

Prescribing amphetamine to amphetamine users as a harm reduction measure¹

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Abstract

Amphetamine misuse is a widespread problem in many countries. This paper briefly reviews the history of amphetamine prescribing, considering experience particularly in Sweden and the UK. The current extent of amphetamine prescribing in the UK is described. From this and from the personal experience of the author, guidelines for prescribing are described. These consider the indications and contraindications, goals of treatment, dosage and form, monitoring and how long treatment should continue. The effectiveness of such prescribing is reviewed and the need for more research in this area as well as the need for services targeted at amphetamine users is noted. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

Amphetamine misuse is a widespread problem in many countries (Yoshida, 1997; World Drug Report, 1997). It has been the principal drug of misuse in Japan and Sweden for many years. The US has had an amphetamine problem since the 1960's and there is some evidence of a resurgence

in its use particularly on the West Coast. Currently in the UK and Australia amphetamine is the most frequently used illegal drug after cannabis.

Many users just take the drug on a recreational basis but there are increasing numbers of heavy dependent users. Many of these people inject the drug (Peters et al., 1997) with the attendant risks of HIV and hepatitis C infection and there are other physical and mental health sequelae of heavy amphetamine use. Criminal activity, violence, and social disruption are all associated with heavy use (Farrell et al., 1997).

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In spite of widespread use and the morbidity associated with heavy use of the drug, there has been relatively little recent research into amphetamine misuse (Klee, 1992). This contrasts markedly with the efforts put into research into cocaine and heroin misuse. This paper looks at one aspect of the treatment of amphetamine misusers that of substitute prescribing. It is important to emphasise that amphetamine prescribing should be only one option in a range of treatment approaches to amphetamine misuse. It is one that is, uniquely, available in the UK.

2. History of amphetamine prescribing

Amphetamine was available as an over the counter medicine from the 1930's onwards. It was used to treat nasal congestion, but there were early reports of its being misused for its stimulant and its fatigue delaying effects. During the Second World War it was widely distributed to troops to enhance their performance and to delay fatigue. In the 1950's doctors prescribed amphetamines as a treatment for depression and for the treatment of obesity. The misuse of amphetamine amongst young people began to be seen in Japan in the late 1940's and 50's and in Sweden in the 1950's. The phenomenon appeared in the US and UK in the 1960's.

In Sweden following a large media campaign in favour of liberalisation of drug policy an experiment with legal prescription of central stimulants and opiates for injection was initiated in April, 1965 (Kall, 1997). The idea was to stop the need to commit crime by supplying the drugs the users wanted and then to gradually reduce the dose and get them off the drugs. The experiment was deemed a failure as there was much leakage onto the black market and users were not getting off the drugs and it was ended after 2 years following the death of a young girl from an overdose of morphine and amphetamine (Bejerot, 1970).

There were two reports of amphetamine prescribing in the UK in the 1960's. In 1968 there was widespread methylamphetamine misuse in London that was brought to an end after a few months following the withdrawal of the drug

from retail pharmacies. A special clinic was set up to provide treatment for these misusers and 12 patients received prescriptions of methylamphetamine for injection (Mitcheson et al., 1976). The results of this trial were considered to be a failure. A second report on amphetamine misusers treated with oral amphetamine at a clinic in London in 1968/69 concluded that such prescriptions were unlikely to be effective (Gardner and Connell, 1972). These experiences were influential for nearly two decades in the UK in discouraging amphetamine prescribing as a treatment.

3. Current situation in the UK

An increase in the amount of illicitly available amphetamine sulphate in the UK in the 1980's resulted in an increase in the number of problematic amphetamine users. These did not often present to drug services, which were principally geared to the treatment of opiate users. The system for registering addicts at the Home Office did not include amphetamine users so there was no measure of the numbers who might require treatment. It was the setting up of the first needle exchange schemes in 1987 that brought to light the problem of injecting amphetamine use. In some places more amphetamine users were accessing these exchanges than opiate users (Stimson et al., 1988). A number of drug services in the UK (including our own in Portsmouth) began to prescribe amphetamine to heavy dependent injecting users (Standing Conference on Drug Abuse, 1989).

Over the past 10 years the number of services that prescribe amphetamine has gradually increased in England and Wales—there is no amphetamine prescribing reported in Scotland. This has occurred as a pragmatic response to the problem users that have presented to services but in the absence of much in the way of scientific evidence to support it. Neither has there been any agreed prescribing protocols to guide practice.

