Case Series: Buprenorphine benefits patients with opioid use disorder (OUD) in the emergency department (ED), but its efficacy for OUD patients with suicidal ideation (SI) in the ED is unknown.

Case Series: We present a case series of 14 OUD patients with SI who were given buprenorphine and a referral to outpatient substance use treatment in the ED. All experienced SI resolution, engaged with outpatient services, and remained in outpatient substance use treatment 30 days after ED discharge.

Conclusion: Our data provide evidence for the feasibility of starting buprenorphine in OUD patients with SI in the ED, and suggest that buprenorphine may be useful in helping to resolve SI for these patients. Future research with larger samples is needed.

Keywords: Opioid-related disorders; buprenorphine; suicidal ideation; emergency service, hospital.
included the patients’ background characteristics, reasons for ED visit, current substance use, mental health symptoms, buprenorphine use during their ED visit, and engagement in outpatient substance use treatment after ED discharge. Variables collected regarding outpatient substance use treatment included referral to the program during the index ED visit (yes/no); number of days between ED referral to the program and the first appointment (defined as the number of days between discharge from the ED and attendance at the first scheduled appointment); attendance at the first scheduled appointment (yes/no); engagement with the program 30 days after the first scheduled appointment (yes/no), defined as having notes documenting services received on and after day 30; number of medical visits during the 30-day period (defined as visits with a physician to discuss medication and side effects); and number of support visits during the 30-day period (defined as visits with a non-physician to discuss issues besides medication and side effects).

Two of the authors conducted the health record reviews. One (RA) completed the initial review using a data-collection form that matched an Excel (Microsoft Corporation, Redmond, WA) spreadsheet where the data were entered. The second (MB) reviewed the data after these were entered into the spreadsheet and did a comparison with the health record for these variables. Any discrepancy was corrected (if simple), or discussed to reach consensus (if more complex).

Baseline characteristics are summarized in Table 1. Patients were 86% male and 86% Caucasian with a mean age of 41.36 years (standard deviation [SD] =12.18, range 26-60 years). Besides opioids, patients reported current cocaine (n = 10), cannabis (n = 4), and alcohol use (n = 7), along with symptoms of mood (n = 12) and anxiety (n = 6) disorders. Two patients had attempted suicide immediately before presenting to the ED; 12 reported SI as a main reason for their visit.

Buprenorphine use during the ED visit and engagement with outpatient substance use treatment after discharge are summarized in Table 2. The doses of buprenorphine given in the ED ranged from 2-16 milligrams (mg) (mean = 8.00 mg, SD = 3.76). None of the patients required an inpatient hospitalization for SI. All patients received a referral to an outpatient substance use treatment program, attended their first scheduled outpatient substance use treatment visit, and remained engaged with the outpatient substance use treatment program 30 days after their first visit. During the 30 days after their first visit, patients attended between 1-8 medical visits and 7-28 support visits at the outpatient substance use treatment program.

**DISCUSSION**

This case series provides evidence for the feasibility and potential benefit of initiating buprenorphine in the ED to OUD patients who present with SI. For all the patients in our observational data, ED-initiated buprenorphine was associated with SI resolution, discharge from the ED, and engagement in outpatient substance use treatment. Given that SI rates remain high among OUD patients in outpatient methadone treatment, medication-based treatment by itself is unlikely to explain why the patients in our series experienced SI resolution. Although other factors besides buprenorphine initiation might have contributed to SI resolution, our results provide evidence that ED-initiated buprenorphine may be helpful in the treatment of OUD patients who present to the ED with SI.

There could be several explanations for our findings. One explanation might involve buprenorphine’s pharmacology as a partial mu-opioid receptor agonist and kappa-opioid receptor (KOR) antagonist. KOR activation is known to worsen depressive states, and buprenorphine’s antidepressant effect is thought to result from its KOR antagonism, a property methadone lacks. Studies have shown that there might be a role for buprenorphine to decrease SI for individuals with and without OUD, and it has been hypothesized that buprenorphine’s anti-suicidal property might result from its KOR antagonism. Although pharmacologically compelling, this mechanism of action remains speculative, and no evidence links the KOR to SI. Studies are needed to determine whether KOR activation causes or worsens SI.

