Alternative ways of using and abusing drugs and complicity of doctors

Adam Winstock, John Strang

Many drugs that have been prescribed by doctors are not taken as directed. Altered dose, frequency and route of administration may lead to misuse of drugs that have been prescribed in good faith. Awareness of the abuse potential of prescribed and over-the-counter drugs is the first point of intervention, followed by monitoring of each doctor's practice.

Medicine has long been preoccupied with the selective proscription of the various pharmacological agents at its disposal. Until recently, because of technological limitations, the routes of administration and potency of preparations were determined by the form (usually vegetable matter) that the natural product took. Until the industrial revolution, the most common route of drug administration was the oral route — either drinking or chewing, e.g. use of alcohol or chewing of coca leaves by Peruvian Indians.

The other common route of administration was smoking (or inhalation of vapours). This required little preparation of the base product, and became widespread with the migration of tobacco into Europe in the later part of the 16th century, and opium in smoking form towards the end of the 19th century. Smoking provided a more rapid delivery system and was the first step in enhancing the potential pharmacological reinforcing qualities of the drug.

In the 17th century, Dutch ingenuity led to improved distillation, permitting mass production of higher potency beverages. It was not until the second half of the 19th century, however, that modification of the active substances allowed the development of further preparations and hence routes of administration. In 1859, Alfred Niemann extracted the active alkaloid in the coca leaf and named it cocaine, and in 1889, the inventor of aspirin processed heroin from morphine, which itself had only been extracted as the active ingredient in raw opium in 1836. The appearance of the hypodermic syringe around the same time opened the floodgates to the most economical and later the most abusable route of drug administration.

The complementary nature of drug form and means of administration is shown by the sale of morphine and cocaine kits, complete with syringes, at Harrods during World War I, under the slogan 'A useful present for friends at the Front'. These were displayed alongside sales of cocaine solution with special nasal atomisers for inhalation (*Figure 1*). Further advances in pharmacological manufacture and development increased the range of drugs and possible routes of administration available to the doctor (and public) exponentially.

This choice in preparation, route and pattern of administration, and widespread availability dictates the alternative ways of using drugs, other than those sanctioned, prescribed or culturally accepted. The lack of attention in the past to the choices available may have compromised medical practice in some areas, e.g. pain relief. It is imperative that all doctors have adequate knowledge of the practical significance of how route, dose, pattern of administration (including combining a number of drugs) and unsanctioned use may modulate the effect and hence use or misuse potential of a drug. This article highlights some of the common alternative ways of using drugs, and how these may modify effect and usage patterns.

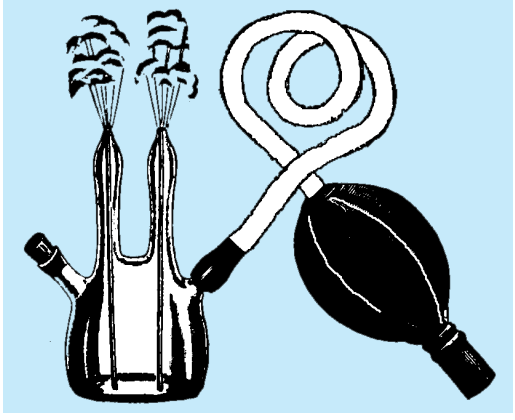

Figure 1. Nasal atomisers for inhalation.

Dr Adam Winstock is Clinical Lecturer in the Addictions and **Professor John Strang** is Professor of the Addictions in the National Addiction Centre, Institute of Psychiatry, London SE5 8AF

Correspondence to: Professor J Strang

ABUSE BY ROUTE

The recommended routes of administration for a particular drug preparation determine, and are themselves determined by, the precise constituents and formulation of the product. Enhanced solubility for intravenous use, slowly distributing preparations for long-acting intramuscular depots, and stability in an acidic environment for oral use are some common examples.

Clearly some routes are associated with inherent body space-specific complications: parenchymal damage and smoking, viral transmission and injecting, gastric irritation and oral consumption (Dinan and O'Flynn, 1994). These route-specific problems are magnified if a preparation specified for one route is inappropriately used by another. Heating and subsequent injecting of temazepam gel capsules designed for oral use led to limb ischaemia and amputation, as the circulating bolus cooled and congealed in major arteries (Strang et al, 1993). Heating methadone suppositories or crushing and injecting methadone tablets causes similar problems because of insoluble particulate matter. Other opiate preparations, e.g. buprenorphine tablets, can be crushed and subsequently injected. An alternative route is generally used to increase the 'bang per buck', although it may also modify the qualitative effects of the drug.

Even in the realm of illicit manufacture a particular preparation may have a preferred route. For example, brown heroin from Eastern Europe is better for smoking than intravenous use since it is less soluble than its whiter Southeast Asian brother. It also has a higher oil content so that it runs on the heated tin foil that is typically used when taking heroin by 'chasing the dragon' (smoking) (Strang et al, 1997). Heroin may be cut with caffeine to enhance its bioavailablity when smoked, while crack cocaine designed for combustion is notorious for the venous damage the freed base causes on injection. There are reports of intravenous use of most drugs of abuse, including amphetamine, MDMA and even alcohol.

