

INJECTABLE HEROIN PRESCRIPTION - THE SWISS EXPERIENCES

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Introduction

In the late 1980s and early 1990s Switzerland faced increasing problems due to the growth of heroin and other illicit drug use, with associated spread of HIV/AIDS and other infectious diseases, a large increase in open drug scenes and a dramatic rise in drug-related deaths. This situation also posed an enormous human and economic burden. The Swiss Federal Council evaluated the situation and devised new ways to reduce the harms of illicit drug use and to control the drug scene, including the medical prescription of injectable heroin for chronic and treatment-refractory heroin-dependent individuals^{1,2}. The main purpose of this treatment approach was to attract and keep patients in treatment in order to improve their health and well-being and to reduce the spread of HIV and other drug use-related problems.

Another advantage of this approach is that the heroin provided to the patients comes in prescription form (Diaphin®) and is relatively safe for heroin-dependent patients, especially if administered in a supervised environment^{3,4}. Most problems occur when the patient takes impure and dilute illicit “street” heroin. Concerns also arise from intoxication due to overdose and co-use of other drugs (i.e. benzodiazepines) in addition to heroin. Hence each treatment facility has developed its own drug testing program to determine if other non-prescribed substances are being used, including “street” heroin in one institution (Basel).

Although the drug testing programs differ across institutions the following parameters were obligatorily tested four times per year in each patient for monitoring and research purposes or spontaneously in suspicious cases: amphetamines (including methamphetamine, MDMA and similar stimulants), barbiturates, benzodiazepines, cocaine metabolite benzoylecgonine, methadone, opiates, THC carboxylic acid and additional, if necessary, chromatographic methods for confirmation and/or differentiation of amphetamines, opiates, cocaine metabolites, and others.

In Switzerland, the medical prescription of injectable heroin for opioid-dependent treatment-refractory patients first became available in the context of a research program called the Medical Prescription of Narcotics or PROVE (acronym of German version: Projekt zur ärztlichen Verschreibung von Betäubungsmitteln) undertaken between January 1, 1994 and December 31, 1996⁴. The Federal Council followed the study report’s recommendations⁴, and on March 8, 1999 authorized maintenance with injectable heroin under supervised conditions as a regular treatment option for those individuals who could not benefit from or be reached by existing treatment methods. The Swiss criteria for this treatment are a current history of severe heroin dependence according to ICD-10 of at least 2 years, a minimum age of 18 years, and evidence of substantial health and/or social problems. Further, participation in other approved treatments must have failed on several occasions and/or current health status does not allow for other treatments.

This report presents an overview of the Swiss study results obtained in patients on heroin-assisted treatment between January 1994 and December 2000.

Description of the Swiss National Cohort Study^{4, 5, 6}

The Swiss National Cohort Study of injectable heroin-assisted treatment involved 2166 admissions, corresponding to 1969 patients who were seen between January 1994 and December 2000 at 21 centers in 19 cities. This study was an extension of PROVE. In the framework of the study, heroin-dependent patients received injectable heroin in a comprehensive therapeutic program, including qualified health and psychosocial support services.

The daily intravenous (iv) heroin dose was in the range of 474 ± 206 mg/day (total daily dose) administered 2.6 ± 1.0 SD times a day. If needed, patients received methadone in addition to heroin to prevent night-time withdrawal. (In the opinion of most doctors involved in heroin-assisted treatment many patients would change to oral opioid maintenance treatment after being in heroin-assisted treatment for a certain period of time). A subset of 237 patients who began treatment between January 1, 1994, and March 31, 1995, and stayed for at least 18 months were assessed for somatic and mental health, social integration, and treatment outcomes. Analytical screening programs were no key points of the study (see introduction). Patients were examined and interviewed by treatment staff using standardized questionnaires for data collection when they entered treatment and thereafter every 6 months. The patients were at least 18 years old and had a minimum 2-year history of heroin dependence.

Main Outcomes of the Swiss National Cohort Study

The mean age of the patients in treatment was a little over 31 years, with approximately 80% being male. The mean length of heroin use prior to treatment admission was 10 years. Patients who left treatment were more likely to have used cocaine daily (29%) and to be HIV-seropositive⁵.