**CPC-EM Capsule**

What do we already know about this clinical entity?

Buprenorphine initiation in the emergency department (ED) improves engagement in outpatient substance use treatment for opioid use disorder (OUD) patients.

What makes this presentation of disease reportable?

This is the first report of successfully initiating buprenorphine in OUD patients who present to the ED with suicidal ideation (SI).

What is the major learning point?

Buprenorphine initiation and a referral to outpatient substance use treatment may help resolve SI and promote outpatient substance use treatment engagement.

How might this improve emergency medicine practice?

In the ED, buprenorphine initiation and a referral to outpatient substance use treatment may be successful interventions for OUD patients who present with SI.
Table 1. Characteristics of 14 patients with opioid use disorder and suicidal ideation at presentation to the emergency department

| Patient | Age | Gender | Race | Reasons for ED visit | Self-reported substance use recorded at ED visit | Positive urinalysis at ED visit | Suicidal ideation description recorded at ED visit | Psychiatric symptoms and diagnoses recorded at ED visit |
|---------|-----|--------|------|----------------------|-----------------------------------------------|--------------------------------|-----------------------------------------------|---------------------------------------------------|
| 1       | 59  | Male   | Caucasian | suicidal ideation, chest pain | heroin, cocaine | heroin, cocaine | suicidal ideation with plan | depression, bipolar disorder |
| 2       | 26  | Male   | Caucasian | suicidal ideation, alcohol withdrawal | heroin, alcohol | cocaine, benzodiazepines | suicidal ideation with plan | depression |
| 3       | 45  | Male   | Black   | suicidal ideation | heroin, cocaine, alcohol, cannabis | heroin, cocaine | unknown | substance-induced mood disorder, depression |
| 4       | 35  | Male   | Caucasian | suicidal ideation, nausea/vomiting, depression | heroin, cocaine, alcohol, cannabis, inhalants | heroin, cocaine, cannabis | suicidal ideation with plan | depression, sleep disturbance, anxiety |
| 5       | 60  | Male   | Caucasian | suicidal ideation, substance use disorder | heroin, cocaine | cannabis | passive suicidal ideation with no plan | depression |
| 6       | 27  | Female | Caucasian | suicidal ideation with plan | heroin, cocaine, alcohol, benzodiazepines | alcohol | suicidal ideation with plan | post-traumatic stress disorder, substance-induced mood disorder |
| 7       | 33  | Male   | Caucasian | suicide attempt | heroin, cocaine, cannabis, sedatives | cocaine | suicide attempt | depression, sleep disturbance |
| 8       | 37  | Male   | Caucasian | suicidal ideation, groin rash | heroin, cocaine | heroin, cocaine, morphine, fentanyl | suicidal ideation | attention-deficit disorder, anxiety |
| 9       | 40  | Male   | Caucasian | suicidal ideation | heroin | heroin, cannabis, morphine, fentanyl | suicidal ideation | anxiety, depression |
| 10      | 28  | Male   | Caucasian | suicidal ideation, abdominal pain, mild ear pain | heroin, cocaine | cocaine | suicidal ideation with plan | poor sleep, weight loss, irritability |
| 11      | 31  | Female | Caucasian | suicidal ideation, substance use disorder | heroin, cocaine, cannabis, alcohol | cannabis | passive suicidal ideation | post-traumatic stress disorder, anxiety, bipolar |
| 12      | 50  | Male   | Caucasian | suicidal ideation, substance use disorder | heroin, cocaine, cannabis, alcohol | unknown | passive suicidal ideation | depression |
| 13      | 55  | Male   | Black   | suicide attempt | heroin | heroin | suicide attempt | depression, sleep disturbance, appetite disturbance, anxiety, loss of appetite, weight loss, low energy |
| 14      | 53  | Male   | Caucasian | suicidal ideation, depression | heroin, alcohol | heroin, cannabis | suicide attempt | |

ED, emergency department.