Occasionally the reverse occurs and intravenous preparations are used orally, as with intravenous methadone preparations when the user has difficulty gaining venous access. It should be remembered that routes other than intravenous are associated with potential harm. Snorting any drug intranasally, commonly cocaine or heroin (although there have been reports of benzodiazepines being taken this way), can result in septal perforation, while chewing Betel nuts, common in India, Bangladesh and Taiwan, is associated with oral submucosal fibrosis and squamous carcinoma (Wyatt, 1996). Inhalation of crack cocaine combusting at extreme temperatures has been associated with acute respiratory complications (Khalsa et al, 1992), while intramuscular use of drugs may lead to local fibrosis and scarring.

It appears that no route of administration is immune to abuse potential — reports of enema abuse by those with bulimia are well recognized (Mitchell et al, 1991). It is worth noting that in the emergency resuscitation of opiate overdose with naloxone, where venous access may be difficult, a similarly rapid response may be achieved through subcutaneous administration (Wanger et al, 1998).

DOSE AND FREQUENCY OF ADMINISTRATION

Most dispensed medicines, whether prescribed or over-the-counter (OTC), have directions for the dose and frequency of administration. Unless in hospital, this part of the treatment is rarely observed and controllable, so deliberate alteration of the prescribed dosing is a common means of manipulating a drug's effects. Those attending slimming clinics or receiving treatment for narcolepsy, directed to consume one tablet of dexamphetamine in the morning, may store their weekly supply in order to binge at the weekend.

Opiates such as dihydrocodeine may be taken in excessive doses in order to achieve a sense of euphoria, as can opiate-based cough linctus preparations, e.g. Collis Brown (Seton UK, Oldham). Other OTC preparations, such as Benylin (Warner Lambert (Parke Davis Medical), Eastleigh), that contain diphenhydramine, dextromethorphan, codeine and pseudoephedrine, may be used in doses above those recommended to enhance the pharmacological effects of one or more of the constituents. Among the dependent population, those requesting medication for home detoxification from alcohol may choose to consume their whole 5-day chlormethiazole prescription in a day, so increasing the potential problems of respiratory depression that have made this drug undesirable for medically-assisted detoxification.

The preparation of a drug may be modified to widen the range of therapeutic applications, e.g. LAAM, a longer-acting prodrug form of oral methadone that is non-psychoactive but whose breakdown products produce a slow onset steady state opiate effect, or nicotine as transdermal patches or sublingual spray for treating smokers.

INTERACTIONS WITH OTHER DRUGS

The list of medications that carry a warning that they should not be taken with alcohol are too numerous to mention. Although in some instances this is to prevent uncomfortable interactions, such as flushing seen with metronidazole or ketoconazole, more usually it is because

of the potential enhancement of the CNS depressant activity, which may be a sought after-effect by some. Common examples would be the co-consumption of alcohol with benzodiazepines or antihistamines (Buckley et al, 1994).

Use of both alcohol and temazepam is common in methadone maintenance clients, who claim that it enhances the effects they get from methadone. However, for the doctor who wishes to be sure that the drug he/she prescribes is not abused, this is further complicated by the fact that, with both opiate and alcohol dependence, benzodiazepines may be useful in treating the agitation and insomnia that accompany withdrawal.

Polysubstance abuse seems to be the norm among many who use illicit drugs in today's society. Drug users are often noted to use one drug to counteract the less desirable effects of another. For example, the use of cocaine and heroin intravenously together, known as a 'speedball', may seem counterintuitive, but the cocaine may combat the lethargy and sedation associated with heroin use, while the heroin may reduce the agitation and anxiety associated with cocaine use.

Among crack cocaine users there is a high rate of alcohol abuse, probably in an attempt to combat anxiety and insomnia. There are also anecdotal reports of ecstasy users treating the insomnia associated with stimulant use with benzodiazepines and smokable heroin. Such use is a reminder that the effects of a drug are always dependent upon the unique interaction between the individual, the drugs taken, and the set (the mood state at time of ingestion) and setting (environment in which drugs is taken) of consumption.

NON-SANCTIONED 'ADAPTIVE' USE OF DRUGS

Any drug may be used for a multitude of purposes. Prescription drugs are not necessarily taken for the reasons recommended by the manufacturers, nor are illicit ones always taken for hedonistic reasons. To adapt Humpty Dumpty 'when I use a drug I use it for the reasons I want, no more no less'. For instance, opiates other than methadone and heroin may be used by opiate addicts as a way of withdrawing themselves from drugs. Dihydrocodeine or codeine linctus may be preferred for home efforts at detoxification from opiates (e.g. by the addict who has never had any contact with treatment agencies or a GP about his/her drug problems), since they have a shorter half-life than methadone and can be obtained OTC without the need to declare one's addict status. There have been several reports of fluoxetine abuse in non-depressed individuals (Gross, 1996), commonly those with a prior history of substance abuse. Abuse of L-dopa among patients with Parkinson's disease has been reported, often in those with a past history of substance misuse (Soyka and Huppert, 1992).

