Urine Drug Testing in Pain Management: A Patient-Centered Approach

PainWEEKEND 2017
Douglas Gourlay, MD, MSc, FRCPC, FASAM

Declaration of Potential Conflict of Interest

• The content of this presentation is non-commercial and does not represent any conflict of interest.

Objectives

• Describe a patient-centered approach to urine drug testing (UDT)
  – Explain the differences between the clinical vs workplace/forensic test pool
• Express the importance of “Testing Strategy” in the clinical use of UDT
  – List Common myths / misconceptions of urine drug testing analysis
• Summary
Why do we test?

• Forensics
• Treatment Compliance / Concurrent drug use
• Advocacy
  – With 3rd party, motivate/support behavioral change, identify abuse/addiction: Avoid “gotcha” syndrome
• Risk Management

Non-Clinical vs Clinical Testing

• In non-clinical testing, the majority of donors are expected to be non-users
  – Thresholds are set based on donor characteristics NOT lab capabilities
  – “-ve test results can harm the donor”
• In Pain Practices this is NOT the case
  – Majority of donors are user of common drugs of misuse
  • Difference is they’re legitimately +ve

What’s worse than not doing UDT?

• Doing UDT inappropriately
  – Clinicians (and lab directors) must resist the urge to reach beyond the scientific AND clinical limits of the test
• Using ‘clinical’ test strategies for ‘forensic’ purposes
  – Agreeing to monitor for CPS / Drug Court
  – This is a dangerous practice
When to Test

• Consider urine drug testing (UDT) in all patients
  – Especially those starting opioid therapy
  – When making major changes in therapy
  – In response to aberrant behavior
• Testing Frequency
  – Low risk – initially and yearly if no problems?
  – High risk – weekly? Monthly if stable?
• Cheap, effective and well tolerated by pts
  – Only patients ‘philosophically opposed’ to UDT are
    those patients with problems who don’t want help

How to Test

• There is no ‘right or wrong’ way to test
  – Laboratory Testing
  – Point-of-Care (‘test strips’)
• Never do a test you don’t know how to interpret the results
  – You must have a testing strategy
  – Need an action plan to deal with results

Testing Strategies

• Routine vs Random testing
  – Random more reliable, more complex
  – Routine easier to ‘prepare’ for
• Reliability
  – Witnessed require same-sex observers
  – Can use temperature strips
• How to use the results
  – Avoid “gotcha” syndrome
Testing Techniques

• Presumptive
  – Immunoassay (EMIT)
• Definitive (Identification)
  – GC/MS, LC/MS-MS etc
• Point-of-Care Testing (‘test strips’)
  – Immunoassay

Adulteration, Substitution, Volume Loading

• People do cheat!
• Witnessed vs unwitnessed collection
• Temperature monitoring
  – Min volume, time, within 1°C body temp
• pH, Creatinine, “urine fingerprinting”
• Volume loading
  – Deliberately ingest H2O to lower SG, Cr
    • Cr<1.8mmol/L AND SG<1.003 = suspicion

Drugs of Abuse

• NIDA-5 (aka “Federal Five”)
  – Cocaine
  – Opiates
  – THC
  – Amphetamines
  – PCP
• Benzodiazepines, Barbiturates, Methadone, etc
Cocaine

• Screen for metabolite, benzoylecgonine (BEG) NOT cocaine parent
• Metabolite $t_{1/2} \gg$ parent $t_{1/2}$
• $H_2O$ soluble $\Rightarrow$ does not accumulate
• Detectable at 300ng/mL for 3-5 day
• Cocaine (parent) implies very recent drug use ie hours

Opiates

• Really Codeine/Morphine
  – Cross reacts with many other opioids
• Threshold varies – DOT 2000ng/mL; typically 300ng/mL (total opioids)
• Heroin use confirmed by 6-AM (6-MAM)
  – $t_{1/2}$ short makes detection difficult
  – Never detect heroin parent*
  – Can’t distinguish morphine from heroin/morphine/codeine metabolism

Opioids 101

<table>
<thead>
<tr>
<th>Natural</th>
<th>Semi-Synthetic</th>
<th>Synthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Hydrocodone</td>
<td>Meperedine</td>
</tr>
<tr>
<td>Morphine</td>
<td>Hydromorphone, Diacetyl Morphine</td>
<td>Fentanyl (Sufenta, Alfenta, Remifentanil)</td>
</tr>
<tr>
<td>Thebaine</td>
<td>Oxycodone, Oxymorphone, Buprenorphine, Naltrexone, Naloxone</td>
<td>Methadone, Propoxyphene</td>
</tr>
</tbody>
</table>
THC

- Screen looks for all cannabinoids
- Variable cut-offs (50ng/mL / 15ng/mL)
- Fat soluble
- GC/MS looks only at THC-COOH
- Infrequent users detect for <3d
- Frequent, heavy users >7d (20ng/mL 77days positive)

Amphetamines

- EMIT screens triggered with decongestants, antihistamines
- May react to MDMA (Ecstasy), MDA etc
- Many prescription and OTC drugs give false positive EMIT screens
- Cut-off 1000ng/mL, confirms 500ng/mL
- “Vicks Nasal Inhaler” dilemma (USA)
- Typically detectable for <3 d

PCP

- Phencyclidine (also reacts with Ketamine)
- Low yield except with specific patient populations in certain areas
- Cut-off of 25ng/mL
- Detectable for < 7d
### Other Drugs