The current legal position in the UK with respect to prescribing amphetamine is covered by the Misuse of Drugs Act. Amphetamine is included under Schedule 2, which requires amongst

other things that practitioners conform to certain regulations in the writing of prescriptions. However, any fully registered doctor, either hospital or general practitioner may prescribe amphetamine. In practice such prescribing is almost always undertaken by specialist agencies usually with their own specialist medical staff or sometimes working with local general practitioners. There is also a requirement to inform a regional database on anonymised forms of any drug misuser seeking treatment.

Results from a 1995 survey of community pharmacists in England and Wales (Strang and Sheridan, 1997) concluded that there were an estimated 900–1000 patients receiving amphetamine for the treatment of addiction, 97% in the form of oral preparations. (This compares to an estimated 400 patients receiving heroin prescriptions and 17000 receiving methadone).

We undertook a survey of specialists in drug dependence in England and Wales in 1996 to obtain some information about amphetamine prescribing practices (Bradbeer et al., 1998). We identified 201 doctors and sent them a short questionnaire and obtained a 74% response rate. Of 149 doctors responding, 69 (46%) were prescribing amphetamine. A larger percentage, 60%, agreed that there was a role for the prescription of amphetamine. In addition we have been in touch with several colleagues who have experience of amphetamine prescribing and have asked them about their practice in more detail. This information forms the basis for the following discussion.

4. Prescribing guidelines

4.1. Indications

Prescribing should be limited to primary amphetamine users with heavy problematic use. In the UK this will mean using more than 1 g of street amphetamine sulphate a day. In practice heavy users may take 3 or 4 g a day and will usually have been taking amphetamine regularly for at least several months. Of users presenting

to services 50% are injecting the drug (Department of Health, 1996) and this is the main group for whom substitute prescribing is reserved though some services will consider prescribing for heavy non-injecting users.

The aim is to prescribe only to those users who are dependent on the drug. It used to be considered that though users may become psychologically dependent on amphetamine there was no physical dependence and thus no indication for substitute prescribing. Recent work has shown that both the physical and psychological dependence on amphetamine in regular users has been underestimated and that this is a powerful drive for continued use of the drug (Dackis and Gold 1990; Topp et al., 1995; Topp and Darke, 1997; Cantwell and McBride, 1998)

4.2. Contraindications

These include a history of mental illness, hypertension, heart disease or pregnancy. The issue of mental illness is not always clear cut as heavy amphetamine users often experience paranoid feelings and indeed occasional psychotic episodes. The UK practice generally is to avoid amphetamine prescriptions if there has been an episode of frank psychosis even if this has been associated with drug use, as these sometimes presage the development of a schizophrenic illness.

4.3. Goals of treatment

These are no different from methadone substitution treatment and are principally harm reduction goals. These include a reduction and eventual cessation in injecting activity, and a move to safer injecting practices; reduction in the use of street drugs; improvements in physical and mental health; improved social functioning and this includes a reduction in criminal activity (Lintzeris et al., 1996). Heavy amphetamine misusers are often chaotic in their behaviour and the initial aim is to try and stabilise them and reduce the risks they pose to themselves and others.

4.4. Dosage and form

There is not enough in the way of clinical studies to be able to make very definitive statements about dosage. In the UK, the average purity of street amphetamine sulphate is 5% (Institute for the Study of Drug Dependence, 1997). However, recently amphetamine 'base' has been available which is of much higher purity and this makes it difficult to assess the amount of active drug that a misuser has been taking. The frequency distribution of amphetamine analyses performed on seized drug by the Forensic Science Service in London in 1997 show the modal values remain between 2 and 4%. The mean value is raised in comparison to earlier years because of the small number of higher purity samples, for example 7.6% of samples contained more than 40% amphetamine (personal communication). In general the aim should be to minimise withdrawal symptoms rather than to give an equivalent dose to that used illegally. The pharmacy study found a mean dose for oral amphetamine of 41 mg daily. Our survey gave a mean upper limit of 66 mg. Many practitioners had an upper limit of 60 mg although some prescribed higher doses i.e. 80–100 mg in some cases. Paranoid symptoms were rarely reported as side effects even with the higher dosages. On those occasions when paranoid symptoms were seen it was usually the case that subjects had used illicit amphetamine on top of their prescribed dose.

