4.6 Buprenorphine advances offer safer maintenance therapy for heroin addiction

Findings Two studies have tested advances which make buprenorphine maintenance more of a practical alternative to methadone. Study 1 was the first double-blind test of methadone versus buprenorphine in its commercially available tablet form. Study 2 is the first trial of whether the new buprenorphine-naloxone tablet (intended to deter misuse by injection – if injected the naloxone blocks buprenorphine's effect) remains effective taken every other day.

In study 1 Italian clinics randomly assigned 72 new heroin patients to methadone syrup or buprenorphine. All took daily doses of tablets and syrup at the clinics; for half the tablets were inactive, for half the syrup. Over an induction week daily doses were raised to 8mg buprenorphine and 60mg methadone and then maintained for six months. Though not statistically significant, by the end 47% of patients were retained on buprenorphine and 64% on methadone. Drop out on buprenorphine was highest during induction and (unlike on methadone) was greatest among patients with more severe problems. Reductions in heroin use and in psychological and social problems were similar in both groups.

LINKS Nuggets 2.3

In study 2 47 US opioid addicts were inducted on to buprenorphine-naloxone tablets over two days. This rapidity minimised initial drop out but a quarter complained of withdrawal symptoms. Switching to buprenorphine-only tablets for induction halved complaints. After induction, patients were stabilised on 8mg buprenorphine and 2mg naloxone daily for two weeks, then allocated at random to a further three weeks on these doses, to the same doses but every other day, or to double doses every other day. All patients took the same number of tablets every day, gaps being filled by placebos. Just 14 completed the study, most leaving during stabilisation. Among those who stayed, the dosing regimes did not result in different ratings of withdrawal or opioid effects and heroin use remained common. Retention was (non-significantly) better on the double-dose regime which did not cause adverse effects.

In context Early drop out was a feature of both studies and tended to involve those with greater drug needs and problems. Poor retention has been noted in other studies of buprenorphine as patients opt to (re)turn to methadone or illegal opiates. High-dose heroin users are unlikely to be satisfied by buprenorphine because its effects level off above the equivalent of about 60mg of methadone. Even this ceiling may not have been reached in the current studies.

As in other studies with poor retention, while on alternate day dosing in study 2 patients still had to attend every day. Effectively they lost what for them was the main benefit of this dosing schedule. Retention is better among patients who are allowed to experience this benefit. Patients who stay in treatment usually do at least as well on buprenorphine as on equivalent doses of methadone.

Practice implications Buprenorphine is becoming established as a safer alternative to methadone, especially for clients who could have been maintained on moderate doses. High doses remain safe and while (beyond a certain limit) these do not increase the opiate effect, they do increase its duration, making dosing every two or three days possible. Where methadone is tied to daily on-site consumption, this alone may make buprenorphine more attractive to clients and improve retention. Combined with naloxone, buprenorphine remains effective on a less than daily schedule and is unlikely to be misused by injection, reducing the need to supervise consumption. The net result should be less costly treatment. These safety, cost and convenience factors make buprenorphine attractive for less dependent patients and for primary care settings. Rapid induction to relatively high doses and at first using buprenorphine alone helps overcome retention problems yets presents a low risk of overdose.

Featured studies 1 Pani P.P., *et al*. "Buprenorphine: a controlled clinical trial in the treatment of opioid dependence." *Drug and Alcohol Dependence*: 2000, 60, p. 39–50 2 Amass L., *et al*. "Efficacy of daily and alternate-day dosing regimens with the combination buprenorphine-naloxone tablet." *Drug and Alcohol Dependence*: 2000, p. 143–152. Copies: for both apply DrugScope.

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