POLICY FORUM: DRUG ABUSE

The Heroin Prescribing Debate: Integrating Science and Politics

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Heroin is abused in almost all countries. It is estimated that about 8 million people (0.14% of the world's population) use heroin each year (*1*). Of the illegal drugs, it is associated with the highest mortality and most emergency room episodes, and so is arguably the most problematic from a health perspective (*1*). Along with prevention and law enforcement strategies, treatment is an essential tool for reducing illicit heroin use and its resulting problems.

The ultimate goal of treatment is to help those affected overcome dependence and be fully reintegrated into society. Although dependent users can proceed directly to detoxification and then strategies to prevent relapse, this fails for a large proportion. Nonetheless, many of these individuals may achieve new stability by daily oral administration of methadone, which acts at the same cell surface receptor as heroin. Methadone maintenance greatly reduces illicit drug use and other criminal activities and improves health and social behavior (*2*). It is the most widely practiced treatment for heroin dependence in the developed world (*1*). But some fail to benefit from methadone and other treatments, so that alternatives are needed for these resistant individuals. Consequently, heroin itself has been reconsidered as a treatment option.

The best information about the prescription of heroin as a maintenance drug comes from decades of experience in the United Kingdom and from recent Swiss cohort studies. Clinical trials have also commenced in the Netherlands (*3*), and there is growing debate about initiating trials in other countries. This debate should be informed by scientific evidence and should address political, social, clinical, and scientific concerns.

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What Does Existing Evidence Tell Us?

In the United Kingdom, heroin prescription has existed within an overall policy of prohibition for decades. The 1926 Rolleston Committee (*4*) established the right of medical practitioners to prescribe regular supplies of an opioid drug, including heroin, if this would allow patients to lead "a useful and normal life" that could not otherwise be achieved.

Heroin dependence in youths only became significant in the 1960s, and thus heroin began to be prescribed more widely and in higher doses, especially in the London area. Overprescribing by a small number of practitioners also created a substantial black market (*5*). This was rectified in 1968 partly through restriction of the right to prescribe heroin to specially licensed doctors and the establishment of clinics (*6*). There are, however, widely varying interpretations of the effectiveness of heroin prescription in the UK. Although a randomized controlled trial in which oral methadone was compared with injectable heroin showed that neither was clearly superior (*7*), consensus among clinicians led to a shift away from the prescribing of injectable heroin to injectable and oral methadone in the 1970s.

Since then, heroin has only been prescribed for those with long histories of dependence for whom other treatments have not been effective. Currently around 300 people (between 1 and 2% of those receiving a prescription for the treatment of opioid dependence) receive pharmaceutical heroin (*8*), usually provided as take-home supplies. Of the 109 doctors with licenses to prescribe heroin, fewer than 50 currently use them and about 20 of these account for the bulk of prescriptions (*9*). In a survey of physicians who treat people dependent on heroin, half of the 105 respondents thought heroin prescription was justified sometimes or often (*10*). A recent study that gave 58 long-term dependent users the choice of injecting heroin or methadone showed improvements in health and social functioning and reductions in criminal behavior (*11*).

In Switzerland, a cohort study undertaken from 1994 to 1996 showed that a system of supervised heroin administration at clinics with restricted operating hours was feasible as well as politically and socially acceptable. This result was documented in 17 clinics where a total of 1035 individuals with chronic and treatment-refractory heroin dependence were accepted for maintenance with supervised injectable pharmaceutical heroin (often in combination with take-home oral methadone) in the framework of a comprehensive assessment and care program. Concerns about doses escalating out of control proved to be unfounded, and most participants achieved stable doses in 2 to 4 months. Randomized studies showed that injectable heroin was superior to both injectable morphine and injectable methadone in attracting the target group, preventing premature treatment dropout, and reducing illegal drug use (*12*).

Participants in this study showed substantial improvements in health and well-being and very pronounced reductions in crime (*12*). Crime reduction was verified by examination of police records and the central criminal register. Similar results were found in a randomized controlled study in Geneva (*13*). The results for the cohort study participants were compared with those for 121 newly admitted patients on methadone maintenance who received comparable psychosocial support. Those in the cohort study showed significant reductions in illegal heroin, cocaine, and nonprescribed benzodiazepine use, whereas the methadone patients showed smaller reductions in illegal heroin use. Both groups showed similar improvements in social integration. Thus, heroin prescription can be helpful for those on methadone maintenance treatment who continue to use illegal heroin regularly, as well as for those who have dropped out of existing treatments (*14*).