Concerning the form in which dexamphetamine is dispensed, our preference is for an elixir prepared from amphetamine sulphate powder that is taken orally and is dispensed on several days a week. This minimises the opportunity for diversion. We have had no reports of users injecting the elixir. Most colleagues prescribe oral preparations more often in the form of tablets than in a liquid. The half-life of amphetamine depends on the pH of the urine, and Sherman alkalised the urine to increase the half-life of amphetamine (Sherman, 1990). The average half-life is about 12 h and most practitioners find a single morning dose is effective.

4.5. Monitoring

This is most commonly by urinalysis for the presence of other drugs, and inspection of injection sites. Recently developed techniques allow for the distinction to be made between prescribed and illicit amphetamine in the urine (Tetlow and Merrill, 1996). In addition monitoring should include: mental state, blood pressure and weight and general social stability.

4.6. How long should prescribing continue?

Once again there is little to guide us, and there are differing views amongst practitioners. There is some uncertainty about the long-term effects of amphetamine on the brain (Gawin and Ellinwood, 1988) which has led us to advise that prescriptions should be time limited. However some specialists argue that if users are showing benefit from a prescription—that is that some of the goals of prescribing are being met—and they relapse if the prescription is withdrawn the balance of advantage lies in continuing the prescription. If there is no progress towards any of the goals of treatment then there is little purpose in continuing the prescription. This can be stopped immediately or tailed off. Rates of reduction vary: 5 mg reduction every 1–2 weeks is often used.

5. Issues

5.1. Is amphetamine prescribing effective as a harm reduction measure?

Most of the published reports are of observational and follow up studies and clinical experience and there is little in the way of controlled clinical trials. Klee reports on a study in the Northwest of England of 43 clients presenting to drug treatment services with amphetamine-related problems matched with controls (Klee, 1997). Both groups were followed up for six months. From the treatment group 43% were prescribed amphetamine and it was amongst these that the greatest decline was seen in use of street amphetamine, injecting activity and criminal activity.

McBride et al. (1997) compared a treatment group who received amphetamine with a control group who fulfilled the same criteria but who had attended the same service before dexamphetamine prescribing began. The treatment group used less illicit drugs and showed reduction in injecting activity and had more contact with services.

In addition to these studies there are a number of reports of follow up studies of patients who have received dexamphetamine prescriptions (Sherman, 1990; Fleming and Roberts, 1994; Pates et al., 1996). These have also showed similar benefits. Thus there is an increasing body of clinical work showing the benefit of amphetamine prescribing in the treatment of dependent amphetamine users. These benefits are principally in the area of harm reduction.

5.2. *Other benefits from prescribing*

The perception of many amphetamine users is that current services have little to offer them (Farrell et al., 1997) although if such services did target them they would be more likely to attend. The existence of an amphetamine prescribing programme sends out a message that amphetamine problems are taken seriously. Our own experience (Fleming and Roberts, 1994) has been that following the establishment of such a programme we had a significant increase in self-referrals with amphetamine problems. Interestingly many of these people were not seeking a prescription but were looking for help in reducing and modifying their use of the drug. This is help that a drug service should be providing. Experience with a prescribing service is that in addition to attracting users to services, providing a prescription helps to keep users in treatment (McBride et al., 1997).

5.3. *The need for more research*

Klee noted the lack of research interest into amphetamine misuse (Klee, 1992). Whilst the reports so far have suggested benefits for amphetamine prescribing there is clearly a need for more controlled studies (Mattick and Darke, 1995). The guidelines outlined above have been developed pragmatically from clinical experience.

In this era of clinical effectiveness they need to be firmly based on evidence and this is only going to come from adequate clinical trials. What is lacking at present is any longer term controlled studies into the effect of amphetamine prescribing. We know little about the natural history of heavy amphetamine use and even less about whether a prescription will modify this.

5.4. *Services targeted at amphetamine misusers*

In the UK drug services have historically been directed at opiate users and the needs of stimulant users have been neglected. There is a need therefore to develop specific services targeted at this group (Klee, 1997). As mentioned above services that have offered substitute amphetamine prescribing have found that they attract more amphetamine users to their service not all of them necessarily seeking a prescription. Services should offer help with modifying patterns of use, and general harm reduction advice as well as substitution treatment where this is indicated.

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