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HIGH DOSE METHADONE INDUCTION IN PREGNANCY



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Perinatal Substance Use: From Research to Practice to Public Health

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Disclosure Information

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Consulting Income from McKesson

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Case Example

- Janet 29 y/o G3P1 woman at 18 weeks gestation with OUD previously stabilized on bupe/nlx
 - Returned to use when she lost insurance coverage
 - Now smoking fentanyl every 2-3 hours
- Presented to care wanting a termination, but changed mind in pre-op
- Wants to go back on buprenorphine

Options for patient?



Treatment of OUD in Pregnancy in the age of fentanyl

- Buprenorphine microinduction outpatient blister packs
- Buprenorphine microinduction hospital
- Buprenorphine macroinduction
- Methadone induction outpatient with methadone maintenance
- Methadone induction inpatient with methadone maintenance
- Methadone induction inpatient with transition to buprenorphine concurrently or with the assistance of methadone clinic



Bupe Microinduction Inpatient

- Please initiate scheduled full opioid agonists from days 1-5 and discontinue after day 5 if tolerated. In addition, have prn opioid agonists available for withdrawal or pain.
- Buprenorphine
 - Day 1, ***date, place TWO buprenorphine 20 mcg/h patches
 - Day 2, ***date, place TWO additional buprenorphine 20 mcg/h patches
 - Day 3,***date, buprenorphine 1 mg SL BID (ideally 0.5mg QID)
 - Day 4,***date, buprenorphine 1 mg SL QID
 - Day 5, ***date, buprenorphine 2 mg SL QID
 - Day 6, ***date, buprenorphine 4 mg SL QID
 - Let buprenorphine patches expire and do not reorder

Baumgartner et al Clinical Toxicology 2022
Galati et al Ob/Gyn 2021



Bupe Microinduction Inpatient

- Patient had hospital induction previously and had good memories of it. Sounds like she was heavily sedated and woke up out of withdrawal (but was when she was only using heroin)
- Started on full agonists + adjuncts
 - Oxycodone
 - IV Hydromorphone/morphine
 - Clonidine
 - Ondansetron
 - Hydroxyzine
 - Imodium
 - Lorazepam
- 2 20 mcg patches placed (actually 4 10 mcg). Much consternation by pharmacy
- Miserable and self-directed discharge back to the hospital where she'd had the first induction despite being given methadone 30 mg
- Sent back, as they weren't comfortable with managing her either



High Dose Methadone Initiation

- ◆ Inclusion Criteria
 - ◆ Fentanyl use confirmed
- ◆ Soft contraindication is 'never had methadone before' (but we make exceptions)
- ◆ Exclusion is age 65 or greater, COPD or other pulmonary disease, ESLD, ESRD, and history of sedation on higher doses of methadone.
- ◆ If receiving any benzos, gabapentin, or other sedating medications, place patient on continuous pulse ox



Pregnancy

- ◆ Initial dose 30 mg. If not overly sedated and still experiencing withdrawal at 4 hours, can give an additional 10 mg.
- ◆ Depending on when they receive it, can get 20 mg 12 hours later (again if not overly sedated). Total first day dose 60 mg
- ◆ Day 2 Start with 30 mg in am (can get an additional 10 if not sedated) and 40 mg in pm (if tolerated the 40 mg in am). Total dose 80 mg
- ◆ Day 3 start with 40 mg in am (+additional 10 mg). 50 in pm (if tolerated 50 in am. Total dose 100 mg.
- ◆ Maintain at 50 bid for 4 days. Assess at peak and support with full agonists prn pain or withdrawal
- ◆ Increase by 10 bid after day 6 if needed (again assessing at peak dose)
- ◆ EKG once on 140 mg

Need references



Advantages

- Faster arrival at steady maintenance dose/resolution of symptoms
- Better compliance with hospital stay/less risk of self-directed discharge
- Shorter hospital stay
- Less withdrawal symptoms
- Less use of illicit drugs/injection risk/infection risks
 - Better pregnancy outcomes

Data from chart review/references



Case Follow Up

- Stabilized on 70 mg bid by HD 10
- Started up titration of sertraline (concern of psychiatrist with serotonin syndrome)
- Down titration of clonazepam
- D/c home once stable on dose with no evidence of oversedation and prn oxycodone need gone
- Warm hand off to methadone clinic/Ob provider in her community



Review of Pregnancy Physiology

Table 2

Summary of gestational age associated physiological parameters incorporated into SimCyp healthy population

	Nonpregnant Female	1 st trimester (≤12 gestation weeks)	2 nd trimester (13–28 gestation weeks)	3 rd trimester (≥ 29 gestation weeks)
Physiological and metabolic change				
Cardiac output [31]	100%	Increased 35%	Increased 40%	Increased 50%
Plasma volume [31]	100%	Increased 12.5%	Increased 32.5%	Increased 50%
Red cell volume [31]	100%	Remain same	Remain same	Increased 30%
Haematocrit [32]	100%	Decreased 3%	Decreased 4%	Decreased 5%
Albumin [32]	100%	Decrease 27%	Decrease 27%	Decrease 27%
Activity of CYP3A4 [33]	100%	Increased 35%	Increased 35%	Increased 38%
Parameter used in model				
Cardiac output scalar	1	1.35	1.4	1.5
Plasma volume scalar	1	1.125	1.325	1.50
Red blood cell volume scalar	1	1	1	1.3
Haematocrit (%)	38	35	34	33
Albumin (g l⁻¹)	49	36	36	36
CYP3A4 (pmol mg protein⁻¹)	137	185	185	189

Zhang et al 2018



Summary

- Fentanyl has made initiation of buprenorphine and methadone challenging
- Microdosing and rapid methadone initiation can help facilitate medication initiation and improve outcomes



References

Hemmons P, Bach P, Colizza K, Nolan S. Initiation and Rapid Titration of Methadone in an Acute Care Setting for the Treatment of Opioid Use Disorder: A Case Report. *J Addict Med*. 2019;13(5):408-411. doi:10.1097/ADM.0000000000000507

Bromley, L, Kahan, M, Regenstreif, L, Srivastava,, A, Wyman, J. Methadone treatment for people who use fentanyl: Recommendations. META:PHI. 2021. [Guide_MethadoneForFentanyl.pdf \(metaphi.ca\)](#)

Stone AC, Carroll JJ, Rich JD, Green TC. One year of methadone maintenance treatment in a fentanyl endemic area: Safety, repeated exposure, retention, and remission. *J Subst Abuse Treat*. 2020;115:108031.





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