2.3 Buprenorphine safer than methadone for less dependent patients

Findings Two studies have confirmed the effectiveness of buprenorphine maintenance as an alternative to methadone for less heavily dependent opiate addicts.

Study 1, a double blind trial in three Swiss centres, reported interim results for 58 daily opiate users, 27 randomly allocated to buprenorphine, 31 to methadone. Over a two-week induction period low starting doses were adjusted to (respectively) a maximum of 16mg (generally at least 12mg) and 120mg daily before four weeks of maintenance. During induction drop out on buprenorphine was significantly higher; by the end of the study under 60% remained compared to nearly 100% on methadone. The fact that illegal opiate use (revealed by urinalysis) was not significantly higher may have been an artifact of differential drop out.

Study 2 at an Austrian addiction clinic involved a week of screening when morphine was prescribed, after which 29 opioid dependants were randomised to buprenorphine and 31 to methadone. Over six days doses were adjusted to a limit of 8 and 80mg respectively then maintained for 23 weeks. Daily doses averaged 7.5 and 63mg. Drop out on buprenorphine was not excessive during induction but then became significantly greater, until by the end of the study 38% of patients were retained compared to 71% on methadone. On the (unlikely) assumption that all drop outs resumed illegal opiate use, there was no significant difference on this outcome. However, while in treatment patients on buprenorphine provided significantly fewer opiate positive urines.

In context Buprenorphine's advantages derive largely from its combined opiate and opiate-blocking effects. Compared to methadone, it is less liable to abuse, far safer in overdose, and withdrawal symptoms are mild, yet taken once a day (or even every two or three days) it prevents heroin withdrawal and reduces the desire to take heroin. There are drawbacks: it is best taken by the inconvenient means of holding under the tongue for several minutes; the injectability of the tablets heightens the risk of abuse; and beyond a certain point higher doses do not have more effect, potentially rendering it unsuitable for high-dose heroin users.

These studies suggest that a slow induction phase and limited doses risk higher drop out than with methadone as patients opt to (re)turn to methadone or to illegal use. Studies in the USA and France suggest buprenorphine can work at least as well in primary care settings as in specialist clinics. The US study recorded acceptable retention and drug use outcomes from dosing three times a week, but there primary care treatment is an unusual and (for patients) welcome innovation.

Practice implications For less dependent patients, buprenorphine can be a viable alternative to methadone. Its safety in overdose and (allied to this) the feasibility of prescribing high enough doses to last two or three days suit it to primary care settings and to patients resistant to daily visits. Swiss experience (study 1) commends it as a starting and end point for maintenance, with those not held by the drug being transferred to methadone before (at the end of treatment) easing withdrawal by switching back. Many will be able to manage throughout on buprenorphine with (if injecting can be prevented) a net increase in safety. Care is needed during induction as buprenorphine can precipitate withdrawal, encouraging drop out. Concern over the injectability of the tablets (why UK guidelines recommend supervised dispensing) should be allayed when a combination product becomes available which renders injecting ineffective. In the interim, prescribers should be aware of the history of injecting-related damage from abuse of buprenorphine in the UK.

Main sources 1 Uehlinger C., *et al*. "Comparison of buprenorphine and methadone in the treatment of opioid dependence." *European Addiction Research*: 1998, 4 (suppl 1), p. 13–18 2 Fischer G., *et al*. "Buprenorphine versus methadone maintenance for the treatment of opioid dependence." *Addiction*: 1999, 94(9), p. 1337–1347. Copies: for both apply ISDD.

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