15.1 Depot naltrexone extends opiate abstinence

Findings A long-acting version of the opiate blocking drug naltrexone nearly doubled the time heroin dependent patients were retained in abstinence-based treatment, creating an opiate-free space during which to begin the construction of non-addicted lifestyles. The new formulation is injected into the buttocks, avoiding surgical implantation. Opiate-blocking effects last about four weeks.

The first trial to test this formulation against a placebo injection recruited 60 heroin dependent patients at two US clinics. After inpatient detoxification, their reactions to oral naltrexone were tested for three days before random allocation to two injections either of a placebo solution, of low-dose naltrexone (one injection active), or of full-dose naltrexone (both active). Injections were repeated four weeks later. All participants were offered twice weekly relapse prevention therapy and monthly psychiatric consultations.

While patients stayed in treatment, regardless of the medication 70–80% of urine tests were free of opiates. Where naltrexone made the difference was in enabling them to stay for longer. On the full dose patients stayed for on average seven weeks compared to just under four on placebo, and over two-thirds (68%) remained for the full eight weeks of the trial compared to well under half (39%) the placebo patients. Results for low-dose naltrexone patients were intermediate.

In context Through ads and word-of-mouth, the trial recruited healthy volunteers uncomplicated by a range of psychiatric conditions or co-dependencies, potentially limiting its applicability to heroin users accessing treatment through normal channels, especially those most likely to substitute non-opiate drugs for heroin.

As in normal practice, presumably only patients prepared to irreversibly commit to at least four weeks without the effects of heroin would have entered the study. Nevertheless, without naltrexone only a minority were able to sustain this commitment. It seems that placebo patients tested the blockade by taking heroin, realised they were not insulated from its effects, and then typically were unable to resist dropping out of treatment and (probably) back to dependent use. Perhaps the most encouraging finding is that though the naltrexone patients could have refused the second set of injections, few did so.

Long-acting naltrexone formulations have not been associated with the greatly elevated risk of overdose death seen in patients prescribed oral naltrexone relative to those on methadone or buprenorphine maintenance. Patients at high risk on oral naltrexone have been found to reduce their risk during and following implantation.

Practice implications The trial confirms other less well controlled studies which together suggest that voluntary commitment to a period of enforced abstinence from opiates (or at least, from their effects) might help some patients construct an opiate-free lifestyle. For suitable patients, depot naltrexone is a convenient way to create this space, avoiding the expense, inconvenience and complications of a minor surgical procedure or lengthy residential rehabilitation.

The main unresolved issue is which types of patients *are* suitable. The clearest candidates are those motivated to return to a life without opiate-type drugs (including prescribed substitutes) and who have the resources, stability and support to sustain this, but who when free to experience heroin cannot resist using the drug. Depot injections may also be considered for unstable patients at very high risk of overdose, but who will not accept or do not do well in substitute prescribing programmes. One complication is that the injections negate the medical effects of opiate-type drugs, including pain-relief. Unless carefully managed (and perhaps even then), transfer from an implant or depot preparation to oral naltrexone or to non-medicated aftercare may be a high-risk period for relapse and accidental overdose. Though they can still be prescribed, naltrexone implants and depot formulations are not licensed as medical products in Britain.

Featured studies Comer S.D. *et al*. "Injectable, sustained-release naltrexone for the treatment of opioid dependence: a randomized, placebo-controlled trial." *Archives of General Psychiatry*: 2006, 63(2), p. 210–218. Copies: www.canadadetox.com/English/downloads/InjectableSustainedReleaseNaltrexone.pdf.

LINKS Nuggets 14.3 Nuggette 15.5

Contacts Sandra D. Comer, New York State Psychiatric Institute and College of Physicians and Surgeons of Columbia University, 1051 Riverside Drive, Unit 120, New York, NY 10032, USA, sdc10@columbia.edu.