Executive summary

Health Council of the Netherlands: Pharmacotherapeutic Interventions in Drug Addiction. The Hague: Health Council of the Netherlands, 2002; publication no. 2002/10.

Request for advice

This advisory report, entitled “Pharmacotherapeutic interventions in drug addiction”, is the third and final report that this Committee presents in reply to previously stated requests for advice by the Minister of Health, Welfare and Sport. The first advisory report, “The prescription of heroin to heroin addicts” (1995), has led to a large-scale investigation. The results of that study were published in February 2002. The second advisory report, “Testing for drugs of abuse ”, dealt with the investigation of bodily materials (mainly urine) in order to detect drug use. This advisory report, which appeared in 1998, played a role in the establishment of the Regulation on Urine Control in Penitentiaries promulgated by the Dutch Minister of Justice in June 1999.

The present advisory report deals with the pharmacotherapeutic treatment of addiction to illegal hard drugs. Considering the requests for the treatment of patients that are, alongside these drugs, also addicted to other compounds, the simultaneous use of — as well as addiction to — alcohol, tobacco, benzodiazepines and cannabis will also be discussed.

Approach

In compiling this advisory report, the Committee has taken an evidence-based approach, integrating findings from scientific investigations, pathophysiological insights, clinical experiences and patient preferences. As a first step the Committee summarized all available evidence-based guidelines pertaining to the

pharmacotherapeutic treatment of drug addiction that are currently used in various countries. In a second step, the Committee analysed the results of recently published research (i.e. double-blind, controlled studies). In the advisory report, the Committee combined these various items with clinical knowledge based on experiences in The Netherlands

Drugs, drug use and addiction

As in both earlier advisory reports, the Committee uses the word "drug" in this report in the limited sense of an illegal*, potentially addicting, psychotropic substance.

Most drug use is recreational and causes few, if any, health or other problems in the majority of users. However, repeated or intensive use can induce changes in the cellular function (including stimulus transmission) in certain brain structures. These changes can lead to addiction, if combined with congenital vulnerability, certain developmental factors, and specific personal circumstances. Modern research methods have demonstrated that the neurobiology of the brain of an addicted person is different from that of a non-addicted person, thus showing that addiction is a qualitatively different condition. Considering the factors that play a role in the development and onset of addiction, the Committee considers addiction to be a condition with a biopsychosocial etiology, which tends to run a chronic course. They advise that investigations be directed at the physiological and cognitive processes (conditioning, memory) that constitute the basis for addiction.

Drug addiction in The Netherlands

The Netherlands, a country with approximately 16 million inhabitants, has between 25,000 and 29,000 heroin addicts About 18,500 of them are in contact with the treatment system. The vast majority of the heroin addicts also use cocaine.

The number of primary cocaine addicts in the Netherlands is unknown. It is known, however, that approximately 28,000 people in the general population have used the drug.

About 13,000 people have used amphetamine and about 40,000 XTC. It is not known how many of them are addicted to these drugs.

Treatment of addiction: medical treatment

Treatment of addiction should, as a treatment for any other condition with a tendency towards chronicity, be considered to be part of the medical domain.

The treatment of addiction requires that attention be paid to various aspects. First of all craving: the powerful, often irresistible, urge for drugs, which can occur as a

* Illegal meaning here: scheduled under the Opium act and obtained without prescription.

result of their use. Craving is often considered to be an expression of the sensibilization of brain processes, and is often referred to as incentive sensitisation. Craving is an exclusive characteristic of addiction.

Furthermore, the treatment of addiction requires that attention be paid to possible withdrawal symptoms, tolerance and pharmacological sensitisation. However, the presence of these phenomena in the context of the use of a certain sustance is just an indication (and no prerequisite or evidence) for the existence of addiction to that substance. Conditioning is also not unique to addiction.

Pharmacotherapeutic interventions for addiction should, in general, be directed at preventing the occurrence of withdrawal symptoms, normalising disturbed physiological functions and reducing craving. This entails that the medication must act upon the system that has been changed or unsettled by the use of drugs.

The compounds used for this purpose are generally categorised according to the way they can influence the stimulus transmission between neurones. This is either through (total or partial) inhibition or blockade, or through (total or partial) stimulation. A distinction is made between agonists (compounds that bind to receptors and subsequently cause maximum physiological activity), partial agonists (compounds that bind to receptors but do not cause maximum activation) and antagonists (compounds that inhibit or block the effects of agonists).

In addition to these compounds that act upon the neurotransmitter system, some other compounds are used that either bind and neutralize the drug or influence its metabolism. This can result in a situation where the addictive substance does not reach the brain — and thus no intoxication occurs — or a situation in which certain metabolic products accumulate, causing aversive reactions.

Because addiction is a condition with a biopsychosocial etiology, pharmacotherapy can, in many cases, be no more than just a part of an integrated treatment approach in which also psychosocial and psychotherapeutic interventions play a role. At the end of the advisory report, therefore, the Committee places the pharmacotherapy of drug *addiction* in the larger framework of an integrated, multi-disciplinary treatment of drug *addicts*.

