organized around a target city and its metropolitan area, located in 12 of the 22 administrative regions of France.

Participants were recruited using two successive approaches:

Initially, the researchers responsible for carrying out the interviews made contact with various centres and organizations operating at each site, so that they could facilitate their contact with people who were taking HDB and would be likely to meet the inclusion criteria.

Subsequently, ongoing recruitment proceeded using the ‘snowball’ technique, with each person surveyed being asked to put the researchers in contact with other people taking the medication.

The aim of this multiplication of survey sites and recruitment methods was to avoid the focus of the survey falling on a single centre or on only one specific population.

All of the interviews were carried out during the course of December 2006. They were all held in a neutral place.

2.3 Data collection

The interviews were carried out by a team of researchers trained in psychosociological interviewing methods. They were conducted with the help of a structured pen-and-paper-type questionnaire made up exclusively of closed questions, even if some of them did allow for the inclusion of non pre-coded answers. The expected duration...
of an interview was 45 minutes. The questionnaire, which was devised specifically for the survey, had previously been tested on 6 people to check its comprehensibility, the relevance of its application in relation to the medical history of the interviewees, the range of different types of trajectories encountered and its acceptability.

This questionnaire included 47 items covering the associated consumption of psychoactive substances, the methods used for obtaining, using and administering HDB, the reasons for using it and taking a substitution treatment; 7 of the questions were dedicated to finding out the socio-demographic characteristics of the interviewees.

2.4 Statistical analysis

Comparative analysis of the different groups described above was performed with the aid of the usual tests (Chi-square and Student’s t-tests). The significance thresholds were set at 99% and 95%. The data were processed with the aid of COSI software.

2.4.1 Analysis criteria

A systematic comparative analysis was performed on the different groups of people participating, defined according to whether or not they had obtained HDB exclusively without a prescription during the previous month.

Thus, 3 groups of people were defined as follows:

° The first group included those who had always obtained the HDB they use by methods other than medical prescription. This group was labelled: “never with a prescription”.
° The second group was made up of people who, at earlier stages, had purchased HDB at pharmacies with a medical prescription, but who, during the previous month, had only obtained HDB without having any prescription. This group was called: “without prescription during previous month”.
° The third group comprised people who, during the previous month, had obtained and used HDB both with and without a prescription. This group was defined as being: “with and without prescription during the previous month”.

3. Results

3.1 Number of questionnaires processed

298 questionnaires were gathered and processed

° 56 were given to people who had never received a prescription for high-dose Buprenorphine; these were classified as “never with a prescription” GR1;
° 174 were given to people who had obtained the HDB both “with and without prescription during the previous month” GR3.

3.2 Socio-demographic criteria (Figure 1)

There are no significant differences between the three groups in terms of indicators of sex, age and type of income. It should, however, be noted that the proportion of women (33.9%) and of those who were earning a salary (33.3%) was highest in the group who had obtained HDB both with and without prescription during the previous 2 months. Besides this, a higher proportion of the people in this same group were living as one of a couple (33.9%) and had stable accommodation (57.5%); these proportions were significantly different from those in the group who had not received a prescription for HDB over the course of the previous month (only 35.3% of these patients had stable accommodation, and the percentage for women patients was as low as 19.1% - p<0.01).

3.3 Social-welfare cover (Figure 2)

Those who had never received a prescription for HDB were the least likely to be affiliated to the CMU (universal medical cover) (42.9%) and those most likely to have no social security cover (32.1%). These proportions differ significantly from those of the group as a whole (total group) and from the group who had obtained HDB both with and without a prescription during the previous month (p<0.05).

3.4 Associated uses (Figure 3)

The patients who had obtained HDB both with and without a prescription over the course of the previous month poly-consume less than the others: 82.8% also used opiates and/or stimulants over the course of the previous month, compared to 95.6% of the group who had
was, however, significantly less frequent (p<0.05) in this group (33.9%) than in the group who had never obtained HDB on prescription (50%).

There is, however, no difference between the groups as far as the snorting of HDB is concerned: this practice affected between 24.5% and 33.9% of the interviewees.

60.9% of those who also had HDB on prescription

3.5 Ways of taking HDB (Figures 4, 5 and 6)

The average amount of the most recent quantity of HDB consumed for the group as a whole was 10.2 mg, ranging from 9.46 mg in the group of people who had obtained it both with and without prescription to 12.25 mg in the group that had never obtained it on prescription; these differences were not significant. Was this daily amount taken in one or several quantities over the course of the day? The questionnaire does not permit a response to this question.

The injection of HDB is a factor in all the groups, including the group that obtained it with and without prescription during the previous month; this practice was, however, significantly less frequent (p<0.05) in this group (33.9%) than in the group who had never obtained HDB on prescription (50%).
over the previous month were taking HDB every day, which significantly differentiates this group (p<0.01) from the total group (43.6%), from the group who had never received a prescription for HDB (19.6%) and from the “without prescription during previous month” group (19.1%).

In parallel, the highest proportion of people using HDB about once per week (19.6%) or less frequently (21.4%) was found in the group who had never been given a prescription for HDB. These patients showed a notable difference with respect to the group who had obtained HDB with and without a prescription (2.9% for each of these frequencies - p<0.05) and with the total group (8.4% and 7.7%).

3.6 Reasons for obtaining HDB without a prescription. (Figures 7 and 8)

The main reasons why the interviewees needed to obtain HDB by another means during the previous month are, for those who obtained it exclusively without a prescription over the course of the previous month, not wanting to go and see a doctor (65.3% of the group). For those who had seen a doctor during the preceding month or previously, the main reason given was that the quantity prescribed to them was insufficient (68.2% for the total group and 67.2% for those who had also obtained it on prescription over the preceding month).

3.7 Reasons for using HDB (Figure 9)

Half of the patients (50%) stated that they had been using HDB in order to stop taking heroin permanently, and this reason was the one most commonly given (63.2%) among those who had obtained HDB both with and without prescription over the previous month (a significant difference (p<0.01) with respect to the two other groups).

The story is very different for those who had not been given a prescription for HDB over the course of the previous month and those who had never been given an HDB prescription. Of these groups, 61.8% and 57.1%, respectively, stated they had used HDB only when they were unable to use heroin. These proportions were significantly different from the group that also obtained HDB on prescription during the previous month (31% - p<0.01) and the total group (42.9%).

3.8 Number of doctors consulted

Those who obtained HDB both with and without prescription during the previous month state that they have one doctor only in 71.8% of cases, and, when they have several doctors, the average is 2.47.

4. Discussion

The aim of our survey was to describe the population groups on the basis of the way in which they accessed HDB. The three groups showed different initial characteristics according to whether they had received a prescription for HDB during the previous month or had never been given one, while the third group was located between these two positions.

There were more people who were employed with a salary, had stable accommodation, were living as a
couple, and also more women, in the group that had a prescription for HDB during the previous month. Despite its lower incidence than in the other groups, the injection of HDB among those who had received a prescription during the previous month was not negligible. However, the fact of having had a prescription in the previous month did result in better observance of treatment, since the treatment substance was taken every day in a very large majority of cases.

For the group of patients who had HDB on prescription during the previous month, HDB was mainly being taken as a means for permanently getting off heroin, whereas in the other two groups most patients used it when they were unable to obtain heroin.

