Investigation of Propofol in Post-Mortem and Ante-Mortem Specimens by GC/MS

Mike Frontz, Robert Rodriguez, Gary Kunsman
Bexar County Medical Examiner’s Office, San Antonio, TX

Brad Hall, Patricia Schroeder, Rod McCutcheon
Travis County Medical Examiner’s Office, Austin, TX
Acid/Neutral Drug Screen

Bexar County Medical Examiner's Office
Forensic Toxicology Laboratory

Assay: Acid/Neutral Drug Screen
File ID: D:\HPCHM\2\DATA\NOV2002\1113RR13.D
Sample Info: FTL: 02-0207
Misc. Info: 0.20 ML Blood
Analyst: Rodriguez, R.
Date/Time: 11/13/02 10:54:26 AM
Instrument: HP 5890 Gas Chromatograph #2
Seq Line: 13
Vial Number: 13

Graph showing drug analysis results.

Bexar County MEO
All in a day’s work

- Travis Co. (Austin) identifies propofol overdose in death ruled accidental
- Bexar Co. (San Antonio) identifies propofol in intoxication assault case
- 3 other PM cases from San Antonio examined
Overdose points to holes in system

Doctor's death attributed to drugs stolen from operating room

By LEIGH HOPPER
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Last summer, a medical school graduate and triathlete from Tennessee accepted a coveted post in Baylor College of Medicine's anesthesiology training program. Dr. Daniel Jacks, newly married, moved to Houston in June. Six months later he was dead from an overdose of drugs filched from the operating room. Colleagues found Jacks' body Dec. 12, still in blue surgical scrubs, in a Ben Taub General Hospital restroom. An autopsy revealed at least 17 needle marks on his body, evidence of recurrent use…
Abuse case
50 y/o Caucasian female
Surgical nurse
Found unconscious in bathroom
Syringe in arm
5 empty and 1 unused vials of propofol
Femoral blood – 0.24 mg/L propofol

- 29 y/o female
- Radiographer
- Accidental overdose fatality
- 2 empty 20 mL vials of propofol
- Femoral blood – 0.22 mg/L propofol
- “The milk of human kindness”
Propofol

- Diprivan®
- 2,6-diisopropylphenol
- M.W. 178.27

Bexar County MEO
Propofol – Clinical

- IV anesthetic, sedative
- Fast onset
- Long duration
- Structurally unrelated to other common anesthetics
- Highly lipophilic
- $V_d$: 2-10 L/kg
Propofol – Clinical

- Preparation
  - Oil emulsion
  - 1-2% propofol
- Used for anesthesia induction and maintenance
  - Bolus dose (adults): 2.0-2.5 mg/kg
  - Maintenance: 50-300 ug/kg/min
  - Monitored anesthesia care sedation
EI – Fragmentation Pattern

Scan 273 (2.103 min): 111.3RR28.0

Bexar County MEO
Travis County – Analytical

- Propofol extraction
  - 1.0 mL sample made acidic
  - Add 20 uL of I.S. (2-isopropylphenol@100 ug/mL)
  - Extract w/ 5.0 mL n-buCl
  - Remove organic, extract w/ 4.0 mL 0.5N NaOH
  - Remove 3 mL of NaOH layer and make acidic
Propofol extraction (cont.)
- Add 100 uL CHCl₃
- Vortex 30 s, then centrifuge
- Inject 1.0 uL on RTX-5 w/ full scan MS
- Use m/z 163 (propofol) and m/z 121 (I.S.) for quantitation
- Calibrators – 0.10, 0.25, 1.0, 2.0 mg/L
- R² – 0.9994
Travis County – Case History

- 56 y/o Caucasian male
- Found, moderately decomposed, in his home by a friend
- Syringe containing a white milky substance in hand
- Several other syringes with the milky substance were found
- Decedent worked in a hospital in the surgery unit
Travis County – Toxicology

- Volatiles – 0.04% EtOH in blood
- Urine EIA
  - Positive – opiates, benzodiazepines
  - Negative – amps, barbs, cocaine-mtb., THC, PCP
- Benzodiazepines
  - Blood – Negative
  - Urine – 7-amino-clonazepam detected
Travis County – Toxicology

- Opiates
  - Blood – morphine (<0.025 mg/L)
  - Urine – morphine detected

- Alkaline screen (blood)
  - Promethazine (0.15 mg/L)
  - Lidocaine (0.29 mg/L)
Travis County – Toxicology

