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EDUCATIONAL SERIES

Opioid Substitution Therapy: Effects on Cognitive and Psychomotor Function

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2018

About the Reviewer



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Peter graduated from the Otago Medical School in 1984. After several years working in general practice, he was inveigled into doing some part-time service for the Christchurch alcohol and drug service. Gradually this commitment grew as he found it was a rewarding, enjoyable and challenging arena of work. He is now engaged in a peripatetic practice, servicing three OST programmes across the mainland.

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This article provides an overview of the potential effects of opioid substitution therapy on cognitive and psychomotor function, with a focus on buprenorphine and methadone. This review is supported by an educational grant from Indivior Pty Ltd.

Introduction

Opioid substitution therapy (OST) is substantially more effective than abstinence-based treatment for patients with opioid use disorders.¹ Buprenorphine and methadone appear to be equally effective as OST,² with buprenorphine being associated with less sedation and respiratory depression.³ However, as psychoactive substances, both methadone and buprenorphine have the potential to affect cognitive and psychomotor function.

Cognitive function

Opioid medications may affect cognitive function because their mechanism of action is mediated via the activation of opioid receptors, which integrates pain modulation with other CNS processes, including cognition.⁴ Despite methodological problems with the literature, a meta-analysis of observational studies suggests that chronic opioid use is associated with deficits in certain neuropsychological domains.⁵ For example, some cognitive impairment is common among chronic pain populations receiving long-term opioid treatment,⁶ and among chronic users of illicit opioids.⁷

In terms of OST, evidence from two small prospective studies indicates less impairment of cognitive function in patients receiving buprenorphine or methadone than in individuals dependent on illicit opioids.^{8,9} Preliminary study evidence also suggests that opioid-dependent patients experience improvements in neuropsychological function after starting OST with either methadone or buprenorphine.^{10,11} However, most drug-induced cognitive impairments in patients with substance dependency diminish or disappear with drastic reduction in consumption or abstinence.¹²

According to a recently published comprehensive systematic review of clinical studies that assessed the cognitive effects of labelled medications used to treat drug dependency, there is a lack of large comparative trials that have assessed the cognitive effects of OST medications.¹³ Additionally, independently of sedative effects, it may be difficult to separate the possible cognitive effects of the OST medication from the effects of drug abstinence itself. Nonetheless, some preliminary conclusions have been drawn from the available clinical study evidence.

Both buprenorphine and methadone appear to impair executive function and general cognition in opioid-dependent patients compared with healthy control subjects.¹³ However, in direct comparisons of buprenorphine- and methadone-treated patients, while some studies have demonstrated no differences between the two medications, most have demonstrated less impairment of cognitive function with buprenorphine.¹³

An improvement of certain cognitive abilities with buprenorphine- compared with methadone-based OST was even evident in some studies.¹³ In a 12-month prospective study, buprenorphine-treated patients improved their performance in working memory to reach a level similar to that of healthy controls while methadone-treated patients remained impaired.¹⁴ Another study reported that OST patients who received buprenorphine performed better than methadone-treated patients in terms of decision-making capacity tested in a gambling task (although not differently compared with healthy control subjects).¹⁵

More recently, a small study assessed whether neuropsychological changes over time in opioid-dependent individuals are linked with depressive symptomatology or adherence to OST with buprenorphine.¹⁶ Increased adherence to buprenorphine, but not depressive symptomatology, was associated with improved neuropsychological functioning. Therefore, facilitating adherence to buprenorphine may benefit learning and memory functioning in OST patients.

Furthermore, a conclusion of a recent review of studies that assessed the effectiveness and side effect profiles of methadone and buprenorphine OST in the primary care setting was that buprenorphine can be recommended for patients whose occupation requires a high level of cognitive functioning or psychomotor performance.¹

Psychomotor function and driving-related skills

Although there is a theoretical potential for opioid agonists to affect driving, a recent comprehensive systematic review of the literature suggests that, notwithstanding the need for more prospective studies, driving-related psychomotor skills are not impaired in people receiving regular therapeutic opioids.¹⁷ This finding is consistent with an earlier literature review that concluded that opioids do not appear to impair driving-related skills in opioid-dependent patients.¹⁸

The influence of long-term buprenorphine use on psychomotor and cognitive function related to driving ability has been assessed in two prospective comparative studies.^{19,20} Compared with matched controls (untreated healthy volunteers), neither opioid-dependent patients receiving buprenorphine OST¹⁹ nor non-cancer patients receiving buprenorphine for chronic pain²⁰ showed significant impairment of complex psychomotor or cognitive performance tests.

These findings are supported by a recent prospective study in which the on-the-road driving performance of chronic



non-cancer pain patients treated with stable doses of long-term prescription opioids did not differ significantly from that of healthy control subjects.²¹

Also contributing to the evidence for limited driving impairment with buprenorphine are the results of a dose-effect study of repeated administration of buprenorphine in opioid-dependent patients that demonstrated minimal impairment in psychomotor performance with increasing doses of buprenorphine.²²

Nevertheless, due to limitations in the overall clinical study evidence base and large

inter-patient variations in test scores in some studies, several researchers have proposed that, in clinical practice, determination of fitness to drive should be assessed on an individual basis.^{20,21,23}

It should also be noted that the co-administration of CNS depressants (e.g., opioid analgesics and antitussives, certain antidepressant and anxiolytic agents, and sedative H1-receptor antagonists) with buprenorphine results in increased CNS depression.²⁴ Reduced alertness can make driving and operating machinery hazardous.

EXPERT'S CONCLUDING COMMENTS

The effect of OST on psychomotor function and cognition is very important. For our patients, attaining employment and/or driving represent significant milestones in progress. The paucity of research is therefore concerning. It is reassuring that research shows patients on OST are less cognitively impaired than those using illicitly. Tentative, but suggestive, is the finding of improved neuropsychological function with OST treatment.

While there is now abundant evidence showing the benefit of OST for the individual and society, the impact still needs to be individually assessed. My experience, plus that of my colleagues, has been that a significant minority of patients transferring to buprenorphine/naloxone from methadone report a noticeable improvement in clarity of thought and alertness. A smaller group found this aversive, as I suspect it made their past and present life situation too stark and clear.

TAKE-HOME MESSAGES

- Buprenorphine and methadone are equally effective as OST in opioid-dependent patients, with buprenorphine having a lower risk of overdose.
- Limited clinical study evidence suggests less cognitive function impairment with buprenorphine than with methadone in OST patients.
- Limited clinical study evidence suggests minimal impairment of driving skills with long-term use of buprenorphine.
- Buprenorphine may be a better OST option for patients with occupations requiring a high degree of cognitive function or psychomotor performance.
- The fitness of patients receiving OST to drive should be based on an individual assessment.

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