Thoracic Epidurals (TEA) in Adult Surgical Patients: An Overview, Clinical Pearls & Lessons Learned 1 Year After Introducing Opioid Free TEA

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Conflict of Interest Disclosure

Authors Conflicts of Interest:

- Jason Sawyer. Has received financial compensation from Purdue Pharma for preparing & providing pain management lectures. Last lecture: Winter 2013

- 1212 beds - 677 acute care
- 16,000 operative procedures/year
- 1.2 million patient visits/year
- 10,000+ employees
- 5th largest cancer centre in North America
Acute Pain Service

- 2 Nurse Practitioners Monday-Friday
- Staff or Fellow Anesthesiologist 7 days – Tues-Tues
- 3300-3500 patients/year
- 400-500 surgical epidurals

Agenda

- Losing the battle with postoperative pain management?
- Overview of the advantages of TEA
- Overview of thoracic epidural analgesia (TEA)
  - Anatomy of the epidural space
  - Review of commonly used local anesthetics and opioids
- ASPMN Listserv Survey results (2014)
- Describe common TEA related side effects and their treatment
  - Hypotension, pruritus, nausea, vomiting, urinary retention
- Describe our experience with epinephrine as a substitution for opioid in thoracic epidurals

What Do We Know……

- Pain is still poorly managed postoperatively ([Sawyer et al. 2008, 2010])
- Higher in-hospital pain scores correlate with higher post-discharge pain scores ([Vandenkerkhof, 2006])
- Pain, depression and fatigue account for 1/3 of variation in older adults functional status 1 month after major abdominal surgery ([Zalon, 2004])
- Post-discharge health care utilization is greater in those with higher pain scores in-hospital and post-discharge ([Vandenkerkhof, 2006])
What Do We Know……

- Pain severity adversely effects quality of life in the immediate postop period (Wu, 2003)
- Post-op pain contributes to decreased HRQL 1 month post-discharge, & interfered with ADL’s and sleep (Strassels, 2004)
- Patients that experienced severe pain and utilized the most analgesics the first 7 days postop have ↑ risk of developing chronic post surgical pain (CPSP) (Visser 2006)
If you were given a strong pain killer like morphine after surgery, how worried would you be about becoming addicted?

1. Not worried at all
2. A little bit worried
3. More than a little bit worried
4. Very worried

Would you try to limit how much strong painkillers like morphine you use because you worried about becoming addicted?

1. Yes
2. No
"Oh, Just Give Them PCA".....

- Opioids are not benign
- Opioid Induced Hyperalgesia (OIH)
- Significant increase in addiction to legal opioid prescriptions
- 5-fold increase in prescription opioid related deaths in the US (CDC 2013)

Brief Summary

- Effective postoperative pain management remains an elusive goal
- Severe pain in the postoperative period is a key factor in developing CPSP
  - But not everyone with severe acute pain develops chronic pain
- Patients and families have strong beliefs regarding opioids
- What to do.....what to do.....
Postop matched pair cohorts epidural and PCA (88188 patients) across surgical populations.

Epidural associated with small reduction in 30 day mortality (1.7 vs 2.0; RR 0.89, CI 0.81-0.98, p = 0.02, NNT = 477).

Epidural patients generally had a higher co-morbidity burden.

"Furthermore, the increased burden of co-morbid illness in patients who received epidural anaesthesia would suggest that our study, if anything, is biased against epidural anaesthesia" pg 567.
The analgesic benefits of TEA are well described in the literature across many surgical populations.

Efforts to find reductions in morbidity and mortality are difficult because incidence rates of serious outcomes are very low.