Another explanation might be that the ED referral to outpatient substance use treatment addressed the non-clinical issue of access to care for OUD treatment that had led these patients to experience SI. 14 It is notable that all 14 patients...
Table 2. Buprenorphine initiation and outpatient-treatment engagement for 14 patients with opioid use disorder and suicidal ideation at presentation to the emergency department.

| Patient | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Buprenorphine prescribed at ED visit | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Buprenorphine dose in mg* prescribed at ED visit | 8mg | 4mg | 16mg | 12mg | 12mg | 4mg | 8mg | 8mg | 8mg | 8mg | 8mg | 10mg | 2mg | 4mg |
| Required inpatient hospitalization for SI | No | No | No | No | No | No | No | No | No | No | No | No | No | No |
| Self-harm within 30 days after ED visit | None | None | UK | None | None | None | UK | UK | UK | UK | UK | UK | UK | None |
| Outpatient referral made at ED visit | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Days between ED referral and 1st appointment | 1 | 1 | UK | 5 | 5 | 4 | UK | UK | UK | 4 | UK | UK | 2 |
| Outpatient referral – 1st appointment attended | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Outpatient referral – engaged 30 days after 1st appointment | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Outpatient referral – number of medical visits* attended in 30 days | 2 | 2 | 2 | 2 | 2 | 8 | 3 | 2 | 2 | 1 | 3 | UK | 2 | 5 |
| Outpatient referral – number of support visits** attended in 30 days | 7 | 19 | 10 | 20 | 23 | 11 | UK | UK | UK | UK | UK | 20 | 28 |

*Medical visits = visits with a physician, discussion focused on medication and side effects.
**Support visits = visits with a nurse or counselor, discussion focused on issues other than medication and side effects.

ED, emergency department; mg, milligram; SI, suicidal ideation; UK, unknown.

attended their first outpatient appointment and remained in treatment for 30 days. Other studies of ED-initiated buprenorphine and referral to treatment have found lower percentages of OUD patients attending their first outpatient appointment.7 Many patients did not have to wait long to start outpatient treatment: for the seven patients in our case series whose data are available, the range between the ED referral to outpatient treatment and attendance at the first appointment was 1-5 days. Moreover, by treating both the opioid-withdrawal symptoms and SI, ED-initiated buprenorphine might have illustrated the benefits of continuing buprenorphine after ED discharge to these patients. It might be that the combination of a quick referral to outpatient substance use treatment and the experience of ED-initiated buprenorphine was enough to promote treatment engagement.

Several limitations should be noted. This was a small case series of 14 patients who were not compared with a matched control group that did not receive buprenorphine. We did not examine changes in treatment engagement, opioid use, and SI after 30 days, so we cannot determine how these outcomes might have changed over a longer period of time. We were not able to access data on two variables that might have had an impact on engagement: how patients paid for treatment (eg, insurance, other payment programs, self-pay), or their degree of opioid withdrawal (measured by clinician-rated scores from the Clinical Opiate Withdrawal Scale). It would be useful to know whether any patient experienced self-harm or attempted suicide after the 30 days following their first outpatient substance use visit. Future research should follow patients to examine whether self-harm or suicide attempts occur in the early days of outpatient substance use treatment to evaluate more fully the potential benefit of ED-initiated buprenorphine.

CONCLUSION

The observational data in our case series provide evidence for the feasibility of starting buprenorphine in OUD patients...
Patients with OUD and Suicidal Ideation Treated with Buprenorphine

Spaderna et al.

with suicide ideation in the ED and referring them to outpatient substance use treatment. More rigorous studies are needed to determine the effectiveness of ED-initiated buprenorphine on a larger and more diverse sample of patients.

