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▶ Challenges to antagonist blockade during sustained-release naltrexone treatment.

Kunøe N., Lobmaier P.P., Vederhus J.K. et al.
Addiction: 2010, 105, p. 1633–1639.
Request reprint using your default e-mail program or write to Dr Kunøe at nikolaj.kunoe@medisin.uio.no

Despite being motivated to sustain abstinence and implanted with a drug which should have blocked the effects of opiates, in Norwegian studies most opiate-dependent patients used opiates and about a quarter did so repeatedly.

Summary This account draws on Findings analyses of the two main source studies set in prison and inpatient services respectively.

The featured report recruited opiate-dependent patients allocated to naltrexone implants in three Norwegian studies. Naltrexone is an antagonist which has no psychoactive effects of its own but blocks the effects of heroin and other opiate-type drugs. The implant form of naltrexone is inserted under the skin. In the form used in the studies, blocking effects last for five to six months, avoiding the need to take the medication daily and in theory overcoming the main shortcoming of oral naltrexone − that patients usually stop taking the pills and resume heroin use.

One of the source studies involved prisoners dependent on opiates before their sentence. Sixteen of the 24 who had been allocated to naltrexone were actually implanted before release after being randomly allocated to this or to methadone maintenance to promote continuity of treatment on release and avoid relapse. They were the minority prepared to accept random allocation (most potentially eligible prisoners did not) and who accepted the treatment to which they had been allocated (eight refused the implant).

In a second study, 56 inpatients (of 667 who might have qualified for the study) coming towards the end of their detoxification or residential treatment agreed to be randomly allocated to the implant or to usual aftercare arrangements; 26 of 29 allocated to naltrexone were actually implanted. A third study involved a further six implanted patients.

From these studies 60 implanted patients were recruited for the featured study to assess the degree to which over six months the implants actually did block the effects of opiate-type drugs and prevent opiate use. Of the 60, 42 came from treatment and 18 from criminal justice settings. All but five completed follow-up interviews and for the missing five data was collected from contacts such as families or treatment staff.

Main findings

All the blood samples taken at the end of month five and all but three taken in month six revealed that naltrexone levels had remained above that normally associated with a blocking effect.

Over half (34) of the 60 patients had used illicit opiate-type ('opioid') drugs during the six months when the implants were active; 14 did so on just one or two days, while at the other extreme, nine did so on average at least every other day. Across all the patients, from an average of 18 days per months before implantation, illicit opiate use fell to six days in the final month of the six months of the implant, having risen from even lower levels over the preceding months.

Patients who had tried opioids in the first month of their implants were more likely to try again later. During the six-month follow-up, patients who took opioids were also more likely to be using other types of drugs including benzodiazepines, cocaine, amphetamines and cannabis, more likely to have injected drugs, and more involved with the criminal justice system. By the end of the six months, patients who had avoided opioids were more satisfied with their quality of life and housing, less anxious or depressed, and had found more and better work.

Of the 34 patients who had tried opiate-type drugs, 31 told researchers how it had felt; 22 felt no definite euphoria or 'high' and nine some effect, of whom three said this was a fully fledged high on at least one occasion. The greater the high they had experienced, the more often patients used opioids and also benzodiazepines.

Two patients had sought to overcome the blockade by taking unusually high doses of opiate-type drugs. Among these was one of the two who experienced non-fatal overdoses; the other patient's overdoses were due to use of non-opiate drugs. No further serious adverse events were reported.

The authors' conclusions

On average opioid-dependent patients who received sustained-release naltrexone implants substantially reduced their opioid use but this reduction was unevenly distributed. Almost half did not use at all, while at some point just over half tested the naltrexone blockade, and about a quarter of the sample did so repeatedly. Yet most of this opioid use occurred when naltrexone levels were above those shown previously to block the pleasurable effects of heroin. This repeated use cannot generally be attributed to successful overcoming of the blockade. Many patients confirmed the blocking properties of naltrexone by administering heroin or other illicit opioids, sometimes at high doses, to no effect. Few who tested the blockade reported repeatedly having experienced a full-blown 'high'. When some degree of euphoria was experienced, this may have been due to concurrent use of other types of drugs or due to expectations and conditioned responses.

Whatever the reasons for using heroin or other opioids while on naltrexone, this was associated with poor outcomes. By the end of the six months, patients who had repeatedly tested the blockade had returned to pre-treatment levels of opioid use. Patients who tested the blockade were also more likely to be using non-opioid drugs and to have social adjustment problems, including a more serious involvement in crime.

Rather than being of no significance or a salutary (non)experience, these findings suggest that use of opioids during implant treatment is indicative of the need for urgent clinical attention. In the present study, even patients who used opioids only once or twice tended to report more problem behaviours relative to abstinent patients. Repeated use (with or without reported 'highs') is a warning sign that the patient is at risk of relapsing to a lifestyle involving polydrug use and crime. Services should monitor patients for injecting polydrug use before and during sustained-release naltrexone treatment and where required, offer supplemental interventions to address the wider context of substance use for the individual.

Clinicians who provide this type of medication can expect that many patients will test the blockade by using opioids, some frequently, and some experiencing what they interpret as an opioid 'high'. The latter may warrant blood or urine testing to check naltrexone levels.

FINDINGS Other reports from the Norwegian implant studies have also been analysed by Findings, in analyses which details the findings, place these in the context of related research, and explore UK regulations and experience related to naltrexone implants. Two concerned one of the main source studies for the featured report conducted in prison. One focused on the acceptability of the attempt to randomly allocate prisoners to the treatments, while the second focused on drug use and other outcomes after six months. From the same research team, the other main source study for the featured report tested naltrexone implants versus normal aftercare for opiate-dependent patients leaving Norwegian inpatient treatment centres.

As well as the featured report, data from implanted patients in these and another Norwegian study have been amalgamated in a report on how many of the patients continued the treatment by having a second implant after six months. About half did so.

From these Norwegian reports it seems that six-month naltrexone implants can be an effective and lasting aid to curbing opiate use for the minority of patients motivated to aim for opiate abstinence and prepared to accept that opiate effects may be unavailable to them for six months. Because it does not require the patient to choose to enter aftercare treatment, the option may have a particular role in safeguarding patients emerging opiate-free from prison or other protected environments such as inpatient detoxification centres. However, and despite being motivated to sustain abstinence and being implanted, many if not most patients try opiates again and some do so repeatedly.

This draft entry is currently subject to consultation and correction by study authors.

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