

Rapid methadone induction in the hospital setting: A retrospective observational analysis

INTRODUCTION

- People with opioid use disorder (OUD) are frequently admitted to the hospital, with increases in overdose related encounters since COVID-19^{1,2}
- Hospitalization offers critical opportunity for initiation of medication for OUD like methadone, which improves engagement post discharge³⁻⁵
- Rapid methadone induction may be more feasible in hospital settings with fewer safety concerns than in outpatient settings
- Rapid induction could be particularly important given increased prevalence of fentanyl use and for patients at risk for premature discharge due to undertreated withdrawal and cravings^{6,7}

METHODS

- Retrospective, observational analysis of patients with OUD admitted to Massachusetts General Hospital (MGH), seen by the Addiction Consult Team, who were initiated on methadone from January 1, 2016 to January 1, 2022
 - Patients who were admitted for less than four days were excluded
- Chart review conducted by two reviewers to assess for adverse or safety events during hospitalization and how related such events were to methadone dose
 - Any disagreement was adjudicated by a third reviewer
- Inpatient methadone dosing was extracted from electronic medical record and dose received was calculated for each day of admission
- T test was used to compare mean starting dose in patients with vs. without sedation events
 - Assessed effect of starting dose on likelihood of oversedation controlling for age, sex, length of stay and methadone use within week of hospital admission using logistic regression

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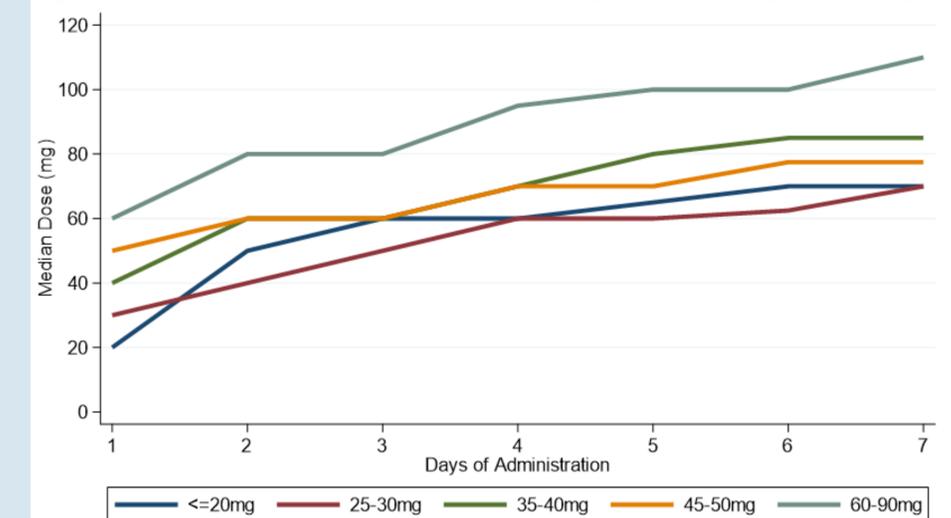
RESULTS

- 112 patients were determined to be new methadone inductions
- Mean age was 37 years old, 38% of patients were female and mean length of hospital stay was 9.4 days
- Mean initial dose administered was 32 mg (SD: 16.9; range: 10 – 90 mg), mean maximum dose was 76.8 mg (SD: 22.0; range: 30 – 165 mg), and mean number of days from initial dose to peak dose was 5.6 days (SD: 3.4; range: 1 – 19 days)
- Overall 30% of patients experienced a safety event with oversedation most commonly reported (Table 1) and 3.5% of patients had a safety event that was definitely or probably related to methadone
- Mean starting dose did not differ between those with vs. without sedation events (34.7 mg vs 31.1 mg, p = 0.306)
 - Starting dose was unrelated to the odds of sedation event (OR: 1.01, 95% CI: 0.98 – 1.04) in adjusted analysis
- 45% (50/112) of the patients received greater than or equal to 40 mg on the first day of administration
- Patients with final dose of 100 mg or higher were more likely to have a safety event that was possibly related to methadone than those with lower ending dose (47.8% vs 12.4%, p < 0.001)

Table 1: Safety events

Event	No Event	Relation of event to methadone induction				Any Event	
		None	Possible	Probable	Definite	N	Percent
Oversedation	80	10	18	3	1	32	28.6%
Depressed respiratory rate	108	0	4	0	0	4	3.6%
Respiratory failure	111	0	1	0	0	1	0.9%
Torsades de pointes	112	0	0	0	0	0	0.0%
Naloxone administration	111	0	1	0	0	1	0.9%
Cardiac arrest	111	0	1	0	0	1	0.9%
Intubation	109	3	0	0	0	3	2.7%
Transfer to intensive care unit	110	2	0	0	0	2	1.8%
Rapid response	109	3	0	0	0	3	2.7%
Code blue	111	0	1	0	0	1	0.9%

Figure 1: Rate of methadone increase on average with starting dose categories



CONCLUSION

- Hospitalized patients who were initiated on methadone utilizing a more rapid titration schedule than currently recommended by OTP guidelines with some patients starting on day 1 doses greater than 40 mg and some escalating doses quicker than usual OTP practice had few observed safety events probably or definitely related to methadone
- Sedation was the most frequent safety event and most of the serious safety events were determined to either not be related or only possibly be related to methadone
- There was no significant difference between starting dose among patients with oversedation vs those without
- Most patients (78%) were successfully connected to an OTP prior to discharge from the hospital
- These findings indicate that inpatient settings may offer opportunity for safe methadone initiation and more rapid titration than utilized in OTPs
- Limitations include inability to definitively determine relation of safety event to methadone due to limited data in chart upon review and methadone titration details were not standardized
- More research is needed to refine inpatient dosing and the safety of this approach in outpatient settings

AUTHORS & DISCLOSURES

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