Operating Room Pharmacy: A Primer

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- Medical University of South Carolina

Objectives

- Understand the role of the pharmacist and pharmacy technician in the operating room environment.
- Explain the underlying principles of regional anesthesia and pharmacy’s role.
- Become more familiar with recent trends in a few key operating room practice areas impacting hospital pharmacies.

Operating Rooms at MUSC

- Ashley River Tower
  - 10 OR’s + “offsites”
  - Services: Gastrointestinal, Vascular, Adult Cardiothoracic, Vascular, Oral Surgery, Plastic Surgery, others

- University Main Hospital
  - 21 OR’s + “offsites”
  - Services: Trauma, Transplant, Pediatric Cardiothoracic, Pediatric General, Urology, Neurosurgery, Orthopedic, ENT, OB-GYN, others

- Rutledge Tower
  - Outpatient Surgery
  - 9 OR’s
  - Services: Ophthalmology, Orthopedic, Pediatric, ENT, Urology, others

Roles of the Operating Room Pharmacy Staff

- Pharmaceutical Services Pharmacist/Technician
- Cost Management Pharmacist/Technician
- Clinical Services Pharmacist
- Operating Room Pharmacy

Pharmaceutical Care Flow

- Preoperative/Holding Area
- Operating Area
- Post-anesthesia care unit (PACU)
- Inpatient Pharmacy

Disclosure

- I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation.
- I will be discussing off label use of medications.
Pharmaceutical Services

- Drug preparation and distribution...STAT!
- SAFETY
- Pre-drawn syringes, pre-made intravenous medications, mini-bags
- Narcotic reconciliation and drug diversion
- Numerous hospital specific systems
- Increase accountability, decrease diversion
- Drug inventory control
  - Centralizing high cost items (i.e. Factor VII, etc)
  - Inventory recovery and re-use
  - OR Satellite Pharmacy and after-hours access

Pharmaceutical Services – Safety and Preventing Harm

- Operating room is a potential “black hole” for medications
- Not in direct observational view of organization
- Higher rates of medication errors
  - Pediatric patients experience disproportionate share of harm
- Very medication intense area of hospital

Drug Diversion

- Anesthesiologists usually comprise 25% of physicians being treated for addiction
  - Opioids, 66%; induction agents, 20%; benzodiazepines, 15%
  - Alcohol, 12%; Recreational drugs 7%; inhalational agents, 5%
  - Fentanyl abuse = 95% are either anesthesiologists or surgeons
- Death
  - Presenting symptom in 7-18% of cases
  - Among residents, 36%
  - Inhalational agents, 26%
  - Propofol: overall 26%, residents 38%

Pharmaceutical Services - Preparation, Distribution and Safety

- Drug cassettes, automated dispensing machine
- LASA drugs (i.e. neuromuscular blockers), MDV vs. SDV, vial color and size
- Patient specific vs general or routine medications
- High-risk and high-potency medications!
Cost Management

- Medication-Use Management
  - Institution guidelines
  - Drug shortages
- Formulary Adherence
- Waste Reduction
- Inventory use and recovery
- Revenue generation: improved billing accuracy

Clinical Services

- Presence in the OR area
- Medication-regimen review
  - Patient specific orders
  - Pharmacokinetics
- Medication-use evaluations
- Institution medication policies
- Code attendance
- Drug information
  - Alternative therapies...drug shortages?
- Research

Regional Anesthesia

- Neuraxial Anesthesia
  - Spinal, Epidural and Caudal Blocks
  - Peripheral Nerve Blocks
  - Paravertebral Blocks

Why Neuraxial Anesthesia?

- Reduced incidence of...
  - Venous thrombosis and pulmonary embolism
  - Cardiac complications
  - Vascular graft occlusion
  - Pneumonia/respiratory depression
  - Surgical site infection
  - Acute kidney injury
- Reduced:
  - Blood/transfusion requirements
  - Use of parenteral opioids
  - Time until extubation/need for mechanical ventilation following abdominal/thoracic surgery

Neuraxial Anesthesia

- Local anesthetic mechanism of action
  - Inhibits voltage gated sodium channels responsible for conduction of nerve impulse
- Types of Blockade
  - Somatic
  - Autonomic
Neuraxial Anesthesia

- Adjunct to general anesthesia
- Sole anesthetic
- Lower abdominal surgery
- Inguinal surgery
- Urogenital surgery
- Rectal surgery
- Lower extremity surgery


Clinical Manifestations

- Cardiovascular
- Pulmonary
- Gastrointestinal
- Renal and Genitourinary
- Metabolic and Endocrine


Contraindications

- Infection at the site of injection
- Patient refusal
- Coagulopathy, bleeding diathesis
- Severe hypovolemia
- Severe aortic/mitral stenosis

Absolute

- Sepsis
- Anticoagulation
- Preexisting neurologic deficits
- Demyelinating lesions
- Left ventricular outflow obstruction

