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Opioid Agonist Treatment for Patients With Dependence on Prescription Opioids

Suzanne Nielsen
University of New South Wales

Briony K. Larance
University of Wollongong, blarance@uow.edu.au

Nicholas Lintzeris
University of Sydney

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Abstract

Clinical Question Are different opioid agonist treatments (eg, methadone vs buprenorphine) associated with differences in efficacy for treating prescription opioid dependence, and is long-term maintenance of opioid agonist treatment associated with differences in efficacy compared with opioid taper or psychological treatments alone? **Bottom Line** For patients who are dependent on prescription opioids, long-term maintenance of opioid agonists is associated with less prescription opioid use and better adherence to medication and psychological therapies for opioid dependence compared with opioid taper or psychological treatments alone. Methadone maintenance was not associated with differences in therapeutic efficacy compared with buprenorphine maintenance treatment. Evidence quality was low to moderate.

Keywords

prescription, dependence, opioids, opioid, treatment, agonist, patients

Disciplines

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JAMA Clinical Evidence Synopsis

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Suzanne Nielsen, BPharm, PhD; Briony Larance, PhD; Nicholas Lintzeris, MBBS, PhD

CLINICAL QUESTION Are different opioid agonist treatments (eg, methadone vs buprenorphine) associated with differences in efficacy for treating prescription opioid dependence, and is long-term maintenance of opioid agonist treatment associated with differences in efficacy compared with opioid taper or psychological treatments alone?

BOTTOM LINE For patients who are dependent on prescription opioids, long-term maintenance of opioid agonists is associated with less prescription opioid use and better adherence to medication and psychological therapies for opioid dependence compared with opioid taper or psychological treatments alone. Methadone maintenance was not associated with differences in therapeutic efficacy compared with buprenorphine maintenance treatment. Evidence quality was low to moderate.

Introduction

The United States is experiencing an opioid overdose epidemic, with recent increases in prescription opioid–related mortality.[1,2] Opioid agonist treatment is recommended for treating prescription opioid dependence by the US Centers for Disease Control and Prevention.[3] This Clinical Evidence Synopsis summarizes findings from a Cochrane review that aimed to summarize current evidence for the treatment of prescription opioid dependence using opioid agonist treatments.[4]

Summary of Findings

Methadone vs Buprenorphine

Three studies compared methadone with buprenorphine (**Table**). No difference was found in the mean number of days of opioid use (assessed during final 30 days of the intervention, 1.51 days [SD, 4.97 days] for methadone vs 2.92 days [SD, 6.38 days] for buprenorphine; mean difference, −1.41 [95% CI, −3.37 to 0.55]; $P = .16$), opioid use as measured by opioid-positive urine drug screening (27 of 79 participants [34.2%] for methadone vs 51 of 117 participants [43.6%] for buprenorphine; risk ratio [RR], 0.81 [95% CI, 0.56 to 1.18]; $P = .28$), and self-reported opioid use (11 of 66 participants [16.7%] for methadone vs 34 of 89 participants [38.2%] for buprenorphine; RR, 0.37 [95% CI, 0.08 to 1.63]; $P = .19$). No between-group difference was found in treatment adherence for methadone (Table).

Evidence Profile

No. of studies: 6 randomized clinical trials

Study years: Conducted: 2002-2014; published: 2003-2015

Last search date: May 13, 2015

Number of participants: 607

Men: 77% **Women:** 33%

Race/ethnicity: 86% white (reported in 3 studies)

Age, mean (range): 32 years (17-60 years; reported in 3 studies)

Setting: Outpatient; 1 study recruited from emergency departments

Countries: United States and Iran

Comparisons: (1) Different opioid agonist maintenance treatments (methadone vs buprenorphine) and (2) maintenance treatment (buprenorphine) vs opioid taper and vs psychological treatment alone.

Primary Outcomes: Illicit opioid use and treatment adherence (attending counseling visits, taking prescribed medication per protocol, or both).

Secondary Outcomes: Pain, injecting behaviors, quality of life, physical and psychological health.

Buprenorphine Maintenance vs Opioid Taper

Three studies compared buprenorphine maintenance with opioid taper or psychological treatment only. No between-group difference was found for mean days of opioid use during past 7 days or 30 days (standardized mean difference, −0.31 [95% CI, −0.66 to 0.04]; $P = .08$). Buprenorphine maintenance treatment was associated with reduced opioid use as determined by urine opioid-positive drug screening (39 of 97 participants [40.2%] vs 67 of 109 participants [61.5%] with opioid taper; RR, 0.63 [95% CI, 0.43 to 0.91]; $P = .02$) and reduced opioid use by self-report (37 of 100 participants [37.0%] vs 62 of 104 participants [59.6%] with opioid taper; RR, 0.54 [95% CI, 0.31 to 0.93]; $P = .003$). Buprenorphine maintenance therapy was associated with greater treatment adherence (83 of 110 participants [75.5%] vs 36 of 137 participants [26.3%] with opioid taper; RR, 0.33 [95% CI, 0.23 to 0.47]; $P < .001$).

Discussion

No difference was found in treatment outcomes between methadone and buprenorphine maintenance therapy in prescription opioid dependence treatment. Maintenance treatment was associated with better substance use and treatment adherence outcomes compared with shorter-term treatments. Updated searches (conducted in August 2016) identified no additional eligible trials.

