CASE REPORTS

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Case One (1)

- KB - 36 y/o WM on Methadone 300 mg insists “not holding” - transfers to DH 8/92
- HX- NO CARDIAC HX, FHX- father with heroin addiction, required >500 mg meth, on no medications
- PE - Marfanoid habitus, bronchitis.
- P/T - 400 ng/110 ng, PE wnl
- Dose Increases begin at 25-35 mg/increase
Case One (2)

- 11/92 - on 435 mg (P/T=532/135), states he feels “10%” better, pushes for > increases
- 12/92 - at 560 mg (P/T=609/155)
- 2/93 - at 600 mg, feeling “30%” better, clinical eval with dilated pupils at trough
- 3/93 - at 660mg ( P/T = 860/344), feels 50% better
- Call from ER - in V. Tach (TdP) with grand mal seizure presentation - threat to call FBI
Case One (3)

- **SUBSEQUENT COURSE**
  - Repeated episodes of V. Tach, QTc = 580 msec
  - Methadone switched to 150 mg Q6h, reduced by 10mg q6h over next 4 days to 100 mg Q6h
  - QTc= 520 msec, ICD and temp pacemaker, medical management
  - Ongoing discussion with cardiology/psych at hospital
  - C/O ongoing w/d sx, dose increased but results in ongoing firing of ICD
Case One (4)

- Ultimately ends up on 420 mg but complains bitterly of ongoing w/d, not holding
- Effort to use LAAM unsuccessful
- Very gradual increase in dose in consultation with cardiologist to 600 mg
- Remains at 600 mg with 1-2X/month firing of ICD despite several anti-arrhythmic meds
TAKE HOME POINTS - Case 1

- Cases of torsades de pointes (TdP) are rare, mostly associated with methadone > 200 mg
- QTc may be prolonged, but some cases have occurred with normal QTc
- Overwhelming majority of prolonged QTc cases do not result in cardiac problems
- CSAT issuing guidelines for monitoring this issue, but there are enormous controversies with little evidence base - more study needed
CASE TWO

- 55y/o WF on MMTP X2 y, on 110 mg, still using cannabis but no other drugs
- Develops heartburn/reflux sx, sees GI doc who prescribes triple therapy with Biaxin
- Doses X3 d. w/o complaint, found down next morning, reports sterterous respirations
- Methadone levels >1000 ng/mg
- Lawsuit brought against methadone program
Case 2 (2)

- Events occurred in early 2005
- Numerous papers in pharm and pre-clinical literature about methadone drug interactions
- CYP3A4 and CYP2D6 inhibitors may increase methadone levels and QTc issues
- Clarithryomycin and erythromycins, anti-fungal agents, antidepressants and neuroleptic agents all implicated
- Warnings went out to prescribers in 2006/07
Case 2 (3)

- Importance of full history, updates, informed consent
- Communication with other prescribers
- ? Computer programs for drug interactions in MMTPs
- Increase in both methadone levels and QTc prolongation with many of these drugs
TAKE HOME POINTS - Case 2

- All clinicians need to be aware of multiplicity of methadone interactions
- Information should be given to patients at intake and at intervals (each counseling event?), and with other prescribers
- Encouraging adding methadone to patient’s home pharmacy records
- When clinical/nursing/medical staff informed of new meds, LOOK THEM UP!!
- Must even consider discontinuation of OLD meds!
CASE 3

• 19 y/o with bipolar disorder, polysubstance abuse- depakote, valproate, seroquel
• States using 10-15 bags of heroin daily, reported to have piloerection, positive UDS, withdrawal sx, also reports ETOH abuse
• Given 20 mg of methadone, 2 hours later an additional 10 mg, also Librium 25mg prn
• Given 30 mg methadone following AM
• Found down at 9 PM, code unsuccessful
Case 3 (2)

- Criticisms of case - >40 mg methadone in first 24 hours
- Polypharmacy treatment
- Lack of scales in diagnosing/monitoring opioid withdrawal
- Exceeding tolerance
- ??? Young age of patient - is tolerance significantly less in younger adults (<23)
Case 3 (3)

- Author has seen 5 cases of inordinate sensitivity to both methadone and long-acting benzos used therapeutically in young adults, esp those 14-20 years
- Consideration of use of alternative therapies, starting low, going slow, esp dose changes
- Buprenorphine is safer alternative in younger adults or those with low tolerance
TAKE HOME POINTS - Case 3

• Young adults may develop significant tolerance for their DOC, but still not tolerate adult doses of methadone, esp with benzos
• Start lower, go slower, have plateaus between dose increases
• Careful clinical assessment, consideration of giving information re: OD to parents, SO’s (sterterous respiration, inability to awaken)
• Consideration of involvement in naloxone programs
Case 4

- 25 y/o with polysubstance abuse, claims to be using 180 mg Oxycodone CR daily
- Seen in MMTP where medical staff review conversion table, decide on methadone 80 mg per day
- Started on 40 mg, raised 10 mg daily to 80 mg
- Misses day 2 and 3, on day 4 given 70 mg
- Misses day 5 and 6, given 80 mg day 7
Case 4 (2)

- Patient found dead on day 8
- Autopsy shows respiratory death, methadone levels of 840 ng/ml, oxycodone/morphine ND,
- No documentation other than patient statement to doctor and + UDS for opiates/benzos
- No documentation of questions or evaluation on each contact
- Missed a number of doses, but no MD contact, dosed despite misses without reconsideration of tolerance
Case 4 (3)

- Majority of deaths in MMTP are during titration in first 1-2 weeks
- Individual tolerance and needs must be determined
- Fixed starting doses and fixed rates of daily increases are the prime factors in titration mishaps
- Policy on missed doses and continued titration should be strongly considered
TAKE HOME POINTS - Case 4

- You can’t keep increasing dose when you don’t know what the previous dose did, and did not allow it to reach steady-state.
- Using equivalency tables is fraught with hazard, best avoided, too much individual metabolic variation.
- Cookbook “one size fits all” titrations need to be reconsidered in ALL programs.
- Individualization remains key.
CASE 5

- 35 y/o AAM with long hx of snorting heroin/oxycontin admitted to MMTP
- Titrated to Methadone 120 mg over first 2 weeks, tolerates well
- FDA/state authority asked for work hardship after he brings in letter from employer about need to be at work at 6 AM
- Given 5 takeout doses per week by week 4
- First 2 UDS neg for substances of abuse
Case 5 (2)

- In month 3 misses several counseling appts, reschedules, unable to provide a urine and is given a warning
- UDS 1 week later is + oxycodone
- One week later, client accused of providing methadone takeout doses at a party, resulting in death of 21 y/o WF
- Lawsuit brought against clinic for allowing takeout doses with evidence of noncompliance
CASE 5 (3)

- Balance between work-related or other hardship doses and patient stability
- Receiving all takeout bottles at next visit
- Random callbacks and bottle counts, UDS on patients on expanded takehomes, ? esp. when given on hardship basis
- What is the clinic’s responsibility to third parties? - similar to driving related issues??
TAKE HOME POINT - Case 5

- Selling/diversion of takehomes may be the most politically explosive issue of MMTPs in many communities.
- Each clinic should develop comprehensive policies regarding eligibility and monitoring.
- Patients whose employment status may indicate request for unearned status should be told up front that this may not be possible.
- MMTPs are not judged like pain programs, patients receiving same drugs by prescription.