Relative

- Absolute
- Spinal deformity
- Absolute
- Left ventricular outflow obstruction

Anticoagulants/Antiplalets

- Hospitalized patients at increased risk for venous thromboembolism
- Low risk: <10%
- Moderate risk: 10-40%
- High risk: 40-80%


Anticoagulants/Antiplalets

- Spinal hematomas
  - Incidence: 1 in 150,000 for epidural; 1 in 220,000 for spinal
  - Manifestation
  - Hemorrhage into epidural space most common with progression to spinal cord ischemia
  - Progression of sensory or motor block, bowel/bladder dysfunction → PARAPLEGIA
  - Full/partial neurologic recovery: 38%

Reg Anesth Pain Med 2010; 35: 64-101

Anticoagulants/Antiplalets

- What class of anticoagulant/antiplatelet?
- What type: thromboprophylaxis versus treatment
- How long before placement of catheter?
- How long after removal of catheter?
- While catheter in place?
- Coagulation testing, CBC
- Neuromonitoring

Reg Anesth Pain Med 2010; 35: 64-101
Local Anesthetics - Allergy

- "My patient is allergic to lidocaine. What local anesthetics can we use?"
- IgE-mediated allergy: true incidence is unknown but estimated to be <1%
- Skin-prick tests and subcutaneous allergy testing may have utility
- True allergy or local anesthetic effect?
  - Vasovagal attack, allergies to other concomitantly administered medications

Local Anesthetics - Allergy

- Esters
  - Cocaine
  - Benzocaine
  - Procaine
  - Tetracaine
  - Chloroprocaine

- Amides
  - Cinchocaine
  - Lidocaine
  - Mepivacaine
  - Prilocaine
  - Bupivacaine
  - Etidocaine
  - Ropivacaine
  - Levobupivacaine

Targeting Dermatomes

Spinal Anesthesia

- Injection of local anesthetic into the sub-arachnoid space (into CSF) at lumbar level
- Site of action at the nerve root with some uptake by spinal cord

Spinal Anesthesia

- Below L1 in adults, L3 in children
- Successful dura puncture verified by free flow of CSF

Critical Factors

- Baricity
- Position of patient
- Drug dosage
- Site of injection

Other Factors

- Age
- Curvature of spine
- Drug volume
- Intrabdominal pressure
- CSF volume
- Patient height
- Pregnancy
Spinal Anesthesia

- Cocaine was the first spinal anesthetic
- Lidocaine, bupivacaine, tetracaine, mepivacaine, ropivacaine, levobupivacaine and chloroprocaine more typically used now
- All-or-nothing single dose

Baricity

<table>
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<th>Specific Gravity</th>
<th>Baricity</th>
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<td>Tetracaine</td>
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<td>1.023</td>
<td>0.554</td>
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<tr>
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<td>1.059</td>
<td>0.957</td>
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<td>Levobupivacaine</td>
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<td>Chloroprocaine</td>
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Epidural Anesthesia

- Injection of local anesthetic into the epidural space
- Lumbar, thoracic or cervical level
- Site of action at nerve root
- Slower in onset and less dense than spinal
Epidural Anesthesia

- Failed Epidural Blocks
- Misplaced injections
- Unilateral block
- Large nerve roots (L5, S1, S2)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Conc</th>
<th>Onset</th>
<th>Sensory Block</th>
<th>Motor Block</th>
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<tbody>
<tr>
<td>Chloroprocaine</td>
<td>2%</td>
<td>Fast</td>
<td>Analgesic</td>
<td>Mild to mod</td>
</tr>
<tr>
<td></td>
<td>3%</td>
<td>Fast</td>
<td>Dense</td>
<td>Dense</td>
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<tr>
<td>Lidocaine</td>
<td>&lt;1%, 1.5%, 2%</td>
<td>Intermediate</td>
<td>Analgesic → Dense</td>
<td>Minimal → Mod to dense</td>
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<tr>
<td>Mepivacaine</td>
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<td>Intermediate</td>
<td>Analgesic</td>
<td>Minimal</td>
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<tr>
<td></td>
<td>&lt;0.25%</td>
<td>Intermediate</td>
<td>Dense</td>
<td>Dense</td>
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<tr>
<td>Bupivacaine</td>
<td>&lt;0.25%</td>
<td>Slow</td>
<td>Analgesic</td>
<td>Minimal</td>
</tr>
<tr>
<td></td>
<td>0.5%</td>
<td>Slow</td>
<td>Dense</td>
<td>Mild to mod</td>
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<tr>
<td></td>
<td>0.75%</td>
<td>Slow</td>
<td>Dense</td>
<td>Mod to dense</td>
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<td>Slow</td>
<td>Analgesic</td>
<td>Minimal</td>
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<tr>
<td></td>
<td>0.5%</td>
<td>Slow</td>
<td>Dense</td>
<td>Mild to mod</td>
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<tr>
<td></td>
<td>0.7%—1.0%</td>
<td>Slow</td>
<td>Dense</td>
<td>Mod to dense</td>
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</table>