The Institutional Review Board approval has been documented and filed for publication of this case report.

Address for Correspondence: Max Spaderna, MD, University of Maryland School of Medicine, Department of Psychiatry, 701 West Pratt Street, 3rd Floor, Baltimore, MD, 21201. Email: mspaderna@som.umaryland.edu.

Conflicts of Interest: By the CPC-EM article submission agreement, all authors are required to disclose all affiliations, funding sources and financial or management relationships that could be perceived as potential sources of bias. The authors disclosed none.

Copyright: © 2021 Spaderna et al. This is an open access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) License. See: http://creativecommons.org/licenses/by/4.0/

REFERENCES

1. Centers for Disease Control and Prevention. Opioid Data Analysis and Resources. 2019. Available at: https://www.cdc.gov/drugoverdose/data/analysis.html. Accessed January 8, 2020.
2. Hedegaard H, Curtin SC, Warner M. Suicide rates in the United States continue to increase. NCHS Data Brief. 2018;(309):1-8.
3. Kuramoto SJ, Chilcoat HD, Ko J, et al. Suicidal ideation and suicide attempt across stages of nonmedical prescription opioid use and presence of prescription opioid disorders among U.S. adults. J Stud Alcohol Drugs. 2012;73(2):178-84.
4. Rockett IR, Kapusta ND, Coben JH. Beyond suicide: action needed to improve self-injury mortality accounting. JAMA Psychiatry. 2014;71(3):231-2.
5. Weiss AJ, Elixhauser A, Barrett ML, et al. Opioid-Related Inpatient Stays and Emergency Department Visits by State, 2009–2014: Statistical Brief #219. 2017. Available at: https://www.ncbi.nlm.nih.gov/books/NBK441648/. Accessed January 8, 2020.
6. Rhodes KV, Gordon JA, Lowe RA. Preventive care in the emergency department, Part I: Clinical preventive services—are they relevant to emergency medicine? Society for Academic Emergency Medicine Public Health and Education Task Force Preventive Services Work Group. Acad Emerg Med. 2000;7(9):1036-41.
7. D’Onofrio G, O’Connor PG, Pantalon MV, et al. Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial. JAMA. 2015;313(16):1636-44.
8. D’Onofrio G, Chawarski MC, O’Connor PG, et al. Emergency department-initiated buprenorphine for opioid dependence with continuation in primary care: outcomes during and after intervention. J Gen Intern Med. 2017;32(6):660-6.
9. Yovell Y, Bar G, Mashiah M, et al. Ultra-low-dose buprenorphine as a time-limited treatment for severe suicidal ideation: a randomized controlled trial. Am J Psychiatry. 2016;173(5):491-8. Erratum in: Am J Psychiatry. 2016;173(2):198.
10. Xu YM, Zhong BL, Chen WC, et al. Suicidal ideation among Chinese methadone-maintained patients: prevalence and correlates. Oncotarget. 2017;8(49):86181-7.
11. Carlezon WA Jr and Krystal AD. Kappa-opioid antagonists for psychiatric disorders: from bench to clinical trials. Depress Anxiety. 2016;33(10):895-906.
12. Kristensen K, Christensen CB, Christrup LL. The mu1, mu2, delta, kappa opioid receptor binding profiles of methadone stereoisomers and morphine. Life Sci. 1995;56(2):PL45-50.
13. Ahmadi J, Jahromi MS, Ehsaei Z. The effectiveness of different singly administered high doses of buprenorphine in reducing suicidal ideation in acutely depressed people with co-morbid opiate dependence: a randomized, double-blind, clinical trial. Trials. 2018;19(1):462.
14. Kroll DS, Karno J, Mullen B, et al. Clinical severity alone does not determine disposition decisions for patients in the emergency department with suicide risk. Psychosomatics. 2018;59(4):388-93.