More evidence required regarding TEA (and ultimately quality pain management):
- Quality of recovery
- Quality of life
- Chronic post surgical pain

Thoracic Epidurals - Some Lingo
- Cephalad/Rostral: towards the head (up)
- Caudal: towards the tail (down)
- Attenuate: dampen
- Lipophilic: fat friendly
- Hydrophilic: water friendly
Where It All Started

August Bier 1861-1949
surgeon

James Leonard Corning 1855-1923
neurologist

1885 Spinal cocaine
1898 Spinal Anesthetic
Assisted by August Hildebrandt

Epidural Anatomy

- Epidural space is a potential space, containing crevices around the epidural contents (fat, veins, lymphatics, nerve roots, dural sac)
- These layers and textures affect the flow of analgesics through the space
- Epidural venous flow is predominantly located anteriorly
- Veins lack valves

McLeod, 2004; Richardson, 2005; Bauer, 2012
Epidural Anatomy

- Ligamentum flavum is non-continuous and not pain sensitive
- Proximity to CSF/Spinal Cord is crucial
- Sympathetic fibres T1-L2

Factors Affecting the Distribution of Neural Blockade by Local Anesthetics in Epidural Anesthesia and a Comparison of Lumbar Versus Thoracic Epidural Anesthesia

Some Effect
- Age
  - 40% less dose for (60-79) vs (20-39)
  - Diminished fatty tissue
  - Decrease in myelinated nerves
  - Increased epidural space compliance
- 4-6 cm threaded into epidural space

Minimal/No Effect
- Height, weight BMI
- Positioning
- Gravity
- Needle direction

Some Effect
- Site of insertion determines distribution
- Total mass of LA more important than concentration or volume

Minimal/No Effect
- Fractional vs single bolus injection
- Epidural pressures
- Pressure in adjacent body cavities
What Analgesics?

- Local Anesthetics
- Opioids
- Epinephrine

Epidural Local Anesthetics

- Primary route of action is spinal nerve roots
  - Weak effect on spinal cord and paravertebral nerves
- Majority absorbed systemically via venous system (peak 10-30 mins)
  - Epidural fat
  - Diffusion across dura
- Lipid soluble
- Ester local anesthetics metabolized by plasma pseudocholinesterase (rarely used for epidural analgesia)
  - Amide local anesthetics metabolized in the liver
    - Most commonly used are bupivacaine and ropivacaine
• Smaller nerves more susceptible to effects of LA
  – Pain, temperature, touch, motor proprioception
• Myelinated fibres are more susceptible to effects of LA
  – Myelination speeds conduction in Nodes of Ranvier which contain high concentrations of Na+ channels
• Positive temperature or pin prick (qualitative) assessments do not necessarily equal analgesia- only let you know where the LA is spreading

**Epidural Opioid Site of Action**

**Substantia Gelatinosa of Spinal Cord**

- Primarily Spinal Effect
- Primarily Supraspinal
- Hydrophilic
- Lipophilic
- Morphine
- Hydromorphone (Dilaudid)
- Fentanyl

**Why THORACIC Epidural?**

- Virtually no Motor Block
  – Vs Lumbar Epidural
- Incision Congruent Placement
- Minimizes the surgical stress response
- Earlier return of bowel function
  – Sympathetic blockade
  – Increases GI blood flow & splanchnic perfusion aiding in return of motility
Earlier return of bowel function (Taqi, 2007; Carli, 2001)
  • Inhibition of splanchnic reflexes (Kehlet, 2001)
  • Inhibition of nociceptive afferents
  • Inhibition of sympathetic efferents
    – Compensatory activation of non anesthetized sympathetic segments (Waurick, 2005)
  • Vasodilation of veins and arteries in blocked area
  • Blockade of spinal reflex arcs
    – (Winterstein, 2001)

Questions Without An Answer

- Ideal mixture of solution (LA and/or opioid) still unknown
  • LA only - no opioid side effects but possibly more hypotension
  • Opioid only no better than systemic opioids and ↑ side effects
  • LA + opioid best?
  • Other adjuncts?