Despite these differences, things are not so clear-cut, because the groups show many similar characteristics, in terms of associated uses, the HDB doses being used and recourse to snorting.

The impression given is, rather, that of a continuum, a progressive approach in which regular visits to a doctor will gradually modify the attitude of patients towards more regular supervision. The role of the prescribing doctor is also central, because, in 71.8% of cases, those who are currently supervised (or who had been given a prescription during the previous month?), have only one doctor.

The amounts taken do, in fact, correspond to the treatment dosages recommended by the AMM (from 9.46 to 12.25 mg/day), and one might well ask whether patients who say they take heroin because the dosage prescribed for them is too low do in fact have a legitimate point, which, if acted on, could permit a significant reduction in abuse.

The benefits of medical supervision have been referred to in previous publications [4, 7-9, 11, 12, 14] but the reasons for abuse are also at issue here, in particular the potential benefits to be won by modifying the HDB dosage.

Even if it is difficult to achieve, the long-term supervision of a cohort group would be appropriate for the study of behavioural modifications among the different groups.

5. Conclusion

Some positive characteristics have emerged from our study but it remains true that further progress can be made.

Substitution with HDB necessarily involves 3 main actors: the patient, the prescriber (but the pharmacist needs to be considered, too) and HDB itself. Potentially, improvement seems to be feasible on the following conditions:

- The patient: regular medical supervision, a sufficient dose and an appropriate way of taking the treatment. A higher dose is both desired and feared by patients
- The prescriber: finding the right dose is an issue that requires the education of GPs about treatment and global take-home care
- The medication: one might consider ways to improve the pharmaceutical form and the addition of an antagonist to HDB treatment, with the aim of improving the correct use of the medicine.

Role of funding source

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Conflict of Interest

The authors has no relevant conflict of interest to report in relation to the present study.

References


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EUROPAD ITALIA 4

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A 10-Year Evaluation of Chronic Pain Patients Treated with Opioids

Forest Tennant

Veract Intractable Pain Center, West Covina, CA, USA

Summary

Over the past 15 years laws and guidelines have been widely promulgated to allow physicians to prescribe opioids for severe, chronic pain patients who have non-malignant conditions. To date little is known about the outcomes of long-term opioid pain therapy. Reported here is an evaluation of 24 patients with non-malignant conditions who have been in continual opioid treatment for at least 10 years. Data collected indicates that some chronic pain patients greatly benefit from long-term opioid therapy. Almost all (22 of 24: 91.7%) patients report that their pain has permanently decreased over time, and the great majority (20 of 24: 83.3%) believe that opioids continue to relieve their pain as well as when treatment was initiated. All patients report they can now do a variety of activities and physical functions they could not do prior to opioid therapy. The major complications of opioid therapy detected to date are hormonal abnormalities which can be easily managed with replacement therapy.

Key Words: Chronic Pain - Opioid Treatment

1. Introduction

The general public has, in recent years, demanded improved pain cure including the use of opioid drugs. A great part of this demand has been implementation of laws and promulgation of regulations and guidelines that permit physicians to prescribe opioids for severe chronic pain. The author resides and practices in the State of California, USA that has, in the past 15 years, allowed physicians to prescribe and patients to receive opioids by enacting an “Intractable Pain Act”, “Pain Patient’s Bill of Rights”, and issuing written guidelines for opioid treatment. Consequently, enough severe, non-malignant pain patients have now been treated with opioids to begin long-term evaluation of this treatment. Reported here is an evaluation of 24 severe, chronic pain patients who have taken daily high dosages of opioid drugs for at least 10 consecutive years. These patients remain in opioid treatment as they have had positive outcomes.

Despite the energetic and forceful efforts to make opioids available for non-malignant pain treatment, there are almost no reports available on the outcome and merits of opioid therapy beyond about three years [5-7].

Information regarding the long-term outcomes of opioid treatments is needed to determine if long-term, opioid therapy produces a quality life with acceptable side-effects, and if opioid treatment may permanently reduce pain.

1.1 Criteria for Admission to Opioid Treatment

24 Patients have been treated at an ambulatory clinic in Los Angeles (West Covina) County, California, USA. All were referred by physicians who had initiated a variety of pain treatments that were incompletely controlling the patient’s pain. Documentation of chronic pain severe enough to treat with opioids was done by medical and pain history, review of past medical records, physical exam showing some evidence of sympathetic discharge (i.e. tachycardia, mydriasis, hypertension,) and family member validation that pain was disabling and interfering with activities of daily living. To be eligible for opioids, patients had to describe their pain as “constant” and report that it impaired some physiologic functions such as sleep, eating, concentration, memory, and endurance.
1.2 Clinical Treatment Procedures

The initial choice of opioid medication was based on previous exposure or experience and the options offered by the patient’s health insurance plan. Initially patients attended the clinic daily or weekly to stabilize following opioid induction and titration. After this period, follow-up visits were monthly. Long-acting opioid dosages were titrated upward over a 4 to 6 week period to reduce baseline pain and suppress sympathetic discharge signs. Short-acting opioids were added to the regimen to provide rescue medication for pain flares or breakthrough pain. All patients were taught stretching and weight-bearing exercises specific to their pathology. All patients were highly encouraged to take daily vitamins and other dietary supplements and to eat a protein-rich diet to provide an abundant supply of systemic amino acids. Periodic opioid blood levels have been determined to verify sufficient therapy, and patients are periodically tested for serum levels of cortisol, pregnenolone, and testosterone.

2. Methods

In preparation for and just prior to this conference, 24 patients who have daily taken opioid medication for a minimum of 10 years were evaluated by chart review and a 19-point questionnaire completed by the patient. Specific questions were asked to provide basic knowledge related to the treatment outcomes of these individuals:
1. Has pain increased, decreased, or remained static?
2. What activities can now be done that couldn’t be done before beginning opioid treatment?
3. What complications from opioids or the pain have developed during treatment?
4. Do opioids still provide pain relief or have they lost potency?
5. What exercise and dietary measures do you do?

Charts were reviewed for details including opioid dosage, serum levels, and medical complications or consequences.

2.1 Characteristics of Patients

This group of patients consists of 16 females and 8 males. Ages range from 30 to 79 years. Major causes of their pain are post-trauma neuropathies and arthropathies, spine degeneration, and abdominal adhesions or neuropathies. (Table 1) The opioids taken are quite varied, but all patients take the long-acting opioid, methadone, or a long-acting morphine, oxycodone, or fentanyl formulation and one or more short-acting opioids for breakthrough pain or emergency pain flares (Table 2). All take a variety of ancillary medications such as muscle relaxants, sleep aids, hormone replacements, and dietary supplements. The majority (22; 96.7%) report they do regular stretching exercises. Most eat a breakfast (18; 75%) and have a protein-rich diet. (20; 83.3%) all take one or more vitamins or other dietary supplements (Table 3).

