



Seminar on Substitution for Methamphetamine users – good practice from abroad

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The experience of prescribing dexamphetamine for dependent amphetamine users

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Where and Why?

- ▶ This presentation describes work undertaken from the mid 1990s onward mainly in Cardiff, a city of 400,000 people in South Wales, UK.
- ▶ Amphetamine use from the 1970s onwards was always more popular than heroin or cocaine because it was cheap and the socioeconomic circumstances of the area.
- ▶ When we established a Community Drug Team in the mid 1980s we became aware that we attracted few amphetamine users. They said “You have nothing to offer us compared to heroin users” (ie methadone)

Where and Why?

But

- ▶ We were aware of the large number of users including high levels of injecting with concomitant risks. We saw people who were amphetamine users attending the needle and syringe exchange.
- ▶ We were aware of a number of chronic users in their 40's having CVAs including a fatal brain haemorrhage.
- ▶ We were aware of the use of amphetamine by many sex workers to get them through their work.
- ▶ We were aware of the incidence of mental health problems associated with amphetamine use.

Amphetamine Substitution Therapy

While the use of methadone (and more recently other opioid drugs) as replacement therapy in the treatment of opiate addiction has been common place for many years in many parts of the world, the use of replacement drugs for the treatment of amphetamine problems has remained controversial and little used with the exception of some projects in the UK. The arguments against replacement prescribing include the fact that there is no obvious long acting drug similar to methadone that could be used and that potentially the same harm could be caused by prescribing amphetamine as caused by street drugs

Amphetamine substitution in the UK

A treatment trial (Mitcheson et al, 1976) during the 1968 “epidemic” of methylamphetamine involved the prescription of methylamphetamine to a group of 12 patients and although one patient showed improvement in social stability and two became abstinent the trial was thought to have been a failure. Mitcheson and colleagues (1976) commented that for these two patients “something considerable was attained – although originally prescribed methedrine they are now off all drugs”.

The drug being used was injectable methedrine so the substitution was of the same drug!

Some Objections to substitute prescribing

- ▶ “The prescription of stimulants is unlikely to lead to desirable changes in behaviour, and carries a number of risks. This is borne out by previous experience in this country of prescribing stimulants regularly to drug misusers, which is generally acknowledged to have been disastrous, resulting in an increase in chaotic behaviour” (ACMD, 1989).
- ▶ The Department of Health Guidelines on clinical management of drug problems also warned against prescribing amphetamines as “the risk of them being diverted (to the black market) is very high” (D.o.H., 1991).

A growing debate

- ▶ Phillip Fleming and colleagues in Portsmouth had started prescribing and had published a paper justifying it.
- ▶ Fleming and Roberts (1994) reported on the first three years of the practice of prescribing dexamphetamine to amphetamine users in Portsmouth. They found that relatively few problematic amphetamine users presented to treatment agencies and commented that injecting amphetamine users are a high risk group as far as HIV transmission is concerned.

The growing debate

- ▶ Fleming and Roberts found that over half of their patients ceased injecting and that there was a considerable reduction by the remainder. Eighty five per cent had not used or shared injecting equipment during the programme. The level of the use of street amphetamine was lower than previously but did not cease .reduced from previously but not ceased. Offending also reduced but there was little change in sexual practices. Most importantly, there was an increase in primary amphetamine users presenting for treatment.

The growing debate

- ▶ I joined the debate: “Prescribing is no panacea. It should be part of a package including services such as counselling, and is not suitable for all amphetamine users, particularly those using small amounts and not injecting. That still leaves many heavy, chaotic users for whom prescribing might provide the opportunity for change” (Pates, 1994)

An important development.

Tetlow and Merrill (1996) developed a method for determining whether those in dexamphetamine replacement treatment were supplementing prescribed dexamphetamine with street amphetamine by separating and quantifying stereoisomers, expressing results as ratios of *l*- to *d*- isomers.