(Winterstein, 2001; Brown, 2004)
SIDE EFFECTS, BIG & SMALL

BIP
Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists

T. M. Cook, D. Connoll and J. A. W. Wildsmith on behalf of the Royal College of Anaesthetists Third National Audit Project

Results. The case review produced a denominator of 207 455 CNB. Eighty-four major complications were reported, of which 32 met the inclusion criteria at the time they were reported. These were: 7 patients died; 12 patients suffered permanent or temporary neurological damage; 15 patients suffered major organ injuries; 25 patients suffered serious non-neurological complications; and 15 patients suffered minor complications. The incidence of permanent injury due to CNB (measured per 100 000 cases) was 0.16 (95% confidence interval 0.11–0.23) and sporadically: 2D; (05–033). Permanent there was 13 dura or parapineal, sporadically five. The incidence of paraplegia or death was sporadically 1.6 per 100 000 (1.0–3.3) and sporadically 0.7 (0.1–1.0). Records of timely debating injuries resolved fully.

Conclusions. The data are reassuring and suggest that CNB has a low incidence of major complications, many of which resolve within 6 months.

Epidural anaesthesia and survival after intermediate-to-high risk non-cardiac surgery: a population-based cohort study

Sides of epidural anaesthesia and survival after intermediate-to-high risk non-cardiac surgery: a population-based cohort study

Table 1: Process of care and outcomes in the propensity-matched pairs

<table>
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<tr>
<th>Process of Care</th>
<th>Matched Pairs</th>
<th>Propensity Score Differences</th>
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<tbody>
<tr>
<td>Preoperative mechanical ventilation</td>
<td>1.03 (95% CI 1.00–1.06)</td>
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<tr>
<td>Postoperative mechanical ventilation</td>
<td>1.02 (95% CI 0.99–1.04)</td>
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<tr>
<td>30-day mortality</td>
<td>1.00 (95% CI 0.99–1.01)</td>
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<tr>
<td>Overall survival</td>
<td>0.99 (95% CI 0.98–1.00)</td>
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*Within 2 years before hospital admission for surgery. - Within 3 days after surgery.
Tolerability of acute postoperative pain management sunshine: Evidence from published data

<table>
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<tr>
<th>Presented as</th>
<th>Pruritus</th>
<th>N=21 461</th>
<th>Nausea</th>
<th>N= 20 606</th>
<th>Vomiting</th>
<th>N=11 423</th>
<th>Urinary Retention</th>
<th>N=12 513</th>
<th>Mild Sedation</th>
<th>N= 9451</th>
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<tbody>
<tr>
<td>All</td>
<td>14.7</td>
<td>25.2</td>
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<td>23</td>
<td>23.9</td>
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<tr>
<td>IV-PCA</td>
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<td>1.2</td>
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<td>1.3</td>
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<tr>
<td>Epidural</td>
<td>16.1</td>
<td>18.9</td>
<td>16.2</td>
<td>20.1</td>
<td>14.3</td>
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<td>14.3</td>
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<td>20.1</td>
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Respiratory and hemodynamic effect of acute postoperative pain management sunshine: Evidence from published data

<table>
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<th>Hemodynamic depression</th>
<th>Respiratory depression by decreased O2 sats</th>
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<td>0.3</td>
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<tr>
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<td>0.1</td>
<td>5.5</td>
<td>1.1</td>
<td>15</td>
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</table>

Do you routinely use etCO2 or continuous pulse oximetry for your patients with thoracic epidurals that contain opioids? n=73

44 Yes

45 No

Review Article
Neuraxial opioid-induced pruritus: An update

• Mechanism of Opioid Induced Pruritus (OIP) is poorly understood
  • Mu opioid receptors seem to play a key role
    – Spinal cord not brain or periphery
  • Histamine release has very little role
    – So antihistamines will most likely not help!
• The more invasive the opioid administration, the higher the incidence of OIP

45
What intervention do you use FIRST for pruritus you suspect is from opioid in the thoracic epidural?

- Administer Diphenhydramine
- Administer Nalbuphine
- Administer Naltrexone
- Administer Naloxone infusion
- Administer Ondansetron
- Reduce/change the opioid in the epidural
- Remove the opioid from the epidural
Urinary Retention

Is Urinary Drainage Necessary During Continuous Epidural Analgesia After Colonic Resection?