3. Results and Outcomes

Twenty Two (22; 96.7%) of 24 patients believe their pain has decreased over time and 22 of 24 (83.3%) believe their opioids still provide the same relief as when they started treatment. The remaining 4 patients report their opioids don’t ‘hold and provide pain relief as well as before’. (Table 4) Patients were asked if they are now able to do a variety of activities and physical functions which they could not do prior to initiating opioid therapy. All patients reported one or more activities or functions that they can now do. For example, a majority reported they can get out of bed everyday, shop or visit friends, take a trip in a car, or take walks. Significant, but less that a majority, reported that before opioid treatment they

<p>| Table 1. Causes of chronic pain requiring opioids (N=24) |
|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Cause</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-trauma with arthropathies and neuropathies</td>
<td>7 (29.2)</td>
</tr>
<tr>
<td>Spine degeneration</td>
<td>6 (25.0)</td>
</tr>
<tr>
<td>Abdominal Adhesions or Neuropathies</td>
<td>5 (20.8)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (8.3)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>3 (12.5)</td>
</tr>
<tr>
<td>Hip Necrosis</td>
<td>1 (4.2)</td>
</tr>
</tbody>
</table>

<p>| Table 2. Opioid currently used (N=24) |
|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>N° of opioids currently used</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 (8.3)</td>
</tr>
<tr>
<td>2</td>
<td>14 (58.3)</td>
</tr>
<tr>
<td>3</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>Opioids currently used</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>6 (25.0)</td>
</tr>
<tr>
<td>Morphine</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4 (16.7)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>9 (37.5)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>10 (41.6)</td>
</tr>
<tr>
<td>Methadone</td>
<td>7 (29.2)</td>
</tr>
<tr>
<td>Meperidine</td>
<td>1 (4.2)</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>1 (4.2)</td>
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<tr>
<td>Levophanol</td>
<td>1 (4.2)</td>
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couldn’t dress without assistance, drive a care, attend church, have normal sexual relations, garden, or care for a pet. (Table 4)

A number of new or emerging medical conditions were identified in this group over the 10-year period. (Table 5) All these conditions directly or indirectly involve the endocrine and cardiovascular systems. All but one male developed hypotestosteronemia. One male developed severe anemia requiring blood transfusions that resolved with testosterone replacement. Five (20.8%) females developed low serum pregnenolone or cortisol levels requiring replacement. Several patients developed osteoporosis (5, 20.8%) or loss of dentition (10, 41.7%). Weight gain, diabetes, and hypertension were common. Neurologic complications of seizures, myoclonus, tremors, hyperalgesia, or dementia have been observed. No hepatitis, renal, or gastrointestinal complications with the exception of minor constipation have been detected. One patient has developed symptomatic coronary arteriosclerosis.

4. Discussion

While several reports of opioid-treatment of non-malignant conditions relate positive results, this report is the only one to evaluate patients with non-malignant conditions who have been treated with opioids for 10 or more years [1, 5-7]. The longest follow-up we can identify is about three years. [5]. A most cogent outcome is that the majority of patients reported that their pain had decreased and their opioid drugs were still effective in relieving their pain. Patients reported a variety of activities and physical functions that were possible with opioid treatment.
In addition to humane, relief of suffering, the ability of patients to be able to have a quality life will continue to drive a public demand for opioid treatment.

Some patients developed medical conditions during opioid therapy. Just how many are pain induced, opioid produced, or simply inherent to the patient is not clear. Opioid therapy is known to lower serum testosterone in males, and this occurrence was found in most male patients [4]. Severe pain is known to over-stimulate the pituitary-adrenal-axis and raise serum cortisol and catecholamine levels that may be related to the development of obesity, diabetes, tooth decay, osteoporosis, hyperlipidemia, tachycardia, and hypertension [3]. No neurologic complications including dementia, hyperalgesia, tremor, or seizures have been detected [2]. It may be that these conditions would be more prevalent and serious in this group if they had not been treated with opioids. It is also very possible that opioids prevented early deaths in this group. Much additional study is needed to determine cause and effect of medical conditions in opioid-main tained patients.

On-going evaluation of long-term pain patients will have to be done without the benefit of comparisons with randomized, placebo controls. It is now considered unethical and even illegal in some states such as California to withhold opioid treatment if a patient requests it.

5. Conclusions

The majority of long-term, opioid treated patients report that their pain has decreased suggesting that opioids may allow or even promote some neurologic healing. It may be that opioid therapy prevents a number of medical complications of pain and prevents early death that may emanate from over-stimulation of the pituitary-adrenal-axis and possibly by excess electrical stimulation produced by damaged nerves. No neurologic complications such as dementia or hyperalgesia have been observed. Even though the number of patients evaluated here is relatively small, the great improvement in their quality of life and physical functioning is so positive and the complications of the therapy so easily managed that long-term opioid therapy should continue to be provided and evaluated.

Role of funding source

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Conflict of Interest

The author has no relevant conflict of interest to report in relation to the present study.

References


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Psychotherapeutic Experiences with Methadone Maintained Patients in the Framework of Multidisciplinary Clinical Institution

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Summary

This communication presents a number of theoretical and clinical formulations that belong to a psychodynamic framework specifically constructed to foster the understanding and treatment of drug addiction. I find this framework useful not merely for the purpose of conceptualizing drug addiction as a clinical category, but also in explaining the complex experiences involved in the therapeutic process to people suffering from that condition. Contemporary psychoanalytic tradition sees drug addiction as an unsuccessful attempt to ward off the unbearable and unmanageable effects through self-medication, but also, more importantly, as a massive disorder originating in early interactions with significant others, resulting in a fragmentation of the self that prompts the individual to self-injury, constant traumatic experiences and a paradoxical fear/pain/pleasure relationship with the drug via addictive fantasies. All of this, enacted in everyday life and in therapeutic sessions, evokes complex emotional experiences on the part of patients, therapists and whole institutions. Relieving, bearing, getting to understand and, crucially, modifying these experiences is seen to be the task at stake in the therapeutic encounter. The final part of the article reflects on some of the advantages for the psychotherapeutic work that derive from methadone maintenance treatment and well-organized team work within a specialized clinic.

Key Words: Methadone Treatment; Psychotherapy.

From a psychotherapeutic point of view, experience can be seen as a combination of affective states, perceptions, representations and memories organized as mental events. We now know, from a variety of developmental studies, that the modification and gradual integration of affects into emotional experiences that can be known and used are determined by complex genetic dispositions, as well as by human relationships, notably by those held with the figures who provided care early in life [7, 9, 18, 20]. This datum testifies to the significant relation between affect representations and internal representations of human relationships which are conceptualized as images of the self and the other in interactions reinforced by affective links or emotional tones. Thus, from a representational point of view, subjective experience includes intersubjective elements. For example, the urge to gain feelings of well-being, which are so important for the development of the self, is experimentally proven to be related to the setting up of a background of safety, connected with the internal models of secure representation of the attachment figure [5]. Any lack of such representations leads to emotional disorganization, and of feelings of fragmentation, or even chaos.

In short, the human ability to tolerate and make use of emotional experience cannot be taken for granted. It is a developmental achievement connected with the capacity for accurate representations of affect - states which are gained through interactions with parental objects capable of empathic mirroring and reflective containment of the infant’s affective expressions [8].

