Bupivacaine Overdose Following Genital Injection

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History of Local Anesthetics

- First clinical operation under anesthesia performed in 1884 using cocaine
- Cocaine widely utilized until toxic effects and death widely reported
- Cocaine was chemically synthesized in 1891, allowing structural amino ester analogs to be produced (tetracaine, benzocaine)
- Between 1898-1972 novel amide local anesthetics produced (procaine, lidocaine, mepivacaine, bupivacaine)
Bupivacaine Uses

- Special interest due to long duration of action (up to 7 hours)
- Most widely used long-acting local anesthetic for surgery and obstetrics
- Bupivacaine HCl doses 12-225 mg
- Doses of 150 mg for peridural anesthesia gave peak plasma concentrations of 1.1 mg/L after 20 mins
- Blood/Plasma ratios 1.2-1.3
- Metabolism likely involves N-dealkylation and hydroxylation; not widely studied in humans
Case History

- Decedent LSA at 8:30 am when spouse left for church
- Wife returned at 1:00 pm
- Husband found dead in upstairs den with pants removed, pornography playing on VCR
- Sexual paraphernalia in the vicinity including magazines, collars, tubing, rope, plastic bags, rubber rings and metal clips
- Syringes, lidocaine cream, xylocaine jelly and three empty vials of Marcaine (5 mg/mL) present
Case History

- Decedent led a “high stress job” as a car salesman
- History of moderate alcohol use
- No history of serious medical or mental health problems
- Postmortem performed 24 hours after the discovery of the body
Postmortem Findings – External Exam

- Laceration and contusion of the lower lip
- Superficial abrasion to left knee
- Small contusion to deep scalp
- Multiple needle punctures on scrotum with contusions
- Mild scrotal edema
- Three small contusions on thorax and abdomen
Postmortem Findings – Internal Exam

- Congestion and edema of the lungs
- Diffuse fibrous adhesions within the scrotum
- Fibrosis and hemorrhage of penis and testicles
- Mild atherosclerotic stenosis of the coronary arteries, nephrosclerotic changes of the kidneys, mild steatosis of the liver
- Remainder of the postmortem was unremarkable
Toxicology

Specimens
- Femoral Blood
- Heart Blood
- Vitreous Humor
- Urine

Tests
- Blood Alcohol
- Drug Screen
- Comprehensive Tox (Basic, acidic, neutral drugs)
Toxicology Methods

Alcohol
- Dual column GC-FID
- HP 6890 GC
- Restek BAC1/BAC2 capillary columns
- N-Propanol, t-Butanol internal standards

Drugs of Abuse Screen
- ELISA
- OraSure Technologies
- Whole blood
- Opiates, Methamphetamine, Benzodiazepines, Cocaine metabolite, Cannabinoids, Propoxyphene, Methadone, Barbiturates
Toxicology Methods

- Basic, Acidic, Neutral Drugs by SPE and GC/MS
- PolyChrom Clin II SPE
- Internal standards (mepivacaine, hexobarbital)
- DB5 capillary column, 30m (0.25mm id x 25µm)
- 160°C (2m); 30°C/min to 230°C (2m); 30°C/min to 290°C (12 m)
- Total run time 20 mins
- Flow rate (He) 1.3 mL/min
2 mL blood + 2 mL Phosphate buffer (pH 6, 0.1M)
↓
Sonicate (15m), Centrifuge (4500rpm, 15m)
↓
Add to SPE
↓
Wash with 1mL DIW, 1mL acetic acid (1M)
↓
Dry (full vac, 5m)
↓
Wash 1 mL hexane
↓
Elute acidic/neural drugs, 1mL ethyl acetate
↓
Wash 1 mL methanol
↓
Elute basic drugs, 1 mL ethyl acetate with 2% NH₄OH
Results

- No ethanol, methanol, acetone, isopropanol
- Drugs of abuse screen negative
- Trace of salicylate in femoral blood
- Bupivacaine only drug of toxicological significance
Bupivacaine Quantitation