Linda Baue, M.D., Mads Werner, M.D., Ph.D., and Henrik Kehlet, M.D., Ph.D.
Side Effects With TEA

- Incidence of nausea, vomiting and naloxone use lower in epidural groups vs IV-PCA
- No single agent will be universally effective for PONV- evidence that algorithms are beneficial in appropriately screened patients (Krancke 2007)
- Most side effects are related to the opioids

Side Effects With TEA

- Incidence of pruritus much higher, but is not histamine mediated. Limited evidence for Ondansetron (Zofran) and opioid reversal agents
- Incidence of urinary retention with TEA is approximately 10% and early removal demonstrates a decrease in UTI
- With the incidence of respiratory depression approximately 0.1%...... Why all the Pulse Oximetry/EtCO2 monitoring, and taking up ICU beds for epidural patients?

Historical TEA delivery at Sunnybrook

- Choice of a single ropivacaine (Naropin) concentration (0.2%) with options for hydromorphone (Dilaudid) 5 or 10 mcg/ml
- No PCEA component
- Trouble shooting involved large doses of lidocaine (Xylocaine)
- High infusion rates not uncommon (15-20ml/hr)
• Perceived excessive failure rate
• Not uncommon to add IV-PCA opioid to epidural
• Suboptimal outcomes for chronic pain/chronic opioid users that receive epidurals
• Despite safely aggressive multimodal analgesia with NSAIDS/Gabapentinoids/Acetaminophen

Lessons Learned Adding Epinephrine

• Quickly
  – Adding epinephrine (Adrenaline) to Ropivacaine (Naropin)/HYDROMorphone (Dilaudid) combination frequently caused pruritus when none existed before (particularly with 10 mcg/ml HYDROMorphone) in the same patient
  – Ropivacaine (Naropin) 0.2% with Epinephrine (Adrenaline) 5mcg/ml did not seem to work consistently as well as we would have liked
History of Epinephrine Use

• Used as an adjunct for saddle block anesthesia in 1950 (Priddle & Andros)
• "The intrathecal use of vasoconstrictors in conjunction with the various local anesthetic agents as a means of increasing the effectiveness of spinal anesthesia dates back some 45 years" (Priddle & Andros 1950 pp 156)
• Small study (3 groups 6 patients total) obstetrical patients
• 3rd group
  - 1mg of epinephrine (1cc of 1:1000 epinephrine with 1cc of 5% dextrose into CSF
  - "complete relief of pain of uterine contraction"
  - No systemic effects noted

How Neuraxial Epinephrine Works

• α2-adreno receptor agonist

• Independently causes segmental hypoalgesia when given epidurally to pinprick (100 mcg) (Curatolo et al 1997) & pinprick/ice (50mcg) (Bromage et al 1983)
• Direct spinal application of epinephrine elevated the nociceptive threshold in an animal model (Reddy et al 1980)
• Absorbed into the CSF and binds to α2 adrenoreceptors in substantia gelatinosa of the dorsal horn (Curatolo et al 1997)
• Epidural Epinephrine (100mcg) reduced peak plasma concentrations of 20ml of 0.5% bupivacaine or 2% lidocaine by 25% in 40 patients undergoing minor general/ortho procedures (Burm et al 1986)
• No delayed peak onset time when added to lidocaine and bupivacaine
• Longer duration of block
• Epidural Epinephrine (100 mcg) decreased peak plasma morphine levels (10mg epidural) by 60% in a study of 3 healthy volunteers (Bromage et al. 1983).
• Profound exacerbation of side effects including resp. depression 6-16 hours post morphine.
• Rostral spread significantly greater at 2-6 hours.
• Similar attenuation of cold pressor test ONLY until 16-22 hrs.

