BUPIVACAINE LIPOSOME (EXPAREL): Adjunct to Regional Anesthesia

NEBRASKA ASSOCIATION OF NURSE ANESTHETISTS
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Sallie Poepsel, PhD, MSN, CRNA, APRN
Director, AANA Region IV

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OBJECTIVES

- Describe the pharmacokinetics and pharmacodynamics of Exparel.
- List the indications for use of Exparel in post-op pain management.
- Identify the benefits and risks associated with Exparel use.
- Using case reports, delineate the post-op pain management outcomes associated with the use of Exparel.
DepoFoam® Encapsulated Bupivacaine

- DepoFoam drug delivery system composed of multivesicular liposomes
- Extended release of bupivacaine for long-acting pain relief
- Analgesic effect localized to injection site

BUPIVACAINE Multivesicular Liposome

In 2011:.......

- 2 positive Phase 3, randomized, double-blind, placebo-controlled trials
- Demonstrated efficacy in 2 representative acute pain models
  1) Hemorrhoidectomy
  2) Bunionectomy
Clinical Studies: Exparel

<table>
<thead>
<tr>
<th>Study</th>
<th>Clinical Setting</th>
<th>Region</th>
<th>Nerve Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>322</td>
<td>Thoracotomy</td>
<td>Thoracic</td>
<td>Intercostal</td>
</tr>
<tr>
<td>323</td>
<td>TKA</td>
<td>Lower</td>
<td>Femoral</td>
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</table>

Multimodal Management Recommended to Manage Acute Postsurgical Pain

- Combines ≥ 2 analgesic agents or techniques that act by different mechanisms to provide better pain relief with fewer opioids
- Usually includes systemic analgesics with local anesthetics

Post-Op Surgical Pain: What we know

- Unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage
- Is as subjective and variable as the perception of pain
- Surgeons interpret and manage pain differently
Post-Op Surgical Pain: What we know

- the treatment of post-surgical pain varies so greatly
- Pharmacological agents remain the mainstay of the management of acute perioperative and postoperative pain
- Treatment requires a combination of multiple pharmacotherapies and routes of delivery

Bupivacaine Liposome Injectable Suspension

Intended Response

- single-dose administration into the surgical site to produce postsurgical analgesia
- blocks the generation and the conduction of nerve impulses
  - increasing the threshold for electrical excitation in the nerve,
  - slowing the propagation of the nerve impulse,
  - reducing the rate of rise of the action potential.
Pharmacokinetics

- **Absorption**: The rate of systemic absorption of bupivacaine is dependent upon the total dose of drug administered, the route of administration, and the vascularity of the administration site.

- **Distribution**: Appear to cross the placenta by passive diffusion.

- **Metabolism**: Are metabolized primarily in the liver via conjugation with glucuronic acid.

- **Excretion**: Kidney is the main excretory organ for most local anesthetics and their metabolites.

Interactions with other Drugs:

- **EXPAREL**: Should not be admixed with lidocaine or other non-bupivacaine-based local anesthetics.

- **EXPAREL**: May be administered after at least 20 minutes or more have elapsed following local administration of lidocaine.

Side Effects

- Systemic absorption of local anesthetics produces effects on the cardiovascular and central nervous systems.

- Changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal.

- Local anesthetics can produce central nervous system stimulation, depression, or both.
EXPAREL

- FDA approved, opioid-free, bupivacaine-based, long-acting local anesthetic
- Bupivacaine used for nearly 50 years
- WHO essential medication
- EXPAREL used more than 3,000x per day via infiltration / field block for safe and effective, long-lasting analgesia
- EXPAREL can reduce postsurgical use of opioids
- Data support broad nerve block indication

DOSAGE & ADMINISTRATION

- intended for single-dose administration only.
- Recommended dose of EXPAREL based on the following factors:
  - Size of the surgical site
  - Volume required to cover the area
  - Individual patient factors that may impact the safety of an amide local anesthetic
  - Maximum dose of 200 mg (20 mL) As general guidance in selecting the proper dosing for the planned surgical

INJECTION GUIDELINES

- EXPAREL should be injected slowly into soft tissues of the surgical site with frequent aspiration to check for blood and minimize the risk of intravascular injection.
- EXPAREL is single-dose administration only.
- EXPAREL should be administered with a 25 gauge or larger bore needle.
- The maximum dosage of EXPAREL should not exceed 266 mg (20 mL, 1.3% of undiluted drug).
- EXPAREL can be administered undiluted or diluted to increase volume up to a final concentration of 0.89 mg/mL (i.e. 1:14 dilution by volume) with normal (0.9%) saline or lactated Ringer’s solution.
DOSAGE & ADMINISTRATION