Retention in heroin-assisted treatment was high, with 83% of patients continuing with the treatment for at least 3 months, 70% for at least 1 year, 50% for at least 2.5 years, and 43% for 5 years and longer (see Figure 1)⁵.

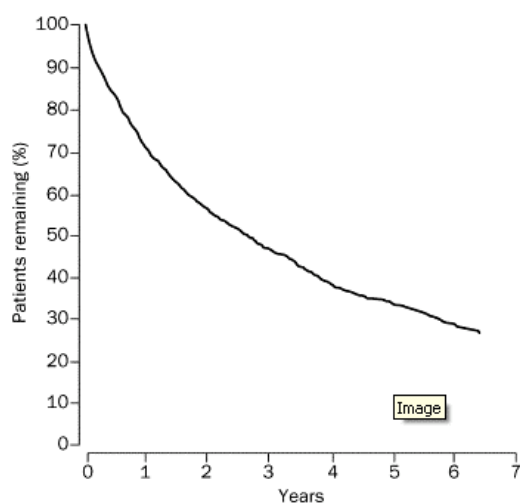


Figure 1 Proportion of patients in treatment over time (with the permission of the authors)⁵

There was a clear relationship between length of stay in treatment and reasons for discharge:

- Within the first 4 months, 9% of patients were discharged in order to proceed to abstinence treatment, whereas 29% were discharged for the same reason after 3 years.
- Lack of compliance was reason for discharge in 30% of patients within the first 4 months, but only 7% after 3 years thereafter.
- Almost all other reasons for discharge were evenly distributed over time.

It was evident that the health of the patients that were followed for 18 months significantly improved with time ($p < 0.05$). Improvements in patients' health status included a reduction of severe somatic and severe mental health problems, a considerable decline in malnutrition anemia and in frequency of epileptic seizures as well as a substantial increase in body mass index. The study also revealed remarkable improvements in patients' socioeconomic status, e.g. unemployment decreased from 44% to 22%. Illicit heroin use based on patient self-reports decreased from 81% during the 6 months before admission to 18% after 18 months on treatment. Use of other illicit drugs after the 18-month treatment period also decreased substantially (cocaine from 29% to 5%, benzodiazepines from 19% to 9%; but there was no change in the use of cannabis and alcohol). At entry to the study, 70% of the patients were involved in illegal activities like sale of hard drugs, shoplifting, sale of cannabis, or handling stolen goods. Eighteen months after treatment admission only 10% still committed illegal activities.

There were no deaths related to the administration of heroin in the treatment setting during the observation period (1994 – 2000). In contrast, the drug-related death statistics of the Swiss Federal Statistics Office for the years 1978 to 2004 shows a peak in 1992 with 419 drug-related deaths (most due to polysubstance use) and a steep decline from 399 deaths in 1994 to a relatively constant level of 180 to 205 between 1999 and 2004⁷. Of course, this change is not only due to the introduction of heroin-assisted treatment. The number of heroin-dependent patients on methadone maintenance, for example, has reached a level of about 15,000 to 18,000 persons since 1994 as compared to only 4,000 in 1989. Since the implementation of heroin-assisted treatment in Switzerland, however, no patient has died of a heroin-related death while in treatment. The most prevalent reasons for death were AIDS, other infectious diseases and accidents.

Discussion

The findings of the cohort study have revealed that heroin-assisted treatment programs are beneficial for chronic and treatment-resistant heroin-dependent individuals. There are now 23 heroin treatment facilities across Switzerland, two of which are prison-based. So far, there has not been one death related to heroin-assisted treatment, and drug-related deaths have sharply decreased in Switzerland since its introduction. The prescription of heroin is covered by health insurance, but overall this system shows cost effectiveness for Switzerland's economy. One patient in treatment costs about 46 CHF/day (~\$US30).

The study results also refute earlier claims that long-term heroin-assisted treatment may undermine the attractiveness and effectiveness of other treatments or may negatively affect patients' motivation because the longer the patients stay in treatment the more likely they are to move on to methadone maintenance or abstinence-based treatment. This suggests that heroin-assisted treatment may increase the patients' readiness to change their drug-related behaviors. According to these findings patients should be advised to stay in treatment for as long as possible (at least 1 year) before considering abstinence-oriented treatment.