• Niemi et al 2001/2002/2003
  • All 3 randomized double blind crossover studies
    – Effect of fentanyl added to bupivacaine/adrenaline
    – Effect of adrenaline added to ropivacaine/fentanyl
    – 3 concentrations of adrenaline added to fentanyl and bupivacaine
      • 2mcg/ml more effective than 1 or 1.5mcg/ml (Niemi & Brevik 2003).

Adding Fentanyl (20 pts) 2001
• Bupiv 0.1% fent & epi 2mcg/ml
• Without fentanyl pain with coughing significantly worse after 3 hours
• Pain decreased within 15 mins and no difference within 1 hr of reintroducing fentanyl
• No change in sensory blockade during non fentanyl times
• No difference in any side effects with or without fentanyl
• No difference in time out of bed

Adding Epinephrine 12 pts 2002
• Ropiv 0.1% & fent/epi 2mcg/ml
• Without Epi pain with coughing significantly worse within 2 hrs
• Pain decreased within 15 mins and no difference within 1 hr of reintroducing epi
• Significant regression of sensory blockade with removal of epinephrine
• Nausea increases significantly when epinephrine removed
• Significantly more mobilization with epinephrine
What Does This Mean Clinically?

- Epinephrine given epidurally:
  - Has its own antinociceptive properties
  - Likely increases the amount of opioid and LA reaching the spinal cord & nerve roots
  - More intense and prolonged analgesic effect
  - Wider sensory coverage
  - Reduced concentrations of each class of analgesia are required
  - (Niemi et al 2002)
  - Reduces systemic absorption of opioids and LA by 25-60%

ASPMN Listserv Survey Results

- Local anesthetics
  - 2/3 bupivacaine (most common 0.1%)
  - 1/3 ropivacaine (most common 0.1-0.2%)
  - Epinephrine (2) Clonidine (1)
- Opioids
  - 55% fentanyl (1-5mcg/ml)
  - 40% Hydromorphone (4-20mcg/ml)
- Vast majority LA/opioid combination
- Very few had multiple options

TEA Management At Sunnybrook October 2014-Present

- Transition to opioid free epidural analgesia regimen
- Continuous infusion + PCA component
- Epinephrine (Adrenaline) 5mcg/ml and Ropivacaine (Naropin) 0.3% standard solution
- Additional solutions available for individualizing TEA
How long, on average, do you keep your thoracic epidurals infusing? (N=74)

- 10.0%
- 20.0%
- 30.0%
- 40.0%
- 50.0%
- 60.0%
- 70.0%

Management of side effects (continue until IV access is discontinued)

- For nausea and vomiting: Follow AWP algorithm for nausea and vomiting (see back of page 2)
  - Dexamethasone 4 mg IV push 8h pm. Dilute in 50 mL of NS or D5W and infuse over 15 minutes.
  - Hydromorphone 0.5 mg - 1 mg every 6h pm
  - Onset of 40 years older or 0.5 mg every 6h pm. See back of page 2
- For pruritus: Naloxone 4 mg IV push 8h pm (do not give a dose if already given for nausea or vomiting in the last 4 hours). Dilute in 50 mL of NS or D5W and infuse over 15 minutes.
  - This order applies to patients receiving opioids. See back of page 2

If you have more than 1 epidural solution to choose from, how do you decide which one to use on your patients? (N=64)

- Anesthesiology preference
- Acute Pain Service preference
- Customized based on patient factors

How long, on average, do you keep your thoracic epidurals infusing? (N=74)
• Ropivacaine plasma concentrations peak in about 67 hrs (of 120 hrs) [2000 Wiedemann]

• Painful Procedure (this is a single procedure!)
  – Small bowel resection, closure of loop ileostomy, abdominal wall hernia repair with components separation, placement of biological mesh (10x25cm), intraperitoneal underlay implant, excision of large skin flaps

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[Graph showing # of Patients With TEA Containing Epinephrine (5mcg/ml)]
# Of Patients Using Each Ropivacaine Concentration

- Pre Opioid Free Epidurals
- Post Opioid Free Epidurals

Trouble Shooting (especially at night!)