- As general guidance in selecting the proper dosing for the planned surgical site:
  a) Example bunionectomy:
     A total of 8 mL (106 mg) was administered
     7 mL of EXPAREL infiltrated into the tissues
     surrounding the osteotomy, and
     1 mL infiltrated into the subcutaneous
  b) Example – hemorrhoidectomy:
     A total of 20 mL (266 mg = 13.3 mg/ml) of EXPAREL diluted with
     10 mL of saline, for a total of 30 mL (8.86 mg/ml), divided into six
     5 mL aliquots, injected by visualizing the anal sphincter as a
     clock face and slowly infiltrating one aliquot to each of the even
     numbers to produce a field block.

COMPATIBILITY CONSIDERATIONS

- The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more.
- When a topical antiseptic such as povidone iodine (e.g., Betadine®) is applied, the site should be allowed to dry before EXPAREL is administered into the surgical site.
- Bupivacaine HCl administered together with EXPAREL may impact the pharmacokinetic and/or physicochemical properties of EXPAREL, and this effect is concentration dependent.

Hernia Repair (inguinal)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine HCl 100 mg</td>
<td>5 min</td>
<td>0-1 hr</td>
<td>8 hrs</td>
</tr>
<tr>
<td>Exparel 266 mg</td>
<td>5 min</td>
<td>P1: 0-2 hrs, P2: 12-24 hrs</td>
<td>72 hrs</td>
</tr>
</tbody>
</table>
Application to the Practice Setting

- There were studies done on the effect of Exparel on patients. Exparel dose demonstrated a significant reduction in pain intensity compared to placebo for up to 24 hours.
- The findings from these studies would be helpful when applied in practice should help practitioner to properly administer and handle the medication.

Dosing:
(following regional blocks: IS or ankle block)

1) added 10 ml of saline to 20 ml vial (266 mg) Exparel (total of 30 ml = 8.86 mg/ml; 5-10 ml injected each layer from the incision line in a fan fashion)
2) 266 mg (20 ml) diluted with 10 ml; injected 15 ml total (half volume = 133 mg) to (20 ml = 177 mg)
3) all tissue injections done before closure.
Dosing: (for hemorrhoidectomy)

1) added 10 ml of saline to 20 ml vial (266 mg) Exparel (total of 30 ml (8.86 mg/ml)
2) divided into six 5 ml aliquots - produce a field block injected in a clockwise fashion by slowly infiltrating one aliquot to each of the even numbers (in the clock) to a total of 30 ml (266 mg)

CASE REPORTS: Pain Scale (IS Block + Exparel)

<table>
<thead>
<tr>
<th>PROCEDURE</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCR (L)</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>RCR (R)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1.5-2</td>
<td>2</td>
</tr>
<tr>
<td>RCR (R)</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>1.5</td>
<td>1.5-2</td>
<td>2</td>
</tr>
<tr>
<td>RCR (L)</td>
<td>0</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
<td>1-1.5</td>
<td>1.5-2.0</td>
</tr>
</tbody>
</table>

Post-Op Pain Progression
### CASE REPORTS:
**Opioids/NSAIDS Use**

<table>
<thead>
<tr>
<th>Case</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCR (R)</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>NSAID</td>
<td>NSAID</td>
</tr>
<tr>
<td>RCR (R)</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>NSAID</td>
<td>Opioid x1</td>
</tr>
<tr>
<td>RCR (R)</td>
<td>none</td>
<td>none</td>
<td>NSAID</td>
<td>NSAID</td>
<td>NSAID</td>
<td>NSAID</td>
</tr>
<tr>
<td>RCR (R)</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>Opioid x1/NSAID</td>
<td>NSAID</td>
<td>NSAID</td>
</tr>
</tbody>
</table>

### Summary
- **Decreases pain**
  - Single timepoint
  - Over time • Multiple surgical models
- **Simple to use:** Single intra-op administration
- **Easy to inject:** Fine gauge needle
- **Decreases opioids:** Amount used & Time to first use
- **Excellent safety**
  - No need for external device
  - No long-term impact

### Summary: con’t
- The benefits of Exparel extend well beyond effective pain control
- other recovery-related outcomes
  - opioid burden,
  - hospital stay
  - time to rehabilitation,
Collectively impact not only institutional costs, but also patient satisfaction (Pacira, 2015)
References


