INTRODUCTION

- Opioids are a class of compounds that bind to mu-receptors in the central and peripheral nervous system eliciting an analgesic and euphoric effect.
- 586,000 and 1.9 million Americans have a substance use disorder involving heroin and prescription pain relievers, respectively.¹
- Cost of opioid dependence in the U.S. is 55.1 billion dollars annually.²
- Substance dependence is the compulsion to seek and take a drug and a loss of control in limiting intake.³
- Ideal treatment is complete abstinence but failure rates are high therefore opioid substitution is the mainstay of treatment.
- Methadone is a full mu-agonist requiring administration in a certified clinic.
- Buprenorphine-naloxone is a partial mu-agonist combined with an orally ineffective mu-antagonist to prevent IV drug use.

CLINICAL QUESTION

Among opioid-dependent individuals does methadone as compared to buprenorphine-naloxone improve retention rates and efficacy in treatment programs?

METHODS

Search Terms: PubMed (methadone AND buprenorphine-naloxone AND opioid dependence), Scopus (methadone versus buprenorphine-naloxone).

RESULTS

Study 1: Methadone and buprenorphine-naloxone are effective in reducing illicit buprenorphine and other opioid use, and reducing HIV risk behaviors: Outcomes of a Randomized Trial. Dhandhuk et al.

**Study Type:** Randomized Control Trial

**Sample Size:** 80

**Length of Program:** 12 weeks with 20-week follow-up

**Objective:** To determine treatment retention with buprenorphine-naloxone or methadone in buprenorphine injection users

**Conclusion:** During daily observed doses of methadone and buprenorphine-naloxone were effective in reducing illicit buprenorphine and other opioid use

**Critique:**

Strengths: Daily observed dosing ensured compliance, limited loss to follow up in initial 12-week study, loss to follow-up addressed by intention to treat approach; Small sample size, short study duration, mostly males subjects, lack of follow-up at 20 weeks.

Trends: Among opioid-dependent individuals does methadone as compared to buprenorphine-naloxone improve retention rates and efficacy in treatment programs?

**Study 2:** Buprenorphine-Naloxone Versus Methadone Maintenance Therapy: A Randomized Double-Blind Trial With Opioid-Dependent Patients. Kamien et al.

**Study Type:** Double-Blind Randomized Control Trial

**Sample Size:** 268

**Length of Program:** 17 weeks

**Objective:** To compare buprenorphine-naloxone with methadone for maintenance treatment of opioid dependence

**Conclusion:** Maintenance treatment with 16 mg buprenorphine-naloxone reduced opioid use at a rate equivalent to that achieved with 90 mg methadone.

**Critique:**

Strengths: Conservative analytic procedures, conducted at licensed, community-based opioid treatment center, exposed patient to buprenorphine-naloxone for longer time periods than previous studies.

Limitations: Uneven number of participants assigned to each of the 4 treatment groups, drop-out rate, loss to follow-up addressed by pre-protocol analysis.

Study 3: Treatment Retention among Patients Randomized to Buprenorphine-Naloxone Compared to Methadone in a Multi-site Trial. Hser et al.

**Study Type:** Open-Label Randomized Control Trial

**Sample Size:** 1,267

**Length of Program:** 24 weeks

**Objective:** To examine patient and medication characteristics associated with retention and continued illicit opioid use in methadone versus buprenorphine-naloxone treatment

**Conclusion:** Methadone appears to be associated with better retention in treatment for opioid dependence than buprenorphine-naloxone, as does the use of higher doses of both medications. Buprenorphine-naloxone is associated with lower continued use of illicit opioids.

**Critique:**

Strengths: First large scale RCT to compare treatment retention of patients in maintenance treatment with methadone versus buprenorphine-naloxone; conducted in community treatment programs in the U.S.

Additional findings: 1. Buprenorphine-naloxone dose related retention treatment. 2. Identified additional participant characteristics predicting dropout (age, ethnicity, other drug use, etc.). Limitations: Limited measures of participant motivation as well as program and community characteristics likely to influence retention. Other limitations are that it was open-labeled and unblinded.

CONCLUSIONS

Buprenorphine-naloxone may be more effective at preventing illicit opioid use than methadone, although this is inconsistent among the three studies. Retention rates are also inconclusive with only one study demonstrating higher retention rates with methadone treatment. With buprenorphine-naloxone demonstrating a better safety profile, fewer withdrawal effects, ease of use and less divergence, we recommend buprenorphine-naloxone over methadone as a first line treatment in opioid-dependent individuals.

ACKNOWLEDGEMENTS

We would like to thank Dr. Kancler and Carolyn Shubert for their support and guidance throughout this project.

REFERENCES