Implicit or unconscious functions of the mind, called defence mechanisms, play an important role, too. They are set to perform adaptive manoeuvres, which have the power to rearrange the representational world. Primitive
mechanisms, such as the splitting of the self and its object, projection, idealization and others, intervene in shaping the representations of the object, modifying them so that they end up resembling the unconscious self-representations. This prevents a more mature establishment of self and object boundaries, and affects the overall integration of internal and external reality. The quality of the emotional interplay with parental responses which provide secure emotional containment, such as the adequate representation of a child’s thoughts and feelings, allows the individual to internalize those very capacities that are seen as prerequisites for symbolic representations of one’s own mental states in terms of wishes, thoughts and beliefs of any kind, not only as devastating and overwhelming expressions of affect. So the mirroring and containing capacities of the caregiver, which are seen as two interwoven processes of replication and acceptance of outward expressions of subjective internal experience – expressions founded on an underlying empathic attitude – provide the infant with representations of its internal state. That state is manageable, while remaining different from the caregivers’ own emotion – features that allow it to be internalized as a self-state and be used for self-regulation [1].

These day-to-day interactive processes play crucial role in establishing a sense of identity and an awareness of oneself as a feeling and thinking being capable of introspection. Alternatively, early parental failures connected with emotional unavailability or disorganized and abusive care-giving may result in serious impairments of self-perception and self-control, affecting the entire personality structure, and leading to an exhausting use of pathological defence mechanisms. Such inabilities in parents, due to their own emotional difficulties, make them react to their children’s negative affect with expressions that may be overwhelming, threatening and even alien in nature and content. Instead of reflecting their children, such parents are likely to defensively push them back, because of a real incapacity to tolerate them; in this way they fail to represent those feelings as belonging to the child, but mark them to be felt as their own states of intolerance. The outcome is that no secondary or symbolic representation of an infant’s affective state can be established. The child will unconsciously attribute the affect to the parent, alienating his/her own emotional experience and, instead of regulating it, the interaction with the caregiver will escalate the negative state, so leading to a kind of traumatization.

The traumatic consequences of the affect produced in these cases can be recognized in various deficits of the personality structure, such as fragmentation of the self, lack of empathic or mentalizing capacities, tendencies to somatize instead of verbalizing emotional experiences; these are none other than some of the typical features of the way the borderline personality is organized [1, 11].

In line with these formulations I now wish to present a summary of the basic psychoanalytical understanding of addiction.

Many recent views on addiction have emphasized that substances are used for the purpose of managing intolerable affective states [3, 6]. Some authors speak of a defect in the stimulus barrier, resulting in incapacity of the self to ward off repeated painful experiences; they have seen substance use as augmenting this defective barrier, or else as a substitute for it. This also suggests that what is normally a developmental process of differentiation, desomatization, and verbalization of affects may turn out to be strongly impaired in addicts. There are specific affective states, including agitated feelings, anxiety, depression, rage, and shame, that addicts attempt to manage through the use of drugs [14, 22].

Khantzian, for example, focused attention on a self-medication hypothesis in which an individual’s choice of drug is the result of the pharmacological action of the drug in alleviating the individual’s principal painful affect. He and coworkers have observed that addicts seem to have a deficit in a group of ego functions involved in the anticipation of danger and in self-protection, which they have called “self-care” functions. They have emphasized the importance of this deficit psychology in substance abusers, a finding that helps to explain the self-destructive nature of drug abuse. Khantzian has also considered a view that addictive behaviour serves as an unconscious attempt at mastery over poorly understood and passively experienced suffering, by creating a dysphoria which is controllable and understandable. Accordingly, some authors have viewed the choice of a drug as dependent on its influence over the most troubling of affect: narcotics are used to reduce or eliminate rage, shame, and feelings of abandonment; amphetamines and cocaine to give a sense of grandeur, or to provide a line of defence against underlying depression, and so on.

From a different perspective, many analysts have described the use of drugs as an object functioning as a substitute for a yearned-for parental figure or object relations. Kernberg [12] saw addictive behaviour as a gratification of primitive, oral instinctual needs; as an enacted wish for reunion with an idealized parental object through an activation of “all-good” self and object images. Similarly, Kohut referred to addictions as “narcissistic behaviour disorders”. He viewed the disturbance in addicts as due to the mother’s failure to function as an adequate idealized self-object, but he saw drugs serving “not as a substitute for loved or loving objects, but as a replacement for a defect in the psychological structure [15]”. Others have also emphasized a “narcissistic crisis” in drug abusers, in which the collapse of a grandiose self, or an idealized object leads to feelings for which drug use is an attempt to respond.

Contemporary with the strong interest being shown in the psychoanalytic literature for borderline states are current views of drug addiction as a traumatic disorder of early relationships where the vulnerabilities of the self are related to neglectful, abusive and chaotic emotional
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Environment, only to be intensified later by the repeated traumatization of a fragile self. The trauma is attached to an emotional chaos where the affect becomes a thing that should be acted upon and manipulated in a very concrete way. Thus the sheer repetition of addictive suffering, inseparable from addictive relief, is a ritual of “repetition enactment” designed to inflict psychophysiological torment, perhaps in the hope that psyche will be able to master unmanageable past and current traumas by structuring and controlling this “event” according to the premeditated ceremony acted out by addicts. Addicts unconsciously prefer to inflict trauma upon themselves rather than finding themselves in a “shock trauma” that leaves them helplessly victimized. In this precise connection, Dodes [6] stresses the role of the drug as a defence against helplessness made possible by creating the paradox of being in control while losing it. Speaking from the perspective of this early trauma, the difficulty of working with the most severe cases of this pathology is related to an internal situation that is imbued with great excitement, because pleasure and pain are perceived in mixed forms once a state of emotional chaos looms nearer, and the bond with the chaotic primary object borders on an experience of mutual destruction involved in what Bollas calls borderline craving [2].

In the context of drug addiction, the concept of “transitional objects” has its place, too. It connotes the infant’s first grasp of the “not-me possession marked by something inanimate and cherished (a soft blanket, toy, teddy bear, etc...), which must have an affective tie to the mother in the course of emotional and physical separation from her”. According to Winnicott, transitional objects are used with the purpose of ameliorating and helping the processes of separation and differentiation from the primary object, but they can also have their pathological function. For the heroin addict, the concept of a transitional object is transformed into a pathological process, while the drug and the equipment used, such as needles, become fetish-like transitional objects, dysfunctional and lacking the most important adaptive cognitive and affective expressions. In this way, transitional objects become available for use with the precise role of inanimate but omnipotent objects; this is one of numerous dysfunctional ways suffering addict has to cope with separation, extreme anxiety and fragmentation [17].

Of course each summary of psychological insights into the meaning and use of drugs is bound to remain incomplete and related to individual cases only, but it will come as no surprise that psychotherapy with drug addicts raises the same issues that arise in any seriously damaged and maladaptively defended patients (for this category, patients with borderline personality disorder are exemplary).