Requirements for New Trials

If the pharmaceutical in question were not heroin and the disease were not heroin dependence, the next step—a double-blind, double-dummy Phase III clinical trial in which the new treatment would be compared to the current gold standard (in this case methadone)—would be straightforward. But pharmaceutical heroin is not simply a replacement for methadone. The British experience and Swiss studies have shown that to achieve stabilization lasting 24 hours, injectable heroin (which is short-acting) is most often combined with a low dose of oral methadone (which is long-acting). In addition, doses of both drugs are

tailored to individual requirements. Thus, fixed-dose comparisons between heroin and methadone make little sense. In addition, unlike a standard clinical trial, participants would be experienced users of both heroin and methadone, so that double-blind, double-dummy studies would not work. For trials targeting those who have failed methadone treatment, the possibility of random assignment to methadone treatment may limit those prepared to participate. A variety of trial designs, each addressing a different issue about heroin prescription, is therefore warranted. No one trial will provide a definitive answer, but interlocking trials will allow decisions about the long-term value of heroin prescription to be reached.

Defining the target population also raises challenges. There are three target populations: those who have not been helped by existing treatments, those currently in treatment who continue to use substantial amounts of illegal heroin, and those who refuse to try currently available treatment options. However, these definitions are problematic. It is common for people to have several treatment attempts before they are successful; continued use of illegal heroin during treatment may be a reflection of too short a time in treatment or of the treatment's inadequacy. Also, most dependent heroin users are reluctant to enter treatment until compelled to do so by social, legal, or economic crises. It can be argued that something other than heroin prescription might be effective. A resolution would be to include a third "arm," testing an alternative therapy, in each clinical trial.

Risks

An Australian feasibility study (*15*) identified strategies to deal with individual and social risks associated with trials of pharmaceutical heroin. Because there is so little empirical evidence about heroin prescription and because the issue is highly politicized, it is difficult to estimate the likely magnitude of the potential risks. There are five risks of overriding concern:

1. Heroin prescription might be linked with more permissive attitudes to illegal drug use, encouraging use especially among young people. This was the reason given by the Australian government for blocking a proposal for a clinical trial of heroin prescription in 1997. However, heroin prescription and permissiveness are not inevitably linked, as the British experience and Swiss studies show.

2. There might be an influx of dependent users to the trial city. This "honey pot" effect can be minimized by enforcement of strict residency criteria, by limiting the number of trial participants, and by close cooperation with the local police (*16*).

3. Heroin prescription may reduce the proportion of participants who become abstinent. There has been little research into the achievement of abstinence because of the long-term nature and expense of the necessary investigations, hence the available figures are limited and dated (*17*). Critics of the Swiss cohort study argue that it has failed because only around 8% of participants moved into drug-free treatments within 18 months (*12*). Yet, over this short time frame, the Swiss results are consistent with existing evidence for chronically dependent people (*17*) and may instead show that heroin prescription does not reduce the rate of achievement of abstinence.

4. The introduction of heroin prescription may undermine the attractiveness and effectiveness of other treatments. There is little evidence on which to assess this risk.

5. Heroin treatment may be unaffordable, especially as ever-increasing health costs are a concern of many governments. Results from the Swiss cohort study, however, indicate significant overall savings (SF45 net per person per day) (*12*).

Conclusions

Assessment of the effectiveness of heroin prescription for the treatment of heroin dependence requires that standard clinical trials be set up. However, the nature of the condition, problems with consent, difficulties in running a double-blind trial, and more than one outcome measure are major problems, although they are not insurmountable.

Is the testing of heroin prescription worth the effort? Research trials will be deemed unnecessary and inappropriate by various parties—by some dependent heroin users and their advocates who believe the benefits are self-evident, and by some who find such an approach offensive and incompatible with the principles of medical practice. But the debates about heroin prescription and the potential hope it offers the chronically dependent cannot be resolved without high-quality empirical evidence.

Where will it all lead? Heroin will not replace oral methadone as the treatment of first choice for stabilization. Its short-acting nature and expense (including the necessary social safeguards) preclude its widespread introduction. The clinical trials are important to determine whether heroin has a role as an adjunct to methadone maintenance—to improve treatment success for those who have failed existing treatments. Finally, the prescribing of heroin is about medicalization, not legalization. The 1961 United Nations Single Convention on Narcotic Drugs places effective constraints on pharmaceutical heroin availability. These "limit exclusively to medical and scientific purposes the production, manufacture, export, import, distribution of, trade in, use and possession of drugs" (*18*). Heroin prescription does not challenge the fundamentals of prohibition. Indeed, the debate about heroin prescription should promote continuing assessment of the scientific evidence underpinning current treatment, law enforcement, and prevention policies, as well as stimulating well-designed empirical investigations to find more effective strategies.

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