Uncontrolled Pain ± Sensory Block
- Bolus epidural with more potent Ropivacaine (Naropin) as opposed to Lidocaine
  - 1% Ropivacaine vials
  - Cassettes with 0.125%/0.2%/0.3% available on high volume unit
  - If satisfactory relief with more potent bolus - start infusion with same

Appropriate Analgesia & Dense Motor Block
- If shutting off until motor block resolution and restarting at a lower rate does not work
- Lower concentration of Ropivacaine

Table I. Maximum doses of local anaesthetics in adults:

<table>
<thead>
<tr>
<th>Local Anesthetic</th>
<th>Pain</th>
<th>Adrenaline</th>
</tr>
</thead>
<tbody>
<tr>
<td>1% Ropivacaine</td>
<td>800 mg (1 ml/kg)</td>
<td>100 mg (14 µg/kg)</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>300 mg (4-6 mg/kg)</td>
<td>500 mg (7 mg/kg)</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>500 mg (7 mg/kg)</td>
<td>600 mg (8.5 mg/kg)</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>300 mg (4-5 mg/kg)</td>
<td>500 mg (7 mg/kg)</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>175 mg (2.5 mg/kg)</td>
<td>220 mg (3 mg/kg)</td>
</tr>
</tbody>
</table>

Reproduced from Miller K. (Anaesthesia, 5th edn. 2000, Churchill Livingstone, Philadelphia, USA)
What do you do FIRST when a patient has an appropriate bilateral sensory block in the surgical area, but still has moderate/severe pain with coughing?

(Epidural solution is Ropivacaine 0.2% + HYDROMorphone 0.010mg/ml, rate 6ml/hr, PCEA 3ml, lockout 15 minutes) Incision is midline. Sensory block is T4-12 bilateral, covering the entire incision. N=57

- Bolus the epidural with more of the same epidural solution infusing through the epidural pump and increase the rate?
- Bolus the epidural catheter with a more potent, different, local anesthetic (e.g. lidocaine), then resume with the same epidural solution.
- Bolus the epidural catheter to comfort with a more potent dose of ropivacaine, then resume the infusion at the more potent dose of ropivacaine.
- Continue the current epidural solution and add IV-PCA/other route of opioid.
- Another route of opioid.
Bedside Patient Education

- There is not a needle in your back
- Sedation/nausea/vomiting/pruritus NOT from your pain medication
- Leave TEA > 3 days to minimize exposure to opioids

- Outline daily the process of epidural removal.
  - What to expect
  - How soon to go home
  - Considering handing out little “key messages”

Clinical Benefits

- No more
  - Pruritus
  - Opioid contribution to ileus
- Reduced systemic absorption when using more potent LA concentrations
- No increased motor block observed to date with increased LA concentration
- Reduction in replacement epidurals
- Reduction in epidural failure rate
- Approximately 15-20% of our major abdominal surgery patients have no exposure to an opioid during their hospitalization

Final Summary

- Epidurals continue to be the main stay for analgesia for many post surgical populations
- It seems they are underutilized in many populations
- We still have not identified the ideal medications/combinations
- Room to improve individuality of epidural analgesia
- Need to dedicate key people to deliver this service and provide continuity of care
- Research should focus on quality of life/recovery, and effect on chronic pain/opioid use
Thank You

“We cannot do everything at once, but we can do something at once”
(Calvin Coolidge)

“Playing small does not serve the world”
(Marianne Williamson)

References


Photo References

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