As already suggested by my choice of topic, the aim of psychotherapy is bound up with the possibility of gradually changing the system of self-regulation by rendering the affects containable and thus providing new opportunities for the organization of self-experience. In Bion’s terms, every psychotherapeutic experience can be seen as a series of transformations that bring together a factual situation, emotional states and representations in hope of discovering the meaning of their links and interdependence. The psychodynamic therapeutic situation invites and allows the patient to actualize or enact feelings, representations and defences in the presence of the therapist in a specially designed setting where transference-countertransference dynamics are found to take centre stage in the process. The term ‘transference’ implies that patients bring to life old models of interaction between self and other, where the mental world of the therapist becomes part of their emotional state. According to Sandler [19], the therapist becomes an embodiment of a wish, a figure offering safety, a victim or a persecutor, depending on the affect that unconsciously prompts the patient to assign roles to the therapist. The open attitude or ‘role responsiveness’ argued for by Sandler allows the therapist to identify the assigned role without fully enacting it; to perform a containing mental function that could later lead to interpretation of the transference and an internalization of new meaning. This is not an easy task, bearing in mind the specific transference manifestations of patients with addictions. Their basic characteristics, following Langs [16], could be presented as direct expressions of affects and inner fantasies maintained with a strong belief in their validity. They are often enacted impulsively in a poorly disguised manner, with their unbearable qualities projected into the therapist. Such transferences usually bring into the open very strong aggressive feelings, which patients with addictions tend to act out in abusive relationships.

Early in her therapy with me a young woman with heroin addiction had left twice in the middle of her previous sessions; later, she went on to tell me that she had gone to a party after she felt so lost and abandoned in her therapy, and had taken a needle from a person with AIDS. Only after a few sessions did she add that she hadn’t used the needle on that occasion, because she was held back by the thought that I might be the only person still capable of believing there was something good left inside her.

Another type is the narcissistic transference in which patients press their need to actualize omnipotent idealizations both of themselves and the therapist, vigorously defending their inner world against feelings of helplessness, uncertainty and dependence. One case of this type is that of Mr. B, who for months came very late to his sessions, just to tell me that he was doing perfectly well, hanging out with his dealer, and having access to free drugs, but not using them, because he was simply enjoying his position of superiority over other users. At the same time, he was constantly saying how grateful he felt for being able to work with me, because he knew that I was the best professional in the clinic.

The term ‘countertransference’, on the other hand,
signifies the emotions which the patient induces in the therapist. More precisely, we speak of ‘countertransference reactions’ where the active conflicts in the therapist are in specific interaction with the projected parts of the patient’s self. That is the reason why most common countertransference reactions in the field of addictions are of the same order as the transference manifestations just mentioned; they inflict feelings of helplessness, frustration, anger and even rage on the therapist, combined with defensive manoeuvres, such as rescue fantasies, withdrawal or rationalized superiority.

For hours and hours on end I felt angry, useless and abandoned by Mr. N, a patient in his third year of treatment, who, after achieving a steady remission from heroin, would come to his sessions well after the agreed time, only to tell me that he did not find any purpose in coming, because with the help of methadone his was doing just fine. Instead of working through these difficult feelings of emptiness and abandonment, I often enacted the active position of a powerful, knowledgeable therapist, who, in the very few minutes left at the end of each session, would make complex, often confusing interpretations of his unconscious wish to put me in his situation of being someone helpless and left alone. Only after I was able to take in seriously the role of being a helpless and abused child and to mourn my own omnipotent saviour fantasies, was I able to become more in touch with my patient. Not words and interpretations, but my acceptance of the role of someone who, even if benevolent, still didn’t know exactly how he could help this patient, prompted Mr. N to make a move, resume his therapy and tell me that what had stopped him for so long was the idea that I would be so triumphantly happy to tell him one day that I had cured him. Now he sees the cure as his own task and at most I can play a role in it.

Several main roles, according to Burian, oscillate in various combinations, between the patient and the therapist through the transference-countertransference dynamics. The idealized, omnipotent saviour, the victim, the perpetrator and the cold mother are a few instances among others [4, 10].

Almost every psychotherapy starts with idealizations which unconsciously bring to life the relationship with all good objects, providing wished-for relationships and states of well-being. These representations are inevitably split off from the bad parts of the self, those imbued with aggression, hate and contempt of oneself, which are easily externalized and disowned by the patient. Patients often expect therapy to work like a drug, producing rapid gratification and predictable responses, and they can feel let down and betrayed when it does not work out in that way. There is a constant swing between goodness and badness, which makes the patient and therapist move between feelings of self-importance and uselessness through projective and introjective mechanisms. Besides feeling unskilled and incompetent, the therapist who takes in patient’s aggressive projections could feel persecuted (a victim) and, at a later stage, a persecutor who does not understand the patient, but only re-enacts his or her internal traumatization. A typical enactment on the part of the therapist in such cases is to give up his benevolent neutrality and become very rigid in his/her thinking and use of technique, building a wall between himself and the patient by applying rules and theories. Or, alternatively, by performing certain boundary violations, he may constantly try to reassure himself and his patient that he will not stop being a good object, even while suffering a constant rejection and disempowerment.

As the therapy progresses, the early relationship patterns are brought into the transference in a very concrete manner. The ambivalence, shame and guilt are no longer tolerated, but totally disowned and externalized to the point where the therapist is perceived as cold, rejecting mother, abandoning its child to internal chaos and unable to protect it from any real or imaginary injury. Once such externalization is achieved, a patient no longer has any interest in his/her relationship with the therapy, which is perceived as undermining their attempts to separate themselves from their disowned parts. They seek to maintain the weak balance in themselves through outside relationships (acting outs), such as marriage, finding a job, or, in the worst scenarios, drug dealing, which often lead to heavy relapses. Survival of the therapist and therapy in these cases proves very difficult, since the therapist feels as if he/she is taking part in the destruction. One case in point is that of Mr. P (of whom I am hearing much in staff supervision); he stopped attending his groups after he took to drug dealing directed at other patients, then locked himself in his home for weeks, and suffered a breakdown while demanding that his parents supply him with money and drugs, while saying he would allow his therapist to see him if only she visited his home. It needed a serious team effort and an even bigger effort from the therapist, who refused to succumb to his demands, but stayed in touch with his suffering through phone calls, to bring this patient back into therapy, in which he now starting his 4th year.

Having made these observations, which cover an inseparable part of the psychotherapeutic experience with addicted patients, one inevitably ends up by asking what actually brings about change in these patients. Of course, there is no mechanical, straightforward answer to that question. It has already been suggested that an empathic mirroring and consistent containment of emotions of the kind implied in the therapeutic setting and attitude, combined with interpretation of here-and-now transference, could lead to minimization of splitting, and bring about a gradual integration of representations and affects [13]. This could be achieved only by constant transformations within the therapist’s mind that require him/her to endure the destruction of, and attacks on his or her good objects, by maintaining the hope that, even in the most severe states of distress and chaos, the patient could go on experiencing the presence of the therapist, who
remains alive and thinking, and so capable of becoming a new part of the mental economy of the affect. This calls for a constant and careful observation of the therapist’s countertransference reactions and regressed profile, the steady application of self-analysis of one’s own vulnerability and inner conflicts, allowing parts of his or her personality to become a home for patients’ experiences without losing the capacity to reflect and symbolize.

In conclusion, I wish to briefly put forward some ideas on the advantages brought to the psychotherapy of heroin addiction by two factors: methadone maintenance treatment and working in a multidisciplinary institution.