The study also demonstrates that heroin-assisted treatment is cost-beneficial by diminishing criminality, decreasing the use of the health care system and producing improvements in social adjustment. However, the study is purely observational and does not meet the gold standard of a randomized, double-blind, placebo-controlled protocol. Thus, it is not clear whether these benefits result from heroin itself, psychosocial counselling, or a combination of both.

Most patients who enter heroin-assisted have been using heroin by injection for many years. Therefore, they often exhibit poor veins complicating iv administration of prescribed heroin and compromising venepuncture for blood sampling⁸. Patients with poor venous access have the possibility to switch from intravenous to intramuscular or oral heroin administration, but the oral route is preferred by treatment providers in order to get patients away from injecting.

The feasibility and effectiveness of oral heroin was examined as an alternative method of supervised administration in a 1-year, prospective, open-label study with two treatment arms⁸. One group of patients was given heroin tablets alone and the other group received heroin tablets in combination with injectable heroin and/or other opioids. The main study outcome was the retention rate after 1 year in treatment. The historical 1-year retention rate for injectable heroin-assisted treatment in Switzerland was 70%⁵, while the retention rate after 1 year for the heroin tablets-only group reached 84%. This result indicates that heroin tablets are an effective way of administering heroin to patients. However, this study reveals a serious methodological problem. Heroin tablets were not compared to methadone tablets, but only to injectable heroin. Due to this shortcoming oral heroin tablets are still not approved. However, as for other routes of administration liquid heroin can be used off-label in Switzerland. In the Dutch heroin trials, heroin was prescribed only in combination with methadone and was also available in an inhalable form. The majority of heroin was given as an inhalant in a 3:1 mixture of heroin base and caffeine to increase the bioavailability of heroin.

Another weakness of the Swiss Cohort Study was that the analytical results of drug of abuse testing were not an outcome parameter, and so the data on drug-use behavior mostly relied on patient self-reports but not on analytical findings. Only the data on cocaine, cannabis and benzodiazepine use were verified by analytical techniques. Thus, the co-use of illicit heroin was merely an estimation based on patient self-reports.

As part of heroin-assisted treatment, some treatment providers conduct an analytical program which has a high influence on the course of the therapy. These programs have expanded the range of analytical parameters and requests as compared to those required by the study protocol. In Basel, for example, a procedure is established since more than 10 years (the same procedure for the full range of substitution regimens, i.e. methadone, buprenorphine, heroin, morphine sulfate).

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References

1. Drug Policy Alliance. Drug Policy Around The World. Available from: <http://www.drugpolicy.org/global/drugpolicyby/westerneurop/switzerland/>. Accessed June 15th, 2007.
2. Drug Policy Alliance. Switzerland's Heroin Experiment. Available from: <http://www.drugpolicy.org/library/tlcnr.cfm>. Accessed June 17th, 2007.

3. Dürsteler-MacFarland KM, Stohler R, Moldovanyi A, Rey S, Basdekis R, Gschwend P, Eschmann S, Rehm J. Complaints of heroin-maintained patients: a survey of symptoms ascribed to diacetylmorphine. *Drug Alcohol Depend* 2006; 81: 231-239.
4. Uchtenhagen A, Gutzwiller F, Dobler-Mikola A, Steffen T, Rihs-Middel M (eds): Prescription of Narcotics for Heroin Addicts. Main Results of the Swiss National Cohort Study. Basel, Karger, 1999
5. Rehm J, Gschwend P, Steffen T, et al. Feasibility, safety, and efficacy of injectable heroin prescription for refractory opioid addicts: a follow up study. *Lancet* 2001; 358: 1417-20.
6. Brehmer C, Iten P X, Medical prescription of heroin to chronic heroin addicts in Switzerland – a review. *Forensic Sci Int* 2001; 121: 23-26.
7. http://www.ejpd.admin.ch/etc/medialib/data/kriminalitaet/statistik/betaeubungsmittel.Par.0001.File.tmp/BMS-d-2004_druckversion_20050617.pdf
8. Frick U, Rehm J, Kovacic S, et al. A prospective cohort study on orally administered heroin substitution for severely addicted opioid users. *Addiction* 2006; 101: 1631-1639.