Drug and Alcohol Dependence 203 (2019) 98

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Letter to the Editor

Galantamine to reduce relapse after agonist taper for individuals with opioid use disorder

Dear Editor,

Current efforts to address the opioid crisis have appropriately focused on broadening access to agonist treatment (buprenorphine or methadone) and encouraging individuals to remain in treatment for several years (National Academy of Medicine, 2019). Conversely, for those who have been treated successfully (e.g., stopped illicit drug use and functioning well in major life spheres) there are no effective strategies for tapering individuals safely and preventing relapse. Tapering from either methadone (Magura and Rosenblum, 2001) or buprenorphine is associated with high levels of relapse (National Academy of Medicine, 2019). Within the Cascade of Care model (Williams et al., 2017), novel strategies are needed to support successful remission for stabilized patients who have achieved good outcomes on agonist treatment. Galantamine, a cholinesterase inhibitor, approved for the treatment of Alzheimer's disease, has also shown promise for addictive disorders including opioid use disorder (Carroll et al., 2019). Galantamine increases synaptic levels of acetylcholine, which may oppose the rewarding effects of dopamine (see Jensen et al., 2018 for a rationale for the brain cholinergic system as a treatment target for opioid use disorder).

We recently completed a small feasibility trial of 6 individuals (5 female, 1 male) who had been stabilized on methadone (n = 3, mean dose at start of taper = 15 mg, *SD* = 4.2; mean 5 years on methadone maintenance, *SD* = 3.6) or buprenorphine (n = 3, mean dose at start of taper = 2 mg, *SD* = 1.5; mean 6 years on buprenorphine, *SD* = 3.6), who were recruited from specialized tapering groups at the APT Foundation in New Haven. The tapering groups were limited to individuals who had been maintained on agonists for several years, had achieved social and medical stability, and who had worked with their clinicians to begin the taper. All had stable living arrangements and no legal problems; 5 were employed and one was supported by disability. Only 1 of the 6 knew any other individuals who had successfully tapered.

After providing written informed consent, participants were randomized to galantamine extended release (n = 3) or identical placebo (n = 3). Once the target dose of 16 mg/day was reached, participants began a supervised medication taper, overseen by a primary care physician. The taper schedule was individualized depending on the individuals level of comfort; all who completed the taper did so within 10 weeks of initiation. All but one (assigned to the placebo group) completed the taper. Participants assigned to galantamine had somewhat lower withdrawal score at end of taper (via Opioid Withdrawal Symptom Checklist) (*m* = 8.7, *SD* = 11.0) than those assigned to placebo (m = 19.0, *SD* = 15.6). Study medication (galantamine/placebo) was continued an additional 4 weeks; with additional follow-up at 3 months. Participants had access to counseling services; all were offered naltrexone as well. Participants were told they could return to agonist treatment immediately on request. As of this writing (3 months after follow-up), only one participant (randomized to galantamine) returned to methadone after a serious unrelated medical illness. These preliminary findings support the feasibility of conducting a randomized clinical trial testing the efficacy of galantamine in preventing relapse to opioid use after agonist taper.

Role of Funding Source

Support was provided by NIDA award P50 DA09241 (Carroll).

Contributors

Authors Sofuoglu, Shi, and Carroll conceived and implemented the trial, oversaw the analysis and wrote the report. All authors read and approved the final manuscript.

Conflict of Interest

None of the authors has any relevant disclosures.

Acknowledgements

We acknowledge with gratitude the support of Sue Henry, RN, Stephanie Dwy and Skye Orazietti, Andre Miguel PhD and Theresa Babuscio as well as the participants in this trial.

References

Carroll, K.M., DeVito, E.E., Yip, S.W., Nich, C., Hunkele, K.A., Sofuoglu, M., 2019. Galantamine effects on illicit opioid use: Secondary analysis of a double-blind placebo controlled trial among methadone-maintained individuals with cocaine use disorder. Am. J. Addict. 28, 238–245.

Jensen, K.P., DeVito, E.E., Yip, S.W., Carroll, K.M., Sofuoglu, M., 2018. The cholinergic system as a treatment target for opioid use disorder. CNS Drugs 32, 981–996.

Magura, S., Rosenblum, A., 2001. Leaving methadone treatment: Lessons learned, lessons forgotten, lessons ignored. Mt. Sinai J. Med. 68, 62–74.

National Academy of Medicine, 2019. Responding to the opioid crisis: Medications save lives. Nationale Academy of Science, Washington DC.

Williams, A.R., Nunes, E.V., Olfson, M., 2017. To battle the opioid overdose epidemic, deploy the "Cascade of Care" model. Health Aff. Blog . (Accessed 17 June 2019). https://www.healthaffairs.org/do/10.1377/hblog20170313.059163/full/.

Mehmet Sofuoglu[a], Julia M. Shi[a,b], Kathleen M. Carroll[a,*]

[a] *West Haven VA Medical Center, 950 Campbell Avenue, West Haven, CT 06516, USA*

[b] *The APT Foundation, Central Medical Unit, 1 Long Wharf, New Haven, CT 06510, USA*

E-mail address: Kathleen.carroll@yale.edu (K.M. Carroll).

https://doi.org/10.1016/j.drugalcdep.2019.05.013
Received 10 April 2019
Available online 03 August 2019