We have an abundant evidence of the stabilizing effects of methadone on the brain. We also know the great advantages of the medically prescribed doses and the beneficial effects of changing the vicious cycle of illicit drug use. Bearing in mind that methadone is a long-acting agonist, we recognize its potential not only as a means of minimizing the tormenting effects of painful affects, but also as enabling the therapist to act on perception and other cognitive functions. Well know is the fact that drug dependence consists not only of taking drugs, but also of withdrawal from them. The loss of the omnipotent state of fusion with the drug during withdrawal periods promotes strong narcissistic crises, which are experienced as real traumatic events. Thus the lack of withdrawal symptoms, along with the behavioural change consequent on taking methadone, open up the way to become free of the great amounts of shame, guilt and helplessness involved in the cycle of illicit use. These are two of the immediate advantages of methadone maintenance. In short, when medically prescribed methadone stabilizes numerous brain functions, the task performed is no less than making long-term psychotherapy with heroin addicts feasible. And by that I don’t mean only the possibility of retaining patients who are notorious for their acting outs and their breaking of relationships in long-term psychological treatment, but also the ability of this medication to ensure a new dimension of psychological functioning by alleviating severe depressive and even psychotic anxieties. It is a matter of level, really, as methadone treatment cannot by itself cure the psychological problems of affect regulation or of integration of personality. Patients’ feelings of dependence on methadone, their rage against the regulated admission of the medication, the hardships of enduring the process of being in treatment as opposed to the omnipotent fantasy of grandeur and the periods of regressive helplessness burdened by feelings of failure are real conflicts that are brought into the open during the therapy. But they are part and parcel of every significant restructuring effort and therapeutic support, which, in the best practice, includes a complex system of care including the efforts of many practitioners, doctors, psychologists and social workers; that is what allows these contradictory and confusing emotions to be endured and made productive in the psychotherapeutic process.

It is difficult, almost impossible, to work psychotherapeutically with addictions outside an institutional framework. The institution, with its overall organization of treatment, providing different levels of interaction, various figures and multiple functions could be seen as a form of mental organization, which communicates and interacts with the patients’ mental organization [4]. A therapeutic team which shares a clear and consistent clinical policy and philosophy allows the patient to enter various relationships and to experience different parallel transferences which make possible a gradual and steady integration in the patient’s mind, through the perception of a whole new object, located within a new social structure, that works as a facilitating environment. The institution itself, with its rules and functions, may play various transference roles like that of powerful mother or forbidding father, but, most importantly, it offers an opportunity to help patients to integrate their otherwise split projections by linking them with their representation of the clinic as a mental and social space, which tolerates triangulation and hierarchy, and behaves like a stable social structure. Of course, like methadone itself, a clinic can always be made the object of fearful attacks. Abusive interactions with members of the staff or perverse relationships with other patients are not rare events in our practice. These acting outs usually serve the purpose of redirecting angry and violent feelings from the often entangled situations that arise in psychotherapy and vis-à-vis the therapist towards other more experience-distant objects, so saving the enfeebled link or threatened therapeutic alliance with the therapist. Certainly, a different movement could also take place: while working in seriously regressed mode in the therapy, a patient who finds difficulty in making progress within the strongly ambivalent situation may use the clinic as a whole, or other staff members, as objects for reparation, in this way strengthening his healthier and more mature parts, via parallel psychic route.

In a nutshell, these observations are consistent and in total accord with the conclusions made by the best known empirical research, conducted in the field by Woody, McLellan, Luborsky and O’Brien [21], stating clearly that psychotherapy is useful and efficient for the treatment of opiate addiction, but only if it is successfully integrated with other important services, drug counseling, methadone treatment and an overall institutional structure. The moral and scientific value of their findings is something that still lays a foundation for adequate practice with addicted patients. The practice of integrated multidisciplinary treatment in cases where patients would not have been available for treatment without methadone, the latter together with the concrete services provided and with drug-focused counselling, are helping them manage addiction and the related social problems, while psychotherapy helps them to achieve significant changes in their internal models and personality structures.
Role of funding source

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Conflict of Interest

The author has no relevant conflict of interest to report in relation to the present paper.

References

Preferences for Buprenorphine/Naloxone (Suboxone®) and Buprenorphine (Subutex®) in Patients Receiving Buprenorphine Maintenance Therapy in France: A Prospective, Multicentre Study

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TO THE EDITOR: We report the results of a multicentre study on the distribution of preferences for buprenorphine/naloxone (Suboxone®) and buprenorphine (Subutex®) in patients receiving buprenorphine maintenance therapy in France.

Background and objectives – A combination formulation of buprenorphine (Suboxone®) containing buprenorphine and naloxone in a 4:1 ratio is now available throughout Europe and many other countries worldwide. Patients previously receiving maintenance therapy with buprenorphine alone (Subutex®) can be transitioned to Suboxone® as part of a global effort to reduce the potential for non-medical use and diversion of buprenorphine. This study evaluated the distribution of preferences between these two formulations in stabilized buprenorphine-maintained patients who were subsequently switched directly to buprenorphine/naloxone.

Methods - A prospective, open-label, multicentre comparative trial using an intent-to-treat (ITT) study design was implemented in France. It included adult opioid-dependent patients who had been receiving buprenorphine for at least 6 months at a stable dose (2 to 16 mg/d). Buprenorphine was given at the patient’s current dose on Days 1 and 2, followed by a direct switch, with the same dose, to buprenorphine/naloxone on Days 3-4-5. Visual analogue scales (0 = worst, 10 = best score) were used by patients to rate the satisfaction felt by them at taking the study drug after each dose across a range of parameters (e.g., overall rating, taste, dissolution time, tablet size). Preference ratings for the two formulations in the ITT population were calculated using covariance analysis (p = 0.05).

Results – Fifty-three patients (15F/38M; mean age: 39±8.6 years) were included. Overall satisfaction with the tablets was high and similar for buprenorphine and buprenorphine/naloxone (p=0.130); the recorded difference in mean scores was 0.4 points. Patients significantly preferred buprenorphine/naloxone with reference to tablet taste (p<0.001, difference 4.3), size (p<0.001, difference 1.1) and sublingual dissolution time (p<0.001, difference 2.8). There was no preference with respect to well-being over 24 hours (p=0.144, difference 0.4) and no significant influence of the treatment dose on any criterion. When asked directly about their preferences at the end of the study, 54% (28/52) of these patients preferred buprenorphine/naloxone, 31% (16/52) pre-
ferred buprenorphine alone and 15% (8/52) expressed no preference. Most patients (71%; 37/52) reported a wish to continue treatment with buprenorphine/naloxone. There were no safety concerns or study discontinuations associated with buprenorphine/naloxone.

**Conclusion** – Buprenorphine-stabilized patients are equally satisfied with Subutex® and Suboxone®, but prefer Suboxone® to Subutex® when it comes to tablet characteristics such as taste, size and dissolution time. Moreover, a majority of patients in this study reported a wish to continue their treatment with Suboxone®.

**Role of funding source**

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**Contributors**

The authors contributed equally to this work

**Conflict of Interest**

The authors have no relevant conflict of interest to report in relation to the present study.
Coordinating Methadone Treatment Providers and Policymakers: Lessons Learned Over 30 Years

Mark W. Parrino
American Association for the Treatment of Opioid Dependence - AATOD

TO THE EDITOR: I am delighted to be able to report that we continue to admit new member state chapters into AATOD in addition to the methadone providers of Mexico. This is all part of AATOD’s work with EUROPAD towards the further development of the World Federation for the Treatment of Opioid Dependence (WFTOD).

I am also grateful for the leadership of Dr. Icro Maremmani, who has worked tirelessly in his efforts with Dr. Marc Reisinger of Belgium and Dr. Andrej Kastelic of Slovenia to solidify the organizational development of EUROPAD. EUROPAD has been working with AATOD since the last Northeast Regional Methadone Conference of 1989. It is useful to review a brief timeline of the development of methadone maintenance treatment in the United States prior to discussing a number of relevant topics, including the World Federation for the Treatment of Opioid Dependence.

The groundbreaking work of methadone maintenance treatment began during the research that Drs. Vincent Dole and Marie Nyswander had initiated at Rockefeller University between 1963 and 1964. The initial research was published in the Journal of the American Medical Association (JAMA) in 1965 and Dr. Mary Jeanne Kreek, also of Rockefeller University, was also directly involved in these early trials and published extensively on their groundbreaking research from the beginning.

It is also important to note that President Nixon appointed Dr. Jerome Jaffe to be the Director of the White House SAODAP Office as heroin addiction was rampant throughout the United States. This was a time when tabloid headlines in newspapers throughout the country were publishing pictures of heroin users overdosing in jails and even public bathrooms. Fortunately, Dr. Jaffe’s appointment led to the major expansion of methadone treatment services throughout the United States through a massive federal investment in treatment.

Soon after this appointment, the Food and Drug Administration (FDA) established the federal regulations, which would govern methadone treatment services to the present date. It was believed that such regulations were necessary to ensure basic standards of treatment and to provide guidelines for the programs in order to protect the well-being of the patients and the public.

Congress passed the Narcotic Addiction Treatment Act (NATA) in 1974, which further defined the “closed panel system” of methadone treatment programs in the United States. Only licensed treatment programs were authorized to dispense and use methadone maintenance treatment for chronic opioid addiction. This “closed panel” continues at the present.

The treatment system continued to develop in the United States and AIDS was detected in 1981 in California and New York State. Several years later, HIV would be identified as the cause of AIDS in 1984. Many of the programs in the United States also noted in 1985 that AIDS-related illnesses were identified as the major causes of patient deaths for the treatment programs. For those clinicians, who were working in the treatment programs at the time, they were horrified to see once healthy patients rapidly deteriorate through enormously quick weight loss. These clinicians also found that the patients were also subject to contracting severe opportunistic infections.

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Congress created the Center for Substance Abuse Treatment (CSAT), one of the three subagencies within the Substance Abuse and Mental Health Services Administration (SAMHSA) in 1992. CSAT would later emerge as the primary federal agency having direct federal oversight of methadone treatment programs and would also provide the oversight to physicians using buprenorphine to treat chronic opioid addiction in their private medical practices.

During the late 1980s and early 1990s, methadone treatment programs were coming under increasing federal scrutiny. The General Accounting Office (GAO - now Government Accountability Office) published a report in 1990, responding to the Congressional Select Committee on Narcotic Abuse and Control. The GAO Report determined that methadone regulations were inadequately implemented and treatment programs were not using the pharmacology of methadone properly. Many patients were receiving sub-therapeutic doses of methadone during this period. The Institute of Medicine (IOM) was subsequently commissioned by the Food and Drug Administration to examine the federal regulations for methadone treatment and their comprehensive report was published in 1995. One of the most profound recommendations of the IOM Report was to suggest the creation of an accreditation-like system to provide better clinical oversight of patients within the treatment programs. The Report also concluded that reports of methadone diversion from the treatment programs did not create any significant risk when measured against the benefit of treatment.

The National Institutes of Health (NIH) also developed a Consensus Statement calling for the expansion of methadone treatment services, which were published in 1997. One of the most salient recommendations of this report was to expand access to such treatment services for patients under legal supervision. This included inmates, who are opioid-addicted and incarcerated in jails and prisons in addition to people who were on probation and parole. Unfortunately, this breakthrough recommendation has been impeded in its development as a result of the stigma associated with narcotic addiction and methadone maintenance treatment services. The European policies have been far more progressive by comparison in providing such treatment opportunities to incarcerated opioid-addicted individuals.

The Food and Drug Administration continued its regulatory oversight for methadone treatment programs until 2001, when such oversight was transferred to the Center for Substance Abuse Treatment within SAMHSA. As a result, treatment programs were required to follow a series of new clinically oriented accreditation standards and all of the existing 1,203 OTPs within the United States have been surveyed by federally approved accreditation entities.

Finally, the most significant new development in treating chronic opioid addiction was officially launched in 2002 after buprenorphine had been approved and the Narcotic Addiction Treatment Act (2000) was passed by Congress and signed into law by President Clinton. Buprenorphine represented the second most widely used medication to treat chronic opioid addiction in the United States and was also used extensively through the private medical practices of federally approved physicians, who participated in an 8-hour training course.

**Advances in Clinical Practice and Policy**

Throughout the 40 years that medication-assisted treatment has been used to effectively treat chronic opioid addiction, we recognized that medication alone was insufficient to treat the complex illness of opioid addiction. Dr. Vincent Dole made this comment in 1989 in the book, "Addicts Who Survived."

"The problem was one of the rehabilitating people with a complicated mixture of social problems on top of a specific medical problem, and that (practitioners) ought to tailor their programs to the kind of problem they were dealing with. The strength of the early programs as designed by Marie Nyswander was in their sensitivity to individual human problems. The stupidity of thinking that just giving methadone will solve a complicated problem seems to me beyond comprehension."

The need to provide comprehensive treatment services for chronic opioid addiction has been repeatedly documented by numerous research studies over the years. Patient outcome improves substantially when medications (methadone and buprenorphine) are combined with comprehensive medical and psychosocial services.

We have also learned that providing access to such medication-assisted treatment services represents a very good return to society on its investment based on the reduction of crime, HIV infection and other related illnesses associated with chronic opioid addiction. Research has also found that the average cost per year for treating an opioid addict is far less than society will bear in its costs for untreated addiction at $45,000.00 per year. Drs. Vincent Dole, Don Desjarlais and Herman Joseph made such a determination in publishing a policy paper for the New York State Division of Substance Abuse Services in 1991. Dr. John Ball’s seminal research also documented the extraordinary decrease in crime as patients were enrolled and remained in methadone treatment programs (1988).

**Current Realities**

At present, there are 1,203 opioid treatment programs (OTP) operating in 46 states of the US in addition to the District of Columbia, the US Virgin Islands, American Samoa and Puerto Rico. All of these programs are under the jurisdiction of the Center for Substance Abuse Treatment and treat approximately 260,000 patients on any given day. This patient number has doubled from 10 years ago.
CSAT has been publishing Treatment Improvement Protocols (TIP) guiding the work of clinicians and policymakers since 1993, when the first TIP, “State Methadone Treatment Guidelines,” was published. There have been updates of these guidelines, the most recent being published in 2005, “Medication Assisted Treatment for Opioid Addiction in Opioid Treatment Programs.”

One of the most critical and challenging issues to confront the opioid treatment programs in the United States has been the increasing number of methadone-associated mortalities. The clear majority of these mortalities (more than 4,500 in 2006 alone) are the primary result of the use of methadone hydrochloride products to treat chronic pain through medical practices in the United States. This phenomenon has been extensively reported over the past five years and there have been increasing calls for greater oversight for the private practice physicians, who are using such medication to treat pain management.

The Development of the World Federation for the Treatment of Opioid Dependence

EUROPAD and AATOD worked together over the years to launch the first World Conference for Medication Assisted Treatment for Opioid Addiction during July 2007 in Ljubljana, Slovenia. The conference was chaired by Dr. Andrej Kastelic of Slovenia and directly brought the organizational authority of EUROPAD and AATOD together to agree upon a Charter for this Federation. The Federation Charter was revised at the Italian EUROPAD conference in Pietrasanta, Italy during November 2007 and has been in force ever since. The future ambitions of this World Federation will be to work with national and international agencies, including the United Nations and its member agencies to increase access to the evidence based use of medication-assisted treatment wherever it is needed throughout the world.

Once again, I am grateful to Dr. Icro Maremmani and his associates for their collective leadership in working with AATOD and its Board of Directors through EUROPAD and AATOD conferences to improve the quality of training for the people who work in our field. Patients will continue to benefit in gaining access to this proven treatment intervention throughout the world as a result of these efforts.

**Conflict of Interest**

The author has no relevant conflict of interest to report in relation to the present paper.

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Saturday, May 9, 2009

EUROPEAN OPIATE ADDICTION TREATMENT ASSOCIATION (EUROPAD)

Expanding Access and Improving Treatment

TIME: 10:00 - 18:30

Chairman: Marc Reisinger, MD
Brussels, Belgium, EU

10:00 Providing Addiction Treatment for All Who Want and Need It: Barriers and Prerequisites
Robert Newman (New York, NY, USA)

10:30 Treating Opiate Addicts as Normal Patients. Principles and Practice
Marc Reisinger (Brussels, Belgium, EU)

11:00 Why Drug Dealers Left the City
Icro Maremmani (Pisa, Italy, EU)

11:30 Has Norway Anything to Learn from Other Countries?
Martin Haraldsen (Sandefjord, Norway)

12:00 Why Are Some Norwegian Addicts Seeking Help Abroad?
Johnny Teigland (Bergen, Norway)

12:30 Discussion

13:00 Break

15:00 Models and Results in Central Norway
Berit Nordstrand (Trondheim, Norway)

15:30 Structural Aspect of Multidisciplinary Approach to Drug Addiction Treatment. Obstacles and Possibilities.
Carl Fredrik Dalaker (Bergen, Norway)

16:00 A Seven Year Follow-up of 50 Opiate-Addicted Patients: What Happened to Them
Earling Aaserund (Bergen, Norway)

16:30 Opioid Addiction: Initiating Acute Opioid Agonist Therapy within 6 Hours. Model and Results.
Joe Siri Ekgren (Oslo, Norway)

17:00 Opiate Agonist Treatment in Prison
Andrej Kastelic (Slovenia, EU)

17:30 What Is a Worthy Life? Who Decides?
Gunnar Kristiansen (Oslo, Norway)

18:00 Discussion

18:30 End of Seminar

Sunday, May 10, 2009

10:30 Boat trip in the fjords on a veteran coastal steamer, with fish soup on board
En Route to 90% Retention. ‘Active Rehabilitation’ in Central Norway

Berit Nordstrand
LAR-Midt, Trondheim, Norway

TO THE EDITOR: I would like to report that one third of patients in Central Norway receive buprenorphine/naloxone (bup/nx) combination at average daily doses of 22.4 mg bup/nx, to effectively deal both with craving and with depressive symptoms, and to explain why the team in Central Norway now recommends transferring some stable methadone patients to bup/nx. The high-threshold ‘active rehabilitation’ system has retained an impressive 88.4% of patients in treatment over two years and helped 78.2% of patients to achieve abstinence.

1. Switching over... switching on

In the face of the rising diversion and IV misuse of buprenorphine, which commands a 50% higher street value than the combination product in Central Norway, the decision was taken to switch all eligible buprenorphine patients to bup/nx. Meanwhile, ineligible patients are no longer given take-home dosing privileges for buprenorphine alone. Minimal side-effects were experienced during the transfer, and nearly all adverse effects tapered and disappeared over the subsequent months.

Given bup/nx’s positive impact on depression and alertness, and the lower weight gain observed, the Central Norwegian group now recommends the transfer of methadone patients to it. Being more ‘awake’ may help patients participate and engage with the impressive range of rehabilitation opportunities on offer within the intensive and comprehensive treatment programme that has been made available.

2. Side-effect confusion

We must stress the importance of identifying and adequately treating somatic or psychiatric comorbidities, whose symptoms may masquerade as treatment side-effects and impact treatment compliance. For example, patients can easily mistake the nausea and headache of HCV for a bup/nx reaction; on the clinical plane, comorbid anxiety or the effects of benzodiazepine abstinence may confound patients’ emotional response to further treatment. Meanwhile, underdosing, thyroid dysfunction or drug interactions can all appear in disguise, as if they were the adverse effects of opiate maintenance. My patients are told that naloxone alone has a very low incidence of side-effects and, considering its very short half life, if they are still experiencing an adverse effect 24 hours after dosing, the effect should not be attributed to the naloxone content of bup/nx.

3. Education, education, education

The education process does not end with adverse effects, however. As part of their comprehensive approach to patient support, we must highlight the critical nature of adequate patient (and prescriber) education. In the Central Norwegian system, all those who interact with patients have a range of educational materials that help them to understand every aspect of their treatment package and the maintenance drug prescribed, from finding the right dose, to supervised dosing.

4. Active rehabilitation

The Central Norwegian package’s high level of efficacy is largely due to the intensive package available. According to Norwegian guidelines the indications for starting ORT are the following: 25 years of age and only after they have been unsuccessful with drug-free treatment. These patients, who live in 83 municipalities in Central Norway, receive the ORT-drug and a package comprising access to leisure activities, comprehensive

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treatment for comorbidities and training opportunities in financial management, everyday activities, and vocational areas. Quarterly multi-disciplinary meetings with social workers, doctors and nurses ensure a holistic and systematic approach to patient management.

5. Supporting abstinence

The Central Norwegian system also benefits from inbuilt tools designed to support and promote abstinence. At treatment entry, patients must surrender their driving licenses, which are only given back after 6 months of demonstrated abstinence. Ongoing abstinence earns an increase in take-home privileges with bup/nx; these privileges are lost for 2-3 months after any drug-positive urinalyses. Such relapses are also followed by increased cognitive behavioural support.

International delegates were left in little doubt that patients can achieve outstanding results with such a comprehensive package. Patients in Central Norway with a population of about 700,000 people, can access the Rolls Royce of treatment services and through that accomplish abstinence (78.2%), work or studies (63%) and an self-esteem, dignity and quality of life.

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Conflict of Interest

The author has no relevant conflict of interest to report in relation to the present report.

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Book:

Book Chapter:

Journal names should be abbreviated as they appear in Index Medicus, journals not currently indexed there should not be abbreviated.

Submission Procedure: Submit the files to Icro Maremmani, MD, Editor, <maremman@med.unipi.it> and a Cc copy to <info@aucns.org>

Submissions should be accompanied by a cover letter indicating that the paper is intended for publication and specifying for which section of the journal it is being submitted (Regular Article, Preliminary Communications, Reports, Proposals, Letters to the Editor);

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