Because of the political and moral climate of the day, other drugs that may have therapeutic potential have been denied appropriate investigation through clinical trials. In the past, American physicians have claimed that LSD (lysergic acid), and more recently MDMA (ecstasy), have potential as an adjunct to interpersonal and marital therapy. The recent British Medical Association review (1997) drew attention to the potential therapeutic uses of cannabis, and trials are likely to commence soon to explore what many self-medicating users with neuromuscular disorders (e.g. multiple sclerosis) and other conditions (e.g. glaucoma) have reported for many years — that cannabis has medicinal properties. Although prescription of cannabis cigarettes is unlikely, a range of selective orally-active cannabinoids would then become available on prescription in the future.

ALTERNATIVE WAYS OF USING DRUGS TO REDUCE ROUTE-RELATED HARM

Oral methadone as substitute treatment in opiate dependence has consistently shown itself to be cost effective and useful. Results from the National Treatment Outcome Research Study focusing on different forms of drug treatment (many of them involving methadone) have reported that for every extra £1 spent on treatment, £3 is saved in terms of social costs consequent upon drug use (Gossop et al, 1998).

Providing an alternative route to injecting not only reduces the specific harm and risks that are associated with intravenous use, but also removes the addict from a particular lifestyle. Substitute prescribing of amphetamine elixir (not tablets that could be crushed and injected) to reduce intravenous abuse of amphetamines may have a role in carefully selected and closely monitored individuals (Mattick and Darke, 1995). However, these approaches remain in the realms of experimental practice for the time being.

DOCTORS' PRESCRIBING HABITS

Patients' expectations and perceptions of the nature of their symptoms influence the prescribing practices of doctors. In the face of a more drug conscious and knowledgeable younger population, doctors may find it difficult to acheive a balance between an over-ready prescription pad at one extreme, and paranoia at the other. Whether a drug is misused will depend on the interaction between doctor, patient, drug dose and type, and the dispensing arrangements.

The doctor's awareness of abuse potential

The first step in reducing misuse of prescribed drugs is to ensure that such abuse is not compounded by prescribing practices, thus the doctor must be aware of the abuse potential of the product. Unusual presentations with past medical histories suggestive of intolerance to all analgesics except opiate-based products, should, in the absence of corroborative information, signal caution, as should requests for injectable preparations, higher doses or longer prescriptions. Inquiry into misuse of other drugs, whether licit or illicit, must always be sought, with confirmation through urine analysis being a desirable objective marker.

The patient

Suspicion may be raised if the patient has a prior history of substance abuse or dependence. If the patient is receiving treatment from a drug agency, it may be provident to contact that service. Communication through hospital notes is vital if repeat attendees and script requesters are to be intercepted early. Patients new to a practice or seeking temporary care may be particularly difficult. Patients should be asked directly about prior experience of the drug and duration of use. If doubts remain, confirmation by contacting the GP or other health-care providers should be sought.

The drug

Drugs that may be used in ways other than directed to manipulate their effects have already been described. Of concern is the prescription of drugs of dependence, e.g. methadone and amphetamine in tablet form, since these are easily crushed and injected either by the individual prescribed to or by a subsequent recipient. The grey market (diversion of prescribed drugs onto the street market) of drugs gives prescription drugs value. Methadone can be bought for £1 for 10 mg on the streets of London, and 5 mg dexamphetamine is available for between £1 and £2 (A Winstock, unpublished data, 1998). Any patient requesting such drugs as substitute treatment should either be referred to a statutory drug service or have their reported drug use confirmed by urine analysis before a prescription is given.

KEY POINTS

- Drugs that doctors prescribe are not always taken as directed.
- People do not always take drugs for the reasons the doctor prescribes them and in the way in which they should be taken.
- Adulteration of dose, frequency and route of administration may lead to misuse of drugs that have been prescribed in good faith.
- All practitioners should be aware of the abuse potential of a wide range of prescribed and over-the-counter drugs.
- Careful practice can limit abuse potential of the doctor's prescription pad.

The dispensing arrangements

Any doctor can issue dispensing instructions (e.g. 'dispense daily, except Saturday when pick up for Sunday') to the pharmacist when prescribing medications, and can also direct that the prescription may only be filled at a named pharmacy. To minimize the misuse of drugs by patients, either through binge use (i.e. saving drugs to permit episodic heavy periods of use) or diversion to the grey market, drugs such as dexamphetamine and opiate-based analgesics may be prescribed on a daily pick-up basis. Repeat prescriptions without regular review can only compound the problem, as can poor documentation and communication of patient prescribing between doctors within a single practice.

CONCLUSIONS

Many drugs that have been prescribed by doctors are not taken as directed. Adulteration of dose, frequency and route of administration may lead to misuse of drugs that have been prescribed in good faith. Awareness of the abuse potential of a wide range of prescribed and OTC drugs is the first point of intervention, followed by careful monitoring of each doctor's own practice. Where there is suspicion, seek confirmation; where there is doubt, ask the patient. **HM**

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