1. Acute Postoperative Pain: Context, Outcomes and Clinical Interventions

ACUTE POSTOPERATIVE PAIN: Context, Outcomes and Clinical Interventions

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2007

2. 21st century medical decision making

21st century medical decision making

- Scientific evidence
- Expert opinion
- Experience

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3. 15th century medical decision making

15th century medical decision making

Religious Taboo
Superstition
Folklore
Tradition
Experience
Expert opinion

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4. Quote

Quote

“Evidence based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”

David Sackett, 1991

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5. Acute Postoperative Pain: Context, Outcomes and Clinical Interventions

HK Beecher

The powerful placebo

JAMA
1955;159:1602-6

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6. Articles

Articles

Beecher HK, Todd DP
A study of deaths associated with anesthesia and surgery

Ann Surg 1954;149:2-34
First outcomes study in anesthesia

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7. Randomized controlled trials – 20th century

Randomized controlled trials – 20th century

- 1926 Concept of random allocation used in agriculture – observed difference in yield between fields due to seed or fertilizer being tested
- 1931 First clinical trial that used a form of random assignment - a flip of a coin - to assign patients with tuberculosis to receive sanocrysin (gold compound) versus distilled water
- 1948 Austin Bradford Hill and the British Medical Research Council conducted multicenter trial of streptomycin in patients with tuberculosis. They used random allocation, matching of patients and blinding. Credited with new era of clinical research.

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8. Bandolier

Bandolier

“Evidence based thinking about health care”

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Clinical Practice Guideline: Acute Pain Management

10. Advances in acute pain management

Advances in acute pain management

- Epidurals
- PCA
- Adjuncts
- Preemptive analgesia

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11. Advances in acute pain management, cont.

**Advances in acute pain management, cont.**

- Do they provide better analgesia?
- Do they improve outcome?

12. Effectiveness of acute postoperative pain management

**Effectiveness of acute postoperative pain management**

13. Effectiveness of acute postoperative pain management, cont.

**Effectiveness of acute postoperative pain management, cont.**

- 17-21% reported poor to fair pain relief despite the use of new techniques and “best efforts”
- Goal of reducing unsatisfactory pain control to <5% is probably unrealistic
- Difference between standard (IM) and new techniques (PCA and epidural is smaller than expected)
- Overall mean incidence of premature catheter dislodgement was 5.7% (CI 4-7.4)

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14. Pain relief with different techniques

**Pain relief with different techniques**

![Chart showing pain relief with different techniques](image)

Poor pain relief report by 2-5% pts, poor or fair pain relief by 17-21% pts


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15. Moderate to severe pain at rest

IM 66% (CI 58-76), PCA 36% (CI 31-40), Epidural 21% (CI 18-24)


16. Moderate to severe pain on movement

IM 78% (inadequate data for CT), PCA 25% (CI 8.4-42), Epidural 38% (CI 30-45)

17. **Severe pain**

Severe pain

![](image)

**IM 29% (CI 19-39), PCA 10% (CI 12-21), Epidural 8% (CI 15-23)**


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18. **Epidurals**

Epidurals

![](image)

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19. Local Anesthetics and Opioids

Local Anesthetics and Opioids

Local anesthetics  →  Differential blockade

Opioids  →  Selective spinal analgesia

20. Acute Postoperative Pain: Context, Outcomes and Clinical Interventions

Intra-op and Post-op

Intra-op  →  Epidural anesthesia
            +/−
            Selective spinal analgesia

Post-op  →  Epidural analgesia
          (C fiber + B fiber)
          +
          Selective spinal analgesia
21. Intra-op Post-op

<table>
<thead>
<tr>
<th>Intra-op</th>
<th>Post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓thrombosis relief</td>
<td>superior pain</td>
</tr>
<tr>
<td>↑vascular graft survival</td>
<td>opioid sparing</td>
</tr>
<tr>
<td>↓blood loss mobility</td>
<td>↑bowel</td>
</tr>
<tr>
<td>↓cardiac work</td>
<td></td>
</tr>
</tbody>
</table>

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22. Minor morbidity and catastrophic outcome

Minor morbidity
- Ileus
- Failure to cough, atelectasis, prolonged intubation
- Graft failure
- Excessive blood loss
- Mental status change
- Delayed mobilization
- Prolonged hospital stay

Catastrophic outcome: Death or Life-threatening morbidity
- Thromboembolism
- Infarction
- Cardiac failure
- Pneumonia

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23. 2005

**2005**

Ballantyne et al

Does the evidence support the use of spinal and epidural anesthesia for surgery?

*J Clin Anesth* 2005:

*Systematic review*

Studies support good analgesic efficacy, reduced thromboembolism, reduced blood loss and favorable effects on bowel mobility

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24. 2001

**2001**

Beattie WS et al

Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis

*Anesthesia & Analgesia* 2001; 93:853-8

*Targeted meta-analysis*

Reduced incidence of myocardial infarction

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25. 1998

1998

Ballantyne et al

The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials
*Anesthesia & Analgesia* 1998;86:598-612

Targeted meta-analysis

Improved pulmonary outcome

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26. Do epidurals reduce catastrophic outcome?