The Cardiff study

- ▶ Pates et al (1996) described a pilot programme in prescribing dexamphetamine for amphetamine users in Wales. Wales has had a high prevalence of amphetamine use for many years but few of these users were presenting to services.
- ▶ The aims of the project were not necessarily to bring about abstinence in the patients but a) to reduce the frequency of injecting, b) to reduce the use of street amphetamine c) to stabilise lifestyle as measured by decrease in prostitution, crime and an improvement in general health.

The Cardiff study

- ▶ Doses were commenced at 30 mgs per day and increased to a maximum of 60mgs. At the end of the trial of 24 weeks frequency of injecting had decrease from an average of 38 times per week to an average of 1.3 times per week and four clients had ceased injecting. The use of street amphetamine had reduced from an average of 40.45 grams per week to an average of 1.6 grams with four clients using no street amphetamine. Lifestyle changes were reported with 5 of the 6 patients who had been sex workers stopping working completely and the other working only occasionally; all reported a reduction in crime and an improvement in general health.

The Cardiff study

- ▶ This was not an RCT, there was no control group as it was a pilot study. Fourteen people were recruited of whom one failed to attend the initial assessment, two dropped out and one developed mental health problems.
- ▶ Subjects were seen as a group on four days per week and the dexamphetamine was dispensed on site on these four days.
- ▶ Inclusion criteria included a history of injecting amphetamine, urines positive for amphetamine and negative for opiates, no current mental health issues and no history of non drug related psychoses, use of amphetamine dependently and not recreationally.

McBride et al, 1997

- ▶ McBride et al (1997) also in Wales, compared 63 patients who were receiving dexamphetamine substitution with 25 patients who received treatment before the service started prescribing dexamphetamine. The patients being prescribed dexamphetamine were retained in treatment for an average 11.7 months compared with an average of 1.4 months for the control group.
- ▶ The number of primary amphetamine users increased from 83 to 197, with the proportion of all patients who were primary amphetamine users from 24.3% to 42.7%.

Efficacy in reducing injecting

- ▶ Charnaud and Griffiths (1998) compared the efficacy of dexamphetamine prescribing for injecting amphetamine users with methadone prescribing for injecting opiate users. One hundred and twenty primary opiate misusers were prescribed oral methadone; and 60 primary amphetamine misusers were prescribed dexamphetamine elixir. The level of injection drug misuse at time of discharge for the two groups was similar, with 67% of the opiate misusers and 70% of the amphetamine misusers having stopped injecting.

Other evidence

- ▶ White (2000) surveyed retrospectively the records of 220 subjects who had been prescribed dexamphetamine for the treatment of amphetamine users.
- ▶ They included both intravenous users and oral users. Outcomes were similar for both groups but the intravenous group showed more overall gains in treatment than the oral group. Over 63% of the injectors stopped injecting and 57% of these stopped within 2 months of coming into treatment

RCTs of dexamphetamine prescribing

- ▶ Shearer et al (2001) reported a pilot randomised controlled study of the prescription of dexamphetamine for amphetamine dependence
- ▶ Twenty one patients were randomised to the treatment arm of the project and 20 to the control arm. All subjects received weekly counselling sessions. The treatment arm received prescribed oral dexamphetamine up to a maximum dose of 60 mgs; the dose was reduced to 40 mgs. at week 12.

Mental health issues

- ▶ Carnwath et al (2002) studied specifically dexamphetamine prescription and the effects on mental health, looked at the notes of eight schizophrenic patients who had been prescribed dexamphetamine for co-existing amphetamine dependence
- ▶ In four out of the eight cases they examined the prescription of dexamphetamine led to good progress both in terms of substance use and their mental health.
- ▶ Adherence to neuroleptic regimes increased in most cases and none of the patients suffered an exacerbation of their psychosis as a result of treatment.

RCTs of dexamphetamine prescribing

- ▶ No adverse events were reported, and no psychotic symptoms were reported for any subjects
- ▶ The proportion of MA in the urines decreased in both groups between baseline and week 6 but there was no significant difference between the groups. In the treatment group, urine levels remained stable at 12 weeks but these increased in the control group. Self-reported street drug use declined in both groups as did injecting. Improvements in psychological adjustment, health and a reduction in criminal behaviour were apparent in both groups; there was no significant difference between the groups.