Frequently, various somatic and psychiatric disorders occur in addition (or in relation) to addiction. This is referred to as comorbidity. It is important to keep this in mind and to actually treat patients for these comorbid disorders.

Because addiction is characterised by frequent relapses (even after long periods of apparent recovery), long-term continuation of the treatment is usually necessary.

Treatment objectives

The treatment of a chronic condition (or a condition with a tendency towards chronicity) such as addiction calls for a hierarchy of objectives that runs from cure through stabilisation to palliation.

The first treatment objective is cure of addiction, i.e. the achievement of stable abstinence. This goal is usually not obtainable in the short term.

The next treatment objective is stabilisation of use. The patient will receive some kind of maintenance treatment, which aims to achieve a situation in which the patient no longer uses any illegal substances. When this appears to be not feasible, another type of maintenance treatment, which aims to regulate the drug use of the patient, will be offered. An important secondary goal is to maintain a regular contact with treatment providers, because it creates opportunities for intervention directed at physical and mental health improvements, the prevention of infectious diseases (such as hepatitis, tuberculosis and HIV), and assistance for social problems (housing, finances, daily activities). This treatment goal is also designated as risk minimisation or harm reduction. The treatment goals of risk minimisation and harm reduction also apply to long-term addicted patients for whom no single treatment has been effective over the course of the years.

The last treatment objective is palliation. This involves attenuation of suffering by combating the symptoms that are a result of years of serious addiction and the treatment of the associated conditions in patients with a limited life expectancy.

Treatment of opiate addiction

Objective: abstinence

The achievement of stable abstinence (i.e. cessation of the use of all opiates*) occurs in two phases: the actual detoxification followed by relapse prevention. Actual abstinence is best achieved when that goal is set at the moment when the patient — according to himself and in the opinion of the treating physician — is ready for this and when personal and social circumstances are favourable. Along with the medical history and the wishes of the patient himself, possible existing comorbidity and possible contra-indications also play a role. In general, the best results are obtained with short-term clinical detoxification (i.e. a maximum of three weeks). The Committee has made the following recommendations.

* The literature differs in terms of what is understood by the word “abstinence”. In some cases, abstinence means abstention from all addictive compounds, while in other cases abstinence stands for abstention from all illegal substances or abstention from all (legal and illegal) opiates, and, finally, abstinence sometimes only means abstention from illegal opiates.

- The short-acting intoxicating opiate is replaced with an equivalent dose of long-acting and orally administered *methadone*. The dose is then gradually reduced. If, despite a sufficiently high initial dose and (individually determined) gradual dose reductions, withdrawal symptoms occur, these can be treated symptomatically.
- In the detoxification of heroin addicts, there appears to be a place alongside the complete agonist methadone for *buprenorphine*; a long-acting, partial opiate agonist. The Committee holds the view that it is desirable, for the detoxification of opiate addicts in the Netherlands, that buprenorphine is available in a properly dosed sublingual tablet ("high dose buprenorphine" or HDB*).
- Opiates can be fairly rapidly reduced when the withdrawal symptoms are treated with *α_2-adrenergic agonists*. Treatment with such compounds, therefore, offers a good alternative for certain patients. Because it is desirable that a compound with less hypotensive effects than clonidine is available, the Committee holds the view that it is important for *lofexidine* to be made available to Dutch addiction treatment providers.
- Detoxification with *naltrexone* results in serious withdrawal symptoms. Therefore, the Committee does not consider detoxification with only naltrexone to be advisable. However, satisfying results can be achieved in certain motivated patients via rapid detoxification with naltrexone if proper treatment of withdrawal symptoms is guaranteed. It appears that general anaesthesia offers no added value to this. The Committee cannot, as yet, provide an assessment of the possible benefits of sedation with this procedure.
- The Committee is of the opinion that having patients kick the habit by acutely stopping them from all opiate use, without proper treatment of the withdrawal symptoms ("cold turkey"), is not in the patients' interest and, therefore, not professional.
- When the treatment goal is total abstention from opiates, relapse is a problem for which the currently available pharmacotherapeutic options can offer no effective solution. Naltrexone is the only medicine available for this purpose. Despite the unpopularity of this opiate-antagonist among patients, naltrexone can be a proper means for the prevention of relapse in patients who are motivated for such a treatment. The Committee expects that the use of this treatment option will increase when a long-acting depot formulation of naltrexone becomes available.
- Pharmacological relapse prevention should generally be continued for a year, starting from the last relapse. Detoxification is contra-indicated (due to the risk of overdosing with renewed use and the chance that the continuity of care will be interrupted) in cases where there is no prospect of proper relapse prevention. The Committee therefore holds the view that it is necessary to create conditions under which follow-up treatment after detoxification can be guaranteed.

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* Already registered in a large number of countries (under the brand name Subutex®).