Table. Opioid Agonist Treatments for Prescription Opioid Dependence

Primary Outcomes	No. of Studies	Range, wk: Treatment Duration	Range, wk: Total Follow-up	Methadone: No.[a]	Methadone: Total No.	Buprenorphine: No.[a]	Buprenorphine: Total No.	Risk Ratio (95% CI)	*P* Value	Quality of the Evidence (GRADE)[b]
Studies That Compared Methadone With Buprenorphine										
Illicit opioid use during final 30 d of the intervention	1	24	32	1.51 (4.97)[c]	53	2.92 (6.38)[c]	76	−1.41 (−3.37 to 0.55)[d]	.16[e]	Moderate
Opioid-positive urine drug screening at treatment completion	2	24 to 26	26 to 32	27	79	51	117	0.81 (0.56 to 1.18)	.28[f]	Moderate
Self-reported substance use at end of treatment	2	24 to 26	26 to 32	11	66	34	89	0.37 (0.08 to 1.63)	.19[f]	Moderate
Adherence[g]	3	24 to 26	24 to 32	121	162	125	198	0.69 (0.39 to 1.22)[h]	.20[f]	Low
Studies That Compared Buprenorphine Maintenance With Opioid Taper or Psychological Treatment Only										
				Buprenorphine		Opioid Taper[i]				
Illicit opioid use	2	4 to 14	4 to 14	NA[j]	69	NA[j]	64	−0.31 (−0.66 to 0.04)[d]	.08[e]	Low
Opioid-positive urine drug screening at treatment completion	3	4 to 14	4 to 52	39	97	67	109	0.63 (0.43 to 0.91)	.02[f]	Low
Self-reported opioid use at end of treatment	3	4 to 14	4 to 52	37	100	62	104	0.54 (0.31 to 0.93)	.003[e]	Low
Adherence[g]	3	4 to 14	4 to 52	83	110	36	137	0.33 (0.23 to 0.47)[h]	<.001[f]	Moderate

Abbreviations: GRADE, Grading of Recommendations, Assessment, Development and Evaluations; NA, not available.

[a] Unless otherwise indicated.

[b] Moderate defined as moderately confident in the effect estimate (ie, true estimate is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different); and low, confidence in the effect estimate is limited (ie, the true effect may be substantially different from the estimate of the effect).

[c] Indicates mean (SD).

[d] Indicates mean difference (95% CI).

[e] Calculated using inverse variance.

[f] Calculated using the Mantel-Haenszel test.

[g] Attended counseling visits, took prescribed medication, or both per protocol.

[h] The analyses represents the risk of someone being nonadherent.

[i] Or psychological treatment only.

[j] Had different denominators (ie, past 7 days or 30 days) in different studies; therefore, the results were calculated using the standard mean difference.

Limitations

Most studies were conducted in the United States. No studies used a double-blind method, and all studies had relatively small sample sizes (53-204 participants). Due to the overall low to moderate quality of the evidence and sample sizes, it is possible further research may change these conclusions.

Comparison of Findings With Current Practice Guidelines

The US Center for Substance Abuse Treatment guidelines[5] and A Guideline for the Clinical Management of Opioid Addiction[6] suggest that long-term treatment is preferable to withdrawal treatment alone, consistent with the findings of this review. The American Society of Addiction Medicine guidelines[7] concluded that evidence supports methadone and buprenorphine maintenance, consistent with the results of this review, and that treatment setting (supervised dosing in a drug treatment clinic vs treatment provided in a physician's office) is important when taking into account patient preference and safety considerations.

Areas in Need of Future Study

Further research should include examining the treatment of concurrent chronic pain and opioid dependence and comparing outcomes for psychological treatment and taper. Inclusion of validated pain measures in future studies will facilitate a better understanding of pain as it relates to treatment of opioid addiction. See JAMA opioid microsite (http://sites.jamanetwork.com/opioids/) for further clinical information such as differences between methadone and buprenorphine induction.

ARTICLE INFORMATION

Author Affiliations: National Drug and Alcohol Centre, University of New South Wales, Sydney, Australia (Nielsen, Larance); Discipline of Addiction Medicine, University of Sydney, Sydney, Australia (Lintzeris).

Corresponding Author: Suzanne Nielsen, BPharm, PhD, National Drug and Alcohol Research Centre, University of New South Wales, 22-32 King St, Randwick, New South Wales, Australia 2031 (suzanne.nielsen@unsw.edu.au).

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REFERENCES

1. Han B, Compton WM, Jones CM, Cai R. Nonmedical prescription opioid use and use disorders among adults aged 18 through 64 years in the United States, 2003-2013. *JAMA*. 2015;314(14):1468-1478.

2. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—United States, 2000-2014. *MMWR Morb Mortal Wkly Rep*. 2016;64(50-51):1378-1382.

3. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. *JAMA*. 2016;315(15):1624-1645.

4. Nielsen S, Larance B, Degenhardt L, et al. Opioid agonist treatment for pharmaceutical opioid dependent people. *Cochrane Database Syst Rev*. 2016;(5):CD011117.

5. US Center for Substance Abuse Treatment. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: Treatment Improvement Protocol (TIP) Series 40*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2004.

6. Wood E, Ahamad K, Djurfors C, et al. A Guideline for the Clinical Management of Opioid Addiction. http://www.vch.ca/media/Opioid-Addiction-Guideline.pdf. Accessed June 28, 2016.

7. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med*. 2015;9(5):358-367.