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▶ After the randomised injectable opiate treatment trial: post-trial investigation of slow-release oral morphine as an alternative opiate maintenance medication.

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Slow-release capsules of morphine – the closest drug to heroin – might offer acceptable and effective treatment to addicts who cannot settle on methadone. In England a dozen also being prescribed heroin switched their supplementary methadone to morphine, generally experiencing the benefits they expected and cutting their average dose of heroin.

Summary Editor's note: Once in the brain heroin is rapidly metabolised to morphine, a conversion responsible for its opiate-type effects. The heroin rush is thought to be more intense than that of morphine because heroin's greater fat solubility enables it to penetrate the brain more rapidly, but otherwise the effects of heroin are effectively those of its metabolite, making morphine the closest substitute drug.

Morphine in the form of morphine sulphate is available as a capsule which when swallowed slowly releases the drug continuously over a 24-hour period, providing steady blood levels of the drug [Editor's note: a property which duplicates the main advantage of oral methadone: that it can be taken once a day and evens out the multiple daily peaks and troughs associated with heroin]. Though marketed for medical use in the UK, it is not licensed specifically for the treatment of opioid addiction. However, it is licensed and used for this purpose in some countries of continental Europe and is also used on an individual patient basis in the UK and Australia.

Problem-free transition of patients from methadone to slow-release morphine has been documented, including in Slovenia where at 12 clinics 39 methadone-intolerant patients were transferred to the drug. The featured study trialled a similar process, but among

patients being prescribed oral methadone and injectable heroin within the British randomised injectable opiate treatment trial (RIOTT); those who were unhappy with methadone had this part of their prescription transferred to slow-release morphine capsules but could continue to inject legal heroin.

Patients who having completed the trial were still dissatisfied with oral methadone could not be transferred to buprenorphine because it would precipitate withdrawal since they were also taking heroin. Slow-release morphine capsules offered an alternative long-acting opiate. Transfer to this drug was tried for all 12 patients (11 men and one woman) to report intolerance or dislike of methadone. On average before entering the trial and being prescribed heroin they had been injecting 25 days per month despite being in maintenance treatment, but were now no longer taking any illicit heroin.

Based on earlier reports, the targeted dose of morphine was about 6mg for each mg of methadone. The switch between the two drugs to the full dose of morphine and zero methadone was made gradually over about five days, then for a few weeks the morphine dose was titrated up or down to suit the individual patient. Unlike the patients' prior oral methadone doses, all the medication was taken under supervision. Patients were monitored daily for any discomfort, intoxication and side-effects.

Pre-switch case notes documented the patients' reasons for wanting to switch and what they expected taking morphine would be like. Interviews 8–12 weeks later also recorded in notes documented their actual experiences at a time when they had been stabilised on morphine.

Main findings

Common themes among reasons for and expectations of the switch to morphine included seeing this as a route to reducing dose and/or number of injections of prescribed heroin, and therefore also reducing the frequency of clinic visits in order to take these doses under supervision. A few thought morphine might enable them to stop injecting prescribed heroin altogether. Commonly patients felt methadone hard to withdraw from and that it gave a poor experience compared to heroin, both of which might be improved by morphine.

After having been stabilised on morphine 10 of the 12 patients said the transition had been smooth, quick and problem-free; the other two reported only minor problems which rapidly resolved. Most experienced a noticeable peak effect from the long-acting formulation around three hours after taking it. Once the dose had been appropriately adjusted, all but two found it kept them comfortable for the full 24 hours. Generally no side-effects were noted and none were serious. Most (in each case eight to 10 of 12) said morphine induced feelings of well-being, improved sleep and reduced craving for other drugs, and that they preferred it to methadone.

On average patients ended up taking 7.5mg morphine for each mg of their prior methadone dose. Five reduced their dose of prescribed heroin by over a fifth, two patients reduced the number of days each week when they were prescribed injectable heroin, and after a break in treatment a third preferred to do without heroin altogether and take only morphine. Overall, after 10 weeks the average dose of prescribed heroin had fallen significantly from 382mg to 315mg.

The authors' conclusions

The findings suggest that the option of long-acting oral morphine, a drug more akin to illicit heroin, might help reduce the drop-out rate in methadone and buprenorphine maintenance, offering a palatable treatment continuation route for some dissatisfied with methadone. In this study, all 12 patients who chose to change from oral methadone successfully switched over a few days with no major problems and most experienced greater satisfaction with the new regimen and felt it was more effective and improved their lives. The positive impacts on mood and sleep confirm results from previous trials, and might reduce the need to prescribe sedative, anti-anxiety and antidepressant medications, with consequent improvements in safety.

Before switching, two thirds hoped morphine might provide a route to reduce their heroin doses and gradually detoxify out of opiate substitution treatment. Indeed, after 10 weeks the average daily heroin dose had fallen significantly, and two patients had at least one day a week when they were no longer prescribed injectable heroin, allowing them to be injection-free on that day, as well as freeing the day for non-clinic pursuits. Another maintained a switch away from injecting altogether. In these ways, as anticipated by the patients, transferring from methadone to morphine allowed them to progress in their treatment plans – in particular, to move away from injecting, a valuable harm reduction step for injectors who cannot achieve abstinence. Moreover, the patients' clear preferences for morphine should improve compliance with treatment and reduce illicit drug use.

One challenge posed by this new treatment is the potential for misuse; injecting the oral formulation or crushing and chewing the capsule content delivers a sudden release of several times the oral dose equivalent, risking fatal overdose. In the study patients could not do this because all doses were supervised, an essential safeguard when there are concerns about treatment compliance and diversion of medications to unintended uses.

FINDINGS UK guidance on addiction treatment says that "Oral opioids other than methadone and buprenorphine, such as dihydrocodeine and slow release oral morphine (SROM) preparations, are not licensed in the UK for the treatment of opiate dependence and should not normally be used in the community." British Association for Psychopharmacology guidelines say slow-release oral morphine has been found as effective as oral methadone, but caution that in Austria the product has frequently been abused and dominates the black market. Guidelines produced for the World Health Organization agree that slow-release oral morphine has been found equivalent to methadone in suppressing heroin use but found the research base too thin to make any consequent recommendations. The experts convened by WHO also warned that prescribing this product is complicated by difficulties in supervising doses and in assessing heroin use [Editor's note: the latter because the presence of morphine could otherwise be used to indicate illicit heroin use, a problem which can be overcome].

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