Do epidurals reduce catastrophic outcome?

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1987

Yeager MP et al

Epidural anesthesia and analgesia in high-risk surgical patients
*Anesthesiology* 1986;66:729-36

*Trial – 55 high risk patients*

Significant improvement in morbidity and mortality

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2000

Rodgers A et al

Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials
*British Medical Journal* 2000;321:1493-7

*Comprehensive meta-analysis*

30% reduction in mortality. Significant reduction in morbidity

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2002

Rigg JRA et al

Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial
Lancet 2002;359:1276-82

Multi-center large trial – 915 patients

Only difference, respiratory failure
31. Accelerated recovery programs

Accelerated recovery programs

- Cough/incentive spirometry
- Early feeding
- Early mobilization
- Early discharge

↓ infection
↓ pneumonia
↓ thrombosis

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32. Changes in anesthetic and surgical practice

Changes in anesthetic and surgical practice

Short-acting drugs:
- LMA
- New standards of monitoring & vigilance
- Better optimization of preoperative medical status
- Less invasive surgical techniques
- Accelerated recovery protocols
- Modern thromboprophylaxis

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33. Conclusion

**Conclusion**

Epidurals play an important role in present-day practice because:

1) Their superior analgesic efficacy for selected procedures is indisputable and has become a standard of care in the U.S.

2) Other effects, particularly local anesthetic effects on the bowel, contribute to improvements in surgical morbidity and mortality brought about by accelerative recovery programs.

3) However, benefits demonstrated by older trials, largely attributable to reductions in thromboembolism, have likely been superseded by modern surgical protocols, especially thromboprophylaxis.

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34. PCA

**PCA**

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35. PCA Meta-analysis

PCA Meta-analysis


15 trials, 787 patients


32 trials, 2,072 patients

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36. Results of Meta-analysis

Results of Meta-analysis

- Analgesic efficacy slightly better
- Patient preference confirmed
- No difference in opioid usage, side effects or length of hospital stay
- Cost saving versus cost burden still uncertain

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![Graph showing Days of hospital stay with Patient Controlled Analgesia vs. Days of hospital stay with control.](image1)


38. Acute Postoperative Pain: Context, Outcomes and Clinical Interventions

![Graph showing Percent with at least satisfactory analgesia with Patient-Controlled Analgesia vs. Percent with at least satisfactory analgesia with conventional treatment.](image2)

New technologies

- **Iontophoretic patches**
  electric current causes charged particles to move across the skin into the capillaries below

- **Poration technologies**
  high-frequency pulses of energy temporarily disrupt stratum corneum; current facilitates drug movement but does not transport the drug; 2-stage process

- **Laser light, heat and sound**
  also used to disrupt the stratum corneum for easier drug transport across the skin

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Patient-controlled transdermal fentanyl &\#8211; the evidence...

Patient-controlled transdermal fentanyl – the evidence

Viscusi et al  Patient-controlled transdermal fentanyl hydrochloride versus intravenous morphine pump for postoperative pain. A randomized controlled trial  *JAMA 2004;291:1333-1341*

Ashburn et al  Ionophoretic delivery of morphine for postoperative analgesia  *J Pain Sympt Manage 1992;7:27-33*
41. Transdermal fentanyl

Transdermal fentanyl

- Pharmacokinetics similar to IV – for fentanyl, peak effect at 10 mins
- Comparative cost remains uncertain, but appears favorable
- Obvious advantage for patients without IVs and home use

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42. Transdermal fentanyl

Transdermal fentanyl

**FIGURE 1**

How the Vyteris Iontophoretic Patch Works

- Drug ions are delivered from the reservoir of similar polarity
- Drug flux increases with applied current
- Drug ions compete for current with extraneous ions


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43. Patient-controlled, transdermal pain management system

**Patient-controlled, transdermal pain management system**

IONSYS™ currently being marketed by OrthoMcNeil for release shortly in the U.S.