Caudal Anesthesia

- Predominantly pediatric patients
- Combined with general anesthesia
- Urogenital, rectal, inguinal, and lower extremity surgery
- Caudal blocks usually bolused, adjuncts common

Caudal Anesthesia

- Pharmacy Math!
- Verbal order from pediatric anesthesiologist:
  Ropivacaine 0.15% with epinephrine 1:200,000 and clonidine 2 mcg/ml
  Patient: 6 kg
  Stock: Ropivacaine 0.2%, epinephrine 1 mg/ml, clonidine 1000 mcg/10 ml

Caudal Anesthesia

- Generally 1 ml/kg = 6 ml...will make 20 ml stock
- Ropivacaine
  0.15% → 1.5 mg/ml * 20 ml = 30 mg
  30 mg/(2 mg/ml) = 15 ml of Ropi 0.2%
- Epinephrine
  1:200,000 → 0.005 mg/ml * 20 ml = 0.1 mg
  0.1 ml / (1 mg/ml) = 0.1 ml of epi
- Clonidine
  2 mcg/ml * 20 ml/s = 40 mcg total
  40 mcg/ (1000 mcg/10 ml) = 0.4 ml of clonidine

Caudal Anesthesia

Ropivacaine 0.2% .......................... 15 ml
Clonidine 1000 mcg/10 ml ............ 0.4 ml
Epinephrine 1 mg/ml ..................... 0.1 ml
QS PF Saline (4.5 ml) ....................... 20 ml

Dispense 6 ml in a 10 ml syringe

Paravertebral and Peripheral Nerve Anesthesia

• Paravertebral Nerve Block
  • Injection of local anesthetic into the paravertebral space at the thoracic vertebrae

• Peripheral Nerve Block
  • Cervical plexus, interscalene brachial plexus, supravacular brachial plexus, infracavicular, axillary brachial plexus, forearm and wrist, femoral nerve, sciatic nerve, ankle block, popliteal sciatic nerve, etc.
  • Ultrasound guidance very useful

Ultrasound Guidance

Complications

• Permanent neurologic injury
• Cauda equina syndrome
• Meningitis
• Postdural puncture headache
• High spinal anesthesia
• Cardiac arrest
• Urinary retention
• Inadequate anesthesia or analgesia
• Intravascular injection
• Total spinal anesthesia
• Transient neurologic symptoms
• Backache
• Spinal or epidural hematoma
• Epidural abscess
• Shearing of epidural catheter

Pharmacy’s Role

• All neuraxial, paravertebral and peripheral blocks: PRESERVATIVE FREE!
• Safe, sterile compounding of complex, multi-ingredient extemporaneous medications
• Information resource
• Provide support to anesthesia for management of complications
  • Local anesthetic toxicity (i.e. lipid rescue)
  • www.lipidrescue.org

Operating Room - Trends


Acta Anaesthesiol Scan 2013; 57: 545-552
Anesth Analg 1999; 88: 797-809
Surgical Care Improvement Project (SCIP)
- Joint Commission set of core measures
- Reduce surgical complications
- "...aligns with Centers for Medicare and Medicaid Services (CMS) with respect to performance measures for patients undergoing surgery"

Liposomal Bupivacaine
- FDA indicated liposome injection of bupivacaine into the surgical site to produce postsurgical analgesia for:
  - Bunionectomy
  - Hemorrhoidectomy
- Not approved for:
  - Epidural
  - Intrathecal
  - Regional nerve blocks
  - Patients < 18 y/o
  - Pregnant patients
  - Pre-procedural usage for local/sedation cases
  - paracervical
- Very costly compared to bupivacaine or ropivacaine

Liposomal Bupivacaine
- Supplemental New Drug Application (sNDA)
  - Indication: nerve block
  - "Femoral Nerve Block with Liposome Bupivacaine for Postsurgical Analgesia Following Total Knee Arthroplasty"
  - Study complete (NCT01683071)
  - March 5th 2015 FDA decision

Liposomal Bupivacaine
- TRANSMITTED BY FACSIMILE
  - Dave Black
  - President and CEO
  - Pacira Pharmaceuticals, Inc.
  - 5 Sylvan Way
  - Parsippany, NJ 07054
  - RE: SDA #124655
  - RYVARDIN® (bupivacaine liposome injection suspension)
  - SWIR 22
  - WARNING LETTER
  - Dear Mr. Black:
    As part of its routine monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has been asked to evaluate the safety and effectiveness of RYVARDIN® (bupivacaine liposome injection suspension) as you submitted by Pacira Pharmaceuticals, Inc. (Pacira)

References
- "Local Anesthesia in Regional Anesthesia Practice: Strengths and Weaknesses of Bupivacaine and Ropivacaine Intrathecal Anesthesia. A Comparative Review. February 15, 2015"