- **Specific opioids**
  - Hydromorphone – may need to ask lab for assistance
  - Oxycodone – needs specific assay
  - Hydrocodone
  - Buprenorphine (immunoassay)
  - Methadone/Fentanyl do NOT yield +ve ‘opiate’ screens
- **Benzodiazepines**
  - Difficult to reliably detect, especially clonazepam even when abused – check with lab regarding sensitivity

---

### Poppy Seeds

- Poppy seeds don’t give false positives
  - They lead to TRUE positives
  - Can exceed DOT Cutoffs for several hours
  - May show both morphine and codeine
  - NEVER accounts for 6-MAM
- **People on UDT programs should not eat poppy seeds**

---

### Passive Marijuana

- ‘Incidental’ exposure does not lead to +ve UDT
- Depends on cut off concentration
- Can not easily distinguish prescribed oral THC from smoked marijuana
- Single use does not lead to persistent +ve results
### Passive Cocaine

- Nasal cocaine (cocaine HCl) cannot be put in cigarette to give positive result
  - Crack cocaine can lead to positive result
- Cocaine base sublimates when heated:
  - Found on many surfaces where crack cocaine is used
  - $20 bills frequently test positive for cocaine
- Medical uses result in positive results
  - ENT, ophthalmology, plastic surgery

### Opioid Metabolism

- Codeine → Morphine → 6-MAM → Heroin
  - (Detected <12h) (Not detected)
- Morphine-X-Glucuronides
  - (Not detected with HPLC but detected with GC/MS)

### Drug Testing Traps

- **codeine**
  - >89%
- **morphine**
  - >97%
- **norhydrocodone**
  - >97%

- **hydrocodone**
  - >89%
- **hydromorphone**
  - <3%
- **morphine**
  - >97%
- **Hydromorphone**
  - <3%

---

Baseelt RC. *Disposition of Toxic Drugs and Chemicals in Man.* 7th ed 2004

*Identification of Hydrocodone in Human Urine Following Controlled Codeine Administration*, JM Oyler et al. *Journal of Analytical Toxicology* 24(7): 530-535

**Evidence of Morphine Metabolism to hydromorphone in pain patients chronically treated with morphine**, E Cone et al. *Journal of Analytical Toxicology* 30(1): 1-5
Test Interpretation  
(GC/MS)

<table>
<thead>
<tr>
<th>Test</th>
<th>Codeine</th>
<th>Morphine</th>
<th>6-MAM</th>
<th>Drug(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>+</td>
<td></td>
<td>MH&gt;12h</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td></td>
<td>C/M+C/H&gt;12h</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>H&lt;12</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>H&lt;12h</td>
</tr>
</tbody>
</table>

M = Morphine  
C = Codeine  
H = Heroin

New Use?  
(Consider Creatinine)

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

What to do with unexpected results?

• First, call the lab.  
  – If unexpected +ve, check for legitimate reasons for true positives  
    • ENT cocaine for epistaxis  
    • Morphine in codeine user  
    • Hydrocodone in codeine user (~11% or less)  
  – If unexpected –ve, check for test sensitivity, subthreshold results, dilute sample, lab error
• Speak with patient  
  – Ask about ALL drug use including OTC and time of last use  
    • When truly negative, look for binging (ie running out)  
• Never ignore an aberrant result!
Test Interpretation Traps
Urinary Levels

- Urinary drug and drug metabolite excretion are a function of many factors which may not be static
  - Volumes of distribution, urinary pH, state of hydration, time of last dose, GI absorption effects etc
  - It is unwise to draw any conclusions based solely or largely on urinary analyte concentrations
  - Drug testing is the beginning not the end of discussion – use ‘social engineering’ to solve the problem

Using the Results
(it’s all in the strategy)

- First, do the results “fit”? If yes, could they be ‘hiding’ an abnormal result? i.e.
  - +ve opiates / +ve bzd
    - Beware of the expected analyte
- Compliance Testing
  - What does the –ve mean? Have a diff Dx for the unexpected result
- Can you interpret the results?
  - Ask before collecting sample.
    - New meds? New OTC drugs? Recreational use?

Approaching the Patient

- “Offer” drug testing to the patient
  - Majority of patients will have no problems with UDT
    - If patient is ‘philosophically opposed’ to UDT, bodes poorly for this patient
    - Remind patient that this will severely limit the pharmacologic choices for treating their pain
  - Reassure the patient that UDT is part of a comprehensive risk management strategy
Case Discussion

• Case I
  – “Opiate +ve, no opiate seen” with patient on Cipro
  – Is this a false positive d/t the antibiotic?
    • +/- sub threshold opioid use?
• Case II
  – “Cocaine +ve UDT in patient who recently had dental surgery”
    • Possible explanations?
• Case III
  – “Strongly +ve methadone parent, no EDDP seen”
    • Possible explanations?
• Case IV
  – “EDDP +ve, no parent seen” – possibilities?

Conclusions

• UDT, when done with respect and sensitivity can be an important part of a comprehensive care plan for all, not only high risk patients that
  – reduces patient stigma
  – Improves patient care
  – And hopefully, reduces risk
• The clinical context is essential for proper UDT interpretation
  – Risk management is FOR the patient

Resources

• http://www.UDTmonograph6.com
  – For UDT monograph
• dgourlay@cogeco.ca