- A/N screen
  - Blood – Propofol (3.2 mg/L)
  - Urine – Propofol detected (<0.10 mg/L)
Bexar County – Analytical

- A/N screen
  - Previously described extraction and run conditions
  - Propofol elutes at ~1.8 minutes
  - RRT – 0.685
  - Barbital used as internal standard
- Established linear range: 0.4 – 93 mg/L
- $R^2 = 0.9999$
Quantitative Data

$y = 0.0377x + 0.0051$

$R^2 = 0.9999$

<table>
<thead>
<tr>
<th>Concentration (mg/L)</th>
<th>Response Ratio</th>
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<tbody>
<tr>
<td>0</td>
<td>0.33</td>
</tr>
<tr>
<td>20</td>
<td>1.53</td>
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<tr>
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<tr>
<td>80</td>
<td>3.90</td>
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<td>100</td>
<td>4.62</td>
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Bexar County MEO
Bexar County Case 1 – History

- 8 y/o Caucasian female
- MV accident
- Decedent buckled in front passenger seat with mother
- Airbag deployed
- Spinal cord injury
Case 1 – Toxicology

- Volatiles – none detected

- Alkaline drug screen (heart blood)
  - Lidocaine
  - Fentanyl (0.02 mg/L)

- A/N drug screen (heart blood)
  - Phenytoin (20 mg/L)
  - Propofol detected and quantitated
### Case 1 - Propofol

<table>
<thead>
<tr>
<th>Propofol (mg/L)</th>
<th>Heart blood</th>
<th>Vitreous humor</th>
<th>Bile</th>
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<tbody>
<tr>
<td>19.7 (Avg.)</td>
<td>0.64</td>
<td>42.1</td>
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Bexar County Case 2 – History

- 78 y/o Caucasian female
- Found unresponsive at home
- Taken to ER
- Intubation, CT scan
- Propofol administered
Case 2 – Toxicology

- Volatiles – none detected
- Alkaline drug screen
  - Subclavian blood
    - Bupropion (0.36 mg/L)
    - Erythro/threo metabolite (3.5 mg/L)
    - Midazolam detected (<LOQ)
- Urine
  - Bupropion, metabolite, diazepam, temazepam detected
Case 2 – Toxicology

- A/N drug screen
  - Subclavian blood
    - Phenytoin (240 mg/L)
    - Acetaminophen (11 mg/L)
    - Propofol detected and quantitated
  - Urine – QNS
Case 2 - Propofol

<table>
<thead>
<tr>
<th>Propofol (mg/L)</th>
<th>Subclavian blood</th>
<th>Vitreous humor</th>
<th>Urine</th>
<th>AM blood</th>
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</thead>
<tbody>
<tr>
<td>8.6 (Avg.)</td>
<td>8.6 (Avg.)</td>
<td>ND</td>
<td>ND</td>
<td>0.73</td>
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Bexar County Case 3 – History

- 41 y/o Caucasian male
- Fall at home
- Diagnosed w/ C2-C4 injury
- Extended hospital stay
- Propofol administered – monitored anesthesia care
Case 3 – Toxicology

- Alkaline drug screen (subclavian blood)
  - nordiazepam detected (<LOQ)
- Opiates – morphine (0.29 mg/L)
- Cocaine/metabolites – none detected
- A/N drug screen – none detected
Bexar County Case 4 – History

- 25 y/o Caucasian male
- Intoxication assault
- 2 blood draws
- 80 minute interval
- Treatment details uncertain
Case 4 – Toxicology

- Volatiles
  - Ethanol (first draw) – 0.18 g/dL
  - Ethanol (second draw) – 0.12 g/dL

- Alkaline drug screen
  - Midazolam (1.2 mg/L)
  - Lidocaine

- Opiates, cannabinoids, cocaine and metabolites – none detected
<table>
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<td>Propofol (mg/L)</td>
<td>&lt;LOQ</td>
<td>&lt;LOQ</td>
<td>180</td>
<td>340</td>
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Bexar County MEO
Acknowledgments

- Joe Castorena, Bexar Co. MEO
- Barry Levine, AFIP
- Ashraf Mozayani, Harris Co. MEO
- Julie Wright, Bexar Co. ADA