8.8 Lofexidine safe and effective in opiate detox

Findings Lofexidine has been confirmed as the preferable non-opiate alternative to methadone for opiate detoxification.

The featured study reviews trials of a class of non-opiate drugs known as alpha2 (or 'α_2') adrenergic agonists. These are thought to suppress a neural network whose rebound over-activity in withdrawal causes symptoms such as chills, cramps, and diarrhoea. Clonidine and lofexidine are the major agents. Three studies comparing them found that the time course (typically peaking at two to four days), intensity (not very severe), and pattern of withdrawal symptoms were similar. However, side-effects from lofexidine were fewer, less serious (especially drops in blood pressure) and required less intervention. If anything, detoxification retention and completion rates were better with lofexidine, but there was very little data.

These findings suggest lofexidine will perform at least as well as other α_2 agents (clonidine has been studied most) as an alternative to tapering doses of methadone. In ten comparitive studies, withdrawal severity was similar or slightly greater on these agents but symptoms peaked within a few days while on methadone the peak was around or after the taper reached zero, usually at least 10 days. Compared to methadone, similar or slightly fewer patients successfully completed detoxification. Clonidine caused greater blood pressure reductions than methadone but this was not a problem with lofexidine.

In context Alternatives to methadone have generally been tried on patients taking relatively low doses of opiates and/or after intake has been moderated through lead-in methadone prescribing. The review included outpatient and inpatient regimes but in Britain outpatient procedures are much more common, and one of lofexidine's main advantages is that safety and low abuse potential permit less close supervision. Documented British experience with outpatient lofexidine is mixed. In one study 71% completed detoxification and were opiate-free but in another just 37%. In the first patients were stabilised on methadone beforehand, screened more stringently for motivation, and frequently supported through home visits. In a survey, UK drug dependency units reported a 60% completion rate but the clinics and the patients may not have been representative.

British inpatient studies have tested compressed four or five day regimes. These start with high doses and may combine lofexidine with naltrexone to precipitate withdrawal. Completion rates were around 80% and symptoms remitted more quickly than on conventional lofexidine regimes. Since this works well with clonidine, there seems no reason why the lofexidine/naltrexone regime cannot be conducted on an outpatient basis with close medical supervision for the first day, a procedure tried successfully in Italy.

Buprenorphine is another alternative to methadone. In terms of comfortable completion of withdrawal it seems preferable to clonidine but it is unclear whether it will also better lofexidine. However, its abuse potential may be seen as requiring supervised consumption.

Practice implications Lofexidine is effective and safe in inpatient or outpatient detoxification and can be given in high starting doses with or without naltrexone to reduce the medication phase to a few days. It is particularly suitable for patients prepared to abruptly stop opiate use without inpatient support and (because it creates an opiate-free gap of a few days) lends itself to longer term naltrexone prescribing to prevent relapse, especially if the detoxification itself involved naltrexone. Supervised consumption is not necessary on safety grounds or to prevent diversion or abuse. Screening for suitability, prior stabilisation on methadone (which may also be used to reduce opioid intake to more manageable levels), and frequent patient support (perhaps best achieved through home visits) are probably important ways to maximise completion rates. For other patients, reducing doses of buprenorphine or methadone may be preferred, especially if the chances of abstinence are low. In these cases patients can seamlessly transfer to substitution treatment using the same drug.

LINKS Nuggets 7.1 5.5

Featured studies Gowing L.R. *et al*. "α_2-adrenergic agonists in opioid withdrawal." *Addiction*: 2002, 97, p. 49–58. Copies: apply DrugScope.

Additional reading Strang J. *et al*. "Lofexidine for opiate detoxification." *American Journal on Addictions*: 1999, 8, p. 337–348. Copies: apply DrugScope.

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