

Managing opioid dependence

Comparing buprenorphine with methadone

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West SL, O'Neal KK, Graham CW. A meta-analysis comparing the effectiveness of buprenorphine and methadone. *J Subst Abuse* 2000;12(4):405-14.

Research question

Is buprenorphine as effective as methadone for managing opioid dependence?

Type of article and design

Meta-analysis by three reviewers.

Relevance to family physicians

Community-based family physicians are uniquely suited to care for opioid-dependent patients. Buprenorphine, like methadone, is a substitution treatment for opioid dependence. Buprenorphine is available in Canada only through a special access program, which is not currently enrolling new patients. Now that the United States Food and Drug Administration has approved primary care physicians' prescribing of buprenorphine, we expect it will soon be available in Canada.

Compared with methadone, buprenorphine has certain theoretical advantages. The most notable pharmacokinetic difference is that buprenorphine has a substantially longer half-life than methadone. Methadone patients generally require once-daily dosing, but many buprenorphine patients can be treated once every 2 or 3 days. This has important clinical implications, because many opioid-dependent patients have to go to a pharmacy for supervised ingestion of methadone or buprenorphine. Lessening the burden of daily pharmacy visits might improve some patients' lives. Also, as mentioned in this meta-analysis, many patients have difficulty discontinuing methadone because they suffer interdose withdrawal, which frequently occurs with lower

doses. Theoretically, this should be less of a problem with buprenorphine.

The most notable pharmacodynamic difference is that methadone is a full opioid agonist at the μ -receptor, while buprenorphine is a partial agonist. Buprenorphine is limited in its ability to cause respiratory depression, which makes lethal overdoses less likely. Furthermore, its use potentially results in less severe physical dependence, making detoxification easier.¹

Overview of study and outcomes

MEDLINE and PsycINFO were searched from 1974 to 2000 for articles reporting controlled comparisons of buprenorphine and methadone. To be included, studies had to provide quantifiable data on both treatment efficacy as determined by ongoing illicit opioid use and the total number of subjects testing positive and negative for illicit opioids at the end of the study period. Reviewers excluded studies in which participants had coexisting psychiatric disorders or reported a primary drug of abuse other than an opioid. Of more than 1595 articles found, nine met the inclusion criteria. The only common outcome measure across all studies was urine toxicology screening.

Results

The authors determined the difference between methadone and buprenorphine using the statistical method of "effect size." In this case, the effect size measured the effectiveness of buprenorphine relative to methadone in achieving negative results of urine toxicology screening. Average unweighted effect size across all studies was r -0.0460, with the negative sign indicating a better outcome for methadone. In other words, average people taking methadone did 4.6% better on urine screening than those taking buprenorphine.

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An effect size this small is unlikely to be clinically significant. Using guidelines developed by Cohen,² the authors noted that this effect size is "below the level normally considered small." The authors also tested cumulative significance and found no significant difference between buprenorphine and methadone groups.

The authors noted great variability among studies: outcomes were statistically more spread out than would be expected by chance (χ^2 25.42, $P < .001$). This often indicates that individual study characteristics have influenced effect size. Five articles had no common characteristics that could be examined after the trial. The one characteristic the authors were able to analyze was prior experience with methadone. This analysis pointed out that studies that included patients with a history of methadone treatment showed that buprenorphine was more effective than methadone (z 3.99, $P < .01$).

Analysis of methodology

Patients with coexisting psychiatric disorders were excluded, so we do not know whether these results apply to them. The authors' post-hoc analysis seems appropriate given the great variability in the nine studies included. It also emphasizes the importance of variables other than the treatment drug in effective management of opioid dependence. Patient characteristics (eg, age, sex), treatment drug dosage, length of illicit drug use, to name a few, could all be important in deciding which treatment is best. It is disappointing that the study cannot tell us which variables are important or what effect they have. It is also disappointing that the authors were able to analyze only effectiveness based on urine toxicology. Other measures of effectiveness, such as incarceration rates, levels of employment, and treatment retention rates, are at least as important as urine toxicology. The authors were, of course, limited by the data available to them.

Two other recent well designed studies on the relative effectiveness of buprenorphine and methadone reached similar conclusions.^{3,4} A meta-analysis by Barnett and colleagues³ concluded that subjects who received buprenorphine had a 1.26 relative risk of discontinuing treatment (95% confidence interval [CI] 1.01 to 1.57) and 8.3% more positive urinalyses (95% CI 2.7% to 14%) than subjects taking methadone. They noted that, while this difference might be statistically significant, it is quite small when compared with differences in outcomes in various methadone programs. A recent double-blind, randomized trial⁴ of buprenorphine and methadone demonstrated that subjects in both treatment groups had similar

proportions of opioid-positive urine tests (buprenorphine 62%, methadone 59%).

Application to clinical practice

Current findings suggest that buprenorphine and methadone are relatively equal treatments for opioid dependence. At present, there is very little solid evidence to guide doctor-patient decisions on treatment. Buprenorphine might be more beneficial for patients who find daily visits to a pharmacy very difficult. Buprenorphine might also be a better choice for patients likely to be successful with outpatient opioid detoxification.

While this meta-analysis indicates buprenorphine appears to be more effective than methadone for patients who have had previous methadone treatment, it does not imply that clinicians should switch patients who are currently taking methadone to buprenorphine. There is little controlled experience of transferring methadone-maintained patients to buprenorphine.⁵ Current evidence suggests that buprenorphine's partial agonist properties precipitate opioid withdrawal in patients maintained on >30 mg/d of methadone.⁵

Bottom line

- Buprenorphine is a safe and effective alternative to methadone for managing opioid dependence.
- Buprenorphine might be a particularly effective option for patients with prior, not current, methadone experience. ✱

Points saillants

- La buprénorphine est une option de rechange sûre et efficace à la méthadone pour prendre en charge la dépendance aux opiacés.
- La buprénorphine pourrait être un choix particulièrement efficace pour les patients qui ont eu une expérience antérieure avec la méthadone, mais pas simultanément.

References

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