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44. Active Transdermal Patch

**Active Transdermal Patch**

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45. Adjuncts

46. Opioid-sparing: putative advantages

Better analgesia:
- Less nausea & vomiting
- Less sedation
- Fewer sleep disturbances
- Less urinary retention
- Less respiratory depression
-Earlier return of bowel mobility
47. Opioid sparing: choice of agents

**Opioid sparing: choice of agents**

**NSAIDs**

- COX-2 inhibitors
- Acetaminophen
- Ketamine
- Gabapentin and pregabalin
- Regional anesthesia/analgesia

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48. NSAIDs and COX-2 inhibitors

**NSAIDs and COX-2 inhibitors**


- 30% reduction in N&V
- 29% reduction in sedation
- Effects on urinary retention and respiratory complications uncertain

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49. Acetaminophen

**Acetaminophen**


- 20% morphine sparing
- No difference in morphine related adverse effects or patient satisfaction

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50. Ketamine

**Ketamine**


- 53 trials, 2839 patients
- Maximum pain intensity difference (0-10 scale), -0.89
- Morphine use—15.7 mg
- No difference in morphine-related side effects
- Low incidence of hallucinations except when used without general anesthesia or benzodiazepines

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51. Gabapentin and pregabalin

**Gabapentin and pregabalin**


- Opioid sparing with typical doses of 1200 mg, single dose pre-op
- Dizziness and sedation in 2/8 studies
- No demonstrated reduction in opioid-related side effects

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52. Preemptive Analgesia

**Preemptive Analgesia**

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53. Definition

Any anti-nociceptive therapy that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain

Kissin 2000

54. Evolution of pre-emptive analgesia concepts

Evolution of pre-emptive analgesia concepts

1980s Experimental evidence in animals suggests a central as well as peripheral component to post-injury pain hypersensitivity (Woolf, Nature 1983)

1980s-1990s Pre-emptive analgesia (neural blockade and opioids) shown to be effective in animal models of experimental pain

1990s Mechanism linked to NMDA receptor (Woolf, 91, Mao 92)
55. **Importance**

- Potential reduction in postoperative pain
- Potential reduction in long-term (chronic) pain
- Chronic pain and dysfunction after surgery under-recognized

(Post-herniorrhaphy, Bay-Nielsen 01, post-thoracotomy, Pertunen 99, Ochroch 92, post-prostatectomy, Haythornthwaite 98)

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56. **Putative mechanism**

Attenuation or prevention of changes in the dorsal horn that result in central sensitization

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Central sensitization

Dependent on NMDA activation

- A short-term (wind-up) and long-term potentiation of pain signals
- Associated with the induction of specific genes (C-fos)
- Specific features:
  - Increased neurotransmitter release
  - Expansion of receptive field size
  - Increase in magnitude and duration of responses
  - Changes in response thresholds
  - New nerve growth

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NMDA receptor role in hyperalgesia

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59. Dorsal horn afferent transmitter organization

Dorsal horn afferent transmitter organization

1) C fibers release peptides and EAAs
to evoke excitation in 2nd order neurons (AMPA)

2) Stimulation from multiple interneurons
evokes excitation in WDR neurons (NMDA mediated)

3) Wind-up and central sensitization are secondary effects

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60. Clinical effects of central sensitization

Clinical effects of central sensitization

- Hyperalgesia
- Allodynia
- Pain summation
- Radiation of pain beyond the dermatomal distribution

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61. Preemptive analgesia aims to prevent these changes by:

Preemptive analgesia aims to prevent these changes by:

- Blocking transmission to the spinal cord (local anesthetics)
- Preventing “wind-up” (NMDA antagonists)
- Modifying pain processes within the spinal cord and brain (opioids)?

62. Why it doesn’t always work

Why it doesn’t always work

Can high dose opioids work?

1) Inadequate afferent blockade
2) Timing
3) Central sensitization already present
4) Study flaws
Adequacy of afferent blockade

- Adequate neural blockade with LA
- Anatomic location of surgery
- Severity of surgery

Timing

- Pre- versus post-incision important?
- Secondary phase of injury needs to be taken into account

Moiniche, Anesthesiology 02
Does it work - the evidence

- Multiple studies in surgical patients have mixed results
- Dense neural blockade appears to be the most effective intervention
- Role of high dose opioids is now in question
- NMDA antagonism theoretically attractive, but no clinically useful NMDA antagonist yet identified

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The evidence, cont.

Moiniche et al. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief Anesthesiol 2002;96:725-41

- No benefit demonstrated through the preemptive administration of epidural analgesia, systemic opioids, NSAIDs, NMDA antagonists or local infiltration

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The evidence, cont.


- PRE- versus POST model only (66/102 v. Moiniche’s 80/93 studies)
- Pronounced preemptive effect with epidural analgesia, local infiltration and systemic NSAIDs
- 44-58% reductions in supplemental analgesic consumption
- Results with opioids and NMDAR antagonists were equivocal (question of pain increases with opioids)

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The evidence, cont.


- PRE- versus NO model
- Examined decreases in pain intensity or analgesic use beyond 5 half-lives
- Extended analgesic benefits in 58% studies with ketamine and 67% with dextromethorphan

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69. Summary

Summary

- The use of epidurals for some indications is supported because they provide superior analgesia and reduce delays in recovery (bowel and pulmonary effects). Future assessments should include risk assessment.
- PCA is supported because patients prefer it.
- Opioid sparing using adjuncts is supported in terms of reducing common side effects (N&V, sedation).
- There is early support for preemptive analgesia, particularly using neural blockade.

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