New Trends in Pain Pharmacotherapy

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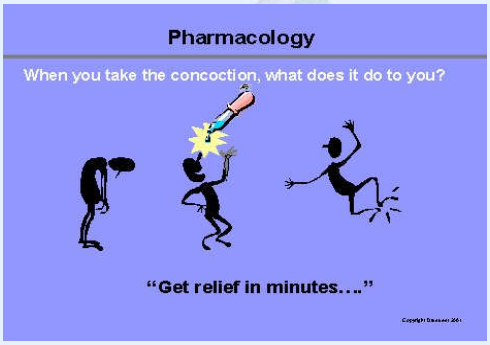
What do we want for pain medications?

- Efficacy → High
- Side effect → No
- Safety → Good
- Patient's satisfaction → Excellent



Safety >= Efficacy > Satisfaction > Side effect

Or

Efficacy >= Safety > Satisfaction > Side effects

Or

Satisfaction > Efficacy > Safety > Side effects

Or

Side effects > Efficacy > Safety > Satisfaction

Or

……..

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An audit of postoperative intravenous patient-controlled analgesia with morphine: Evolution over the last decade

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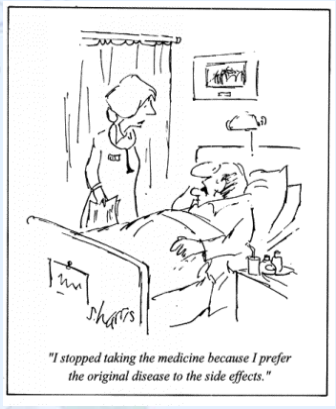
ABSTRACT

The development and refinement of an acute pain service based on the increased availability of clinical evidence would be expected to improve the quality of postoperative pain control. This report reviews the application of postoperative patient-controlled analgesia (PCA) using intravenous morphine in a single institution between 2002 and 2005. More than 5000 patients were evaluated and the results were compared with a similar study performed 10 years ago. Prescription of PCA had increased by more than three-fold. Morphine consumption from post-operative day 1 to day 3 (19.1 vs. 26.1, 8.6 vs. 18.1 and 4.5 vs. 19.0 μg/kg/h, respectively), demand-to-delivery ratio (1.35–1.76 vs. 2.4–2.8) and the incidence of respiratory depression (0.063% vs. 2%) were significantly reduced ($p < 0.001$), but there was no improvement in pain relief. A substantial proportion of patients still experienced postoperative nausea (47%) and vomiting (18.5%) despite a reduction in morphine consumption. Most patients ranked PCA as good and only 0.3% were dissatisfied. We conclude that, in our institution over the last decade, PCA has become more popular for postoperative pain management but with no attendant improvement in pain relief or reduction in side effects. Using PCA alone may result in poorer quality postoperative analgesia. Our findings add to the growing body of evidence that postoperative pain management has not substantially improved despite increased adoption of acute pain services.

- Safety improved
- Opioid consumption much reduced
- Side effect deteriorated
- No improvement in pain relief

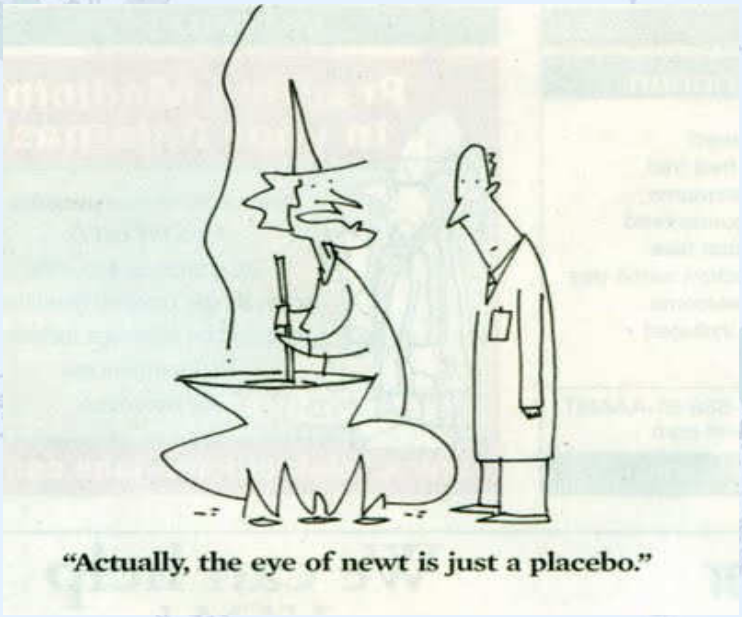


Safety is the first consideration.

Reduced opioid consumption without improvement in pain relief?

Good safety + No side effect

Placebo May Do!



Beliefs

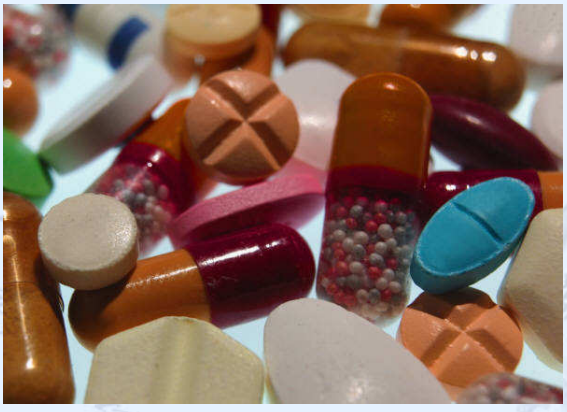
Pre-emptive and Preventive Analgesia

From Pre-emptive to Preventive Analgesia

Ester M, Pogatzki-Zahn and Peter K Zahn.
Current Opinion in Anaesthesiology 2006, 19:551-555

- Timing of analgesic treatment → not important
- Duration and efficacy of analgesic intervention → important
- Preventive analgesia with multimodal analgesia → more important