- Bovine blood fortified with bupivacaine
- Mepivacaine internal standard
- Full scan acquisition
- Quantitation ions (in bold)
  - m/z 140, 84 (bupivacaine)
  - m/z 98, 70 (mepivacaine)
- Calibration range (0-4mg/L)
- $R^2 = 0.999$
- S/N ratio using lowest calibrator (0.08 mg/L) was 341:1
Scan 939 (8.046 min): 1901020.D (-935) (-)

Bupivacaine
<table>
<thead>
<tr>
<th>Tissue</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Blood</td>
<td>2.8 mg/L</td>
</tr>
<tr>
<td>Femoral Blood</td>
<td>3.8 mg/L</td>
</tr>
<tr>
<td>Vitreous Humor</td>
<td>1.3 mg/L</td>
</tr>
<tr>
<td>Urine</td>
<td>11.4 mg/L</td>
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</tbody>
</table>
Genital Injections

- Practice of injecting foreign substances into external genitalia well described in medical literature
- Scrotal inflation with saline most common; oils, gels have also been used
- This practice can lead to local tissue damage or death (if substance enters the vascular system)
- Internet sites describe materials needed, injection sites, what to expect and how to avoid infection
Saline Scrotal Infusion

This text is intended for reading enjoyment, the author claims no medical expertise nor advises you to undertake this procedure. This is a recounting of her experiences and how she has done it.

Saline infusion. A big, full, bouncy, heavy ball sack of fluid. Why, you ask? Because I can, because I like altering human form, it is fun to play and I get off on the control. Men not only let me, they want to experience it for their own assorted, or is that sordid, reasons.
The Encyclopedia of Unusual Sex Practices

A first-class, reference source for those seeking to understand the range of human sexual expression.

Ted Mclvonna, President
The Institute for the Advanced Study, of Human Sexuality

Will fill you with astonishment at the inventiveness of human beings in pursuit of pleasure and novelty.

Filled with more astonishing facts and fancies than most people could ever have imagined, the Encyclopedia of Unusual Sex Practices presents a unique guide to human sexual expression, ranging from the mildly kinky to the truly bizarre.

Carving a path through the mysteries of human behaviour, it records practices and beliefs from cultures world-wide throughout history, as well as from the author's extensive researches into...
Bupivacaine Toxicity

- Since introduction in 1965, CNS and cardiovascular toxicity have been reported
- A stereoselective isomer (levobupivacaine) and ropivacaine (replacement of butyl with propyl) are reported to be less cardiotoxic/increased margins of safety
- Toxicity includes CV collapse, respiratory depression/arrest, arrhythmia, death
- Most frequently associated with seizures
- More cardiotoxic than many structurally related analogs; eliminated from myocardium slower than lidocaine
Bupivacaine Toxicity

- Overlap of adverse/therapeutic concentrations:
- Hypertension, bradycardia, cyanosis, loss of consciousness, convulsions, respiratory arrest reported between 0.7-1.8 mg/L (Holmboe et al 1982; Rosenberg et al 1983; Hasselstrom et al 1984)
- Clinical study using high dose bupivacaine (400 mg) in ten patients produced peak plasma levels averaging 2.5 mg/L (Moore et al 1976)
Case Conclusions

- Decedent injecting bupivacaine into genitalia to enhance/prolong sexual endeavors
- Contusions and internal scarring consistent with long-term activity
- Histology consistent with injection of foreign material
- Minor abrasion on knee and contusion to scalp consistent with terminal collapse
- Laceration to lip consistent with biting (possible seizure activity prior to death)
- Cause of death: Bupivacaine intoxication
- Manner of death: Accidental
Acknowledgements

- Janice Yazzie, B.S.
  Scientific Laboratory Division

- Sean Kelly, M.D.
  Office of the Medical Investigator

- Ross E. Zumwalt, M.D.
  Office of the Medical Investigator