Urine Drug Testing in Pain Management: A Patient Centered Approach
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Declaration of Potential Conflict of Interest

- The content of this presentation is noncommercial and does not represent any conflict of interest
Learning 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

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
Nonclinical vs Clinical Testing

- In nonclinical testing, the majority of donors are expected to be nonusers
  - 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 patients
  - 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 if 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<1.8 mmol/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 $t\frac{1}{2} >>$ parent $t\frac{1}{2}$
- $H_2O$ soluble $\therefore$ 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 2000 ng/mL; typically 300 ng/mL (total opioids)
- Heroin use confirmed by 6-AM (6-MAM)
  - $t\frac{1}{2}$ 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>Meperidine</td>
</tr>
<tr>
<td>Morphine</td>
<td>Hydromorphone</td>
<td>Fentanyl (Sufenta, Alfenta, Remifentanil)</td>
</tr>
<tr>
<td></td>
<td>Diacetyl Morphine</td>
<td></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 (20 ng/mL 77 days 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 1000 ng/mL, confirms 500 ng/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 25 ng/mL
- Detectable for < 7 d
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) can not 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

(Morphine-X-Glucuronides (Not detected with HPLC but detected with GC/MS)

(Detected <12h) (Not detected)

Drug Testing Traps

<table>
<thead>
<tr>
<th></th>
<th>Hydrocodone*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td>&gt;89%</td>
<td>&lt;11%</td>
</tr>
<tr>
<td>morphine</td>
<td>&gt;97%</td>
<td>&lt;3%</td>
</tr>
</tbody>
</table>

norhydrocodone ← hydrocodone ← hydromorphone

hydrocodol → hydromorphe

conjugation

Hydromorphol

Baselt 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) 2000 p530-535

** Evidence of Morphine Metabolism to hydromorphone in patients chronically treated with morphine.

E Cone et al, Journal of Analytical Toxicology 30(1) 2006 p1-5
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>M/H&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</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>

Result

Threshold (Cut-off)

Drug

↓Cr  ↑Cr
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 bingeing (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? ie, +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

  – For UDT monograph
- dgourlay@cogeco.ca

References

7. MROALERT. November 6 , 2006: Vol.XVII; No. 9(1-4)