RCTs of dexamphetamine prescribing

- ▶ Merrill et al (2005) The aims of the study were as follows: a) to investigate the impact of dexamphetamine prescribing for the treatment of amphetamine dependence, b) to assess the practicalities of a research methodology for studying dexamphetamine prescribing in UK clinical settings, c) to assess the effectiveness of dexamphetamine replacement on recognised best available treatment of amphetamine dependence, d) to describe the nature and extent of any benefits or harms on the mental or physical health of those receiving dexamphetamine, e) to contribute to the development of guidelines for best practice in the management of amphetamine dependence.

RCTs for dexamphetamine prescribing

- ▶ There was a reported reduction of in illicit amphetamine use in both groups although this did not differ significantly between groups. There was also evidence of reduced polydrug use in the DEX group during the maintenance phase
- ▶ There was no evidence of reduced injecting behaviour in the DEX group compared with the BATA group.
- ▶ The DEX group showed improvements in physical health outcomes during the maintenance phase with some evidence that this was maintained over the later outcome period.

Merrill et al (2005) – Inclusion criteria

- ▶ Primary drug used amphetamine.
- ▶ Fulfilling DSM IV criteria for dependence.
- ▶ Using amphetamine for four or more days per week for a minimum period of 12 months.
- ▶ Urinalysis confirms recent use of amphetamine
- ▶ Aged 18 years or over
- ▶ Informed written consent to enter trial.

Merrill et al (2005) – Exclusion criteria

- ▶ Pregnancy or lactation
- ▶ Blood pressure when seated over 150/100
- ▶ History of cardiovascular disease, glaucoma or epilepsy
- ▶ Diagnosis of schizophrenia or other serious mental illness
- ▶ Amphetamine psychosis within previous 6 months
- ▶ Body Mass Index below 17.5
- ▶ Opiate dependence
- ▶ Alcohol dependence

RCTs in dexamphetamine prescribing

- ▶ There was a statistical trend showing improvements in psychological health in the DEX group compared to the BATA group in both early and late outcome periods
- ▶ Prescribing dexamphetamine did not have any adverse physical or psychological effects on the participants.

RCTs in dexamphetamine prescribing (Merrill et al, 2005)

- ▶ This pilot study demonstrated the feasibility of conducting a randomised controlled trial comparing the treatment of amphetamine dependence with BATA and BATA supplemented by amphetamine replacement using dexamphetamine tablets (DEX).
- ▶ Both treatments resulted in substantial falls in self-reported amphetamine use during the first month of treatment, which were maintained after the end of the treatment phase.
- ▶ Treatment with dexamphetamine resulted in better physical health early in treatment and trends towards improvements in other problem areas. Although there was a tendency towards better outcomes for treatment with DEX over BATA, the difference was less marked than suggested by previous uncontrolled studies

RCTs in dexamphetamine prescribing (Merrill et al, 2005)

- ▶ The study did not support concerns raised by some that treatment with dexamphetamine confers significant risks to the physical and mental health of patients.
- ▶ . When offered, dexamphetamine should be part of a complete treatment package incorporating psycho-social interventions employed in BATA and clinical monitoring procedures including urine drug screening with the ability to differentiate prescribed from illicit amphetamine, blood pressure checks and mental state reviews.
- ▶ Future studies must involve higher numbers of subjects that are based on power calculations that assume more limited benefits to dexamphetamine prescribing than previously assumed and that anticipate difficulties in recruitment and retention.

Conclusions

- ▶ Although the parallels with methadone prescribing for opiate problems is not exact, promise has been shown for replacement prescribing in terms of stopping or reducing amphetamine and methamphetamine use, reducing or ceasing injecting and improvements in mental health.
- ▶ Most importantly it engages those at high risk in services where help may be offered. Concerns are expressed about diversion, mental health problems etc but all of these may be overcome with adequate service delivery. As with opioid replacement any pharmacological intervention should be accompanied by psychosocial interventions.