Objective: stabilisation

- The first choice with this objective is oral *methadone*. Over the last few years, it has become clear that methadone dosages need to be determined individually. Where 60 mg/day is sufficient to prevent (or to limit as much as possible) withdrawal symptoms and craving in one patient, another patient may require more than 100 mg/day. Long-lasting, sometimes life-long, treatment is often necessary.
- Since not all patients respond to methadone optimally, there is a need in actual practice for alternatives. The Committee expects that *buprenorphine*, when available in adequate doasages, can be helpful in the maintenance treatment of opiate addicts in the Netherlands.
- It is likely that treatment with *heroin* (under clearly circumscribed conditions) can provide good results with chronic, treatment-resistent heroin addicted patients.

Nearly all patients also benefit from supportive psychosocial treatment during maintenance treatment. Material encouragements (incentives) can provide a clear stimulus to comply with treatment.

Objective: palliation

Relief of suffering is the primary goal of palliation. The choice of the most appropriate pharmacological compound varies from patient to patient. A physician who considers palliation can prescribe *heroin* (or a heroin-equivalent opiate) as part of the treatment for the heroin addicted patient.

Treatment of addiction to cocaine, (meth)amphetamine, XTC

There are, currently, no effective pharmacotherapies available for the treatment of addiction to cocaine and amphetamines (amphetamine, methamphetamine, XTC). In general, pharmacotherapeutic interventions are limited to the treatment of the various side effects of these drugs. However, many research programs are currently executed, using different approaches in order to create new possibilities for pharmacotherapy of stimulant addiction. The Committee recommends to support these research activities.

Currently, the best results for cocaine addiction (despite very high drop-out levels) are obtained with intensive individual counselling in combination with group therapy.

There is increasing evidence that the consumption of amphetamines (including XTC) and cocaine may lead to partially irreversible brain damage, even in the absence of addiction.

Treatment of polydrug use

In the treatment of polydrug addicts, the physician has to take into account the pharmacological aspects of the different drugs and their possible (pharmaceutical, pharmacokinetic or pharmacodynamic) interactions. Also other factors have to be taken into account, such as the dosage and the route of administration of the various drugs, the patient's physical condition, biological factors (e.g. heredity and the patient's aptitude, and individual variations in metabolism), the pattern of nutrient and fluid intake, and the context in which drug use occurs.

In general, pharmacotherapeutic interventions should be directed at the various addictions separately. In these patients, psychosocial support is of special importance.

The consumption of certain combinations of drugs should be strongly discouraged. For example, the simultaneous use of cocaine and alcohol creates an increased health risk to the user (sudden death) as well as his fellow man (aggression).

According to the Committee, it is useful to recommend all patients seeeking treatment to discontinue cigarette smoking and to decrease or discontinue alcohol consumption. In order to implement this recommendation, it is necessary to train treatment providers in supporting patients during this trajectory.

Patients with comorbid disorders should be informed about the possibility of unexpected effects following the simultaneous use of drugs and medications prescribed for the treatment of comorbid conditions. They must be advised to stop their use of drugs, and not to stop the use of these medications.

Treatment of the addicted: health care

The available data clearly show that the treatment methods for drug addicts in the Netherlands (i.e. medical, psychological and social care, frequency and the intensity of contacts) and the dosage of prescribed medication vary considerably between institutions. The Committee would like to point out that there is a serious lack of consensus and guidelines. The Committee holds the view that is it improbable that optimal care of the patient can be guaranteed with such variations in the treatment of similar groups of patients. Therefore, in this advisory report, alongside the possibilities for pharmacotherapeutic interventions, attention is paid to other aspects worth consideration when treating addicts.

Firstly, it is of crucial importance that treatment providers from various disciplines cooperate in the treatment of the addicted patient. A lack of cooperation can easily lead to a situation where no one feels responsible for the treatment. The Committee urges that addiction specialists (physicians) be explicitly charged with this responsibility.

However, this alone will not suffice. Addiction treatments can only develop into an optimal health care service if a number of conditions are fulfilled:

- Medical schools should pay attention to the practical aspects of the treatment and management of addicted patients.
- The development of a separate registration or certification of “addiction medicine” for junior doctors, general practitioners and specialists is higly advisable.
- There is a need for practice guidelines. The present advisory report can serve as a starting point. Attention should subsequently be paid to the implementation, and a regular critical evaluation, of these guidelines. The coordination of activities directed at this could rest within the Steering Committee on the Development of Multidisciplinary Guidelines in Mental Health Care.
- Addiction treatment providers who exercise a profession covered by the Individual Health Care Professions Act (Wet BIG) must, too, be properly trained to perform their specific task. This, likewise, applies to other employees that come into contact with addicted patients, such as receptionists and managers.
- From a treatment perspective, treatments services for drug addicts should be low-threshold and, if necessary, stay open seven days per week for all patients, including foreigners an patients without a legal status.
- The organisation and workforce of addiction treatment services should comply with the demands that are placed upon all healthcare services.
- Outpatient addiction treatment services should be financed like any other healthcare service.
- Public information campaigns about the nature of addiction and the treatment options of drug dependent people may contribute to the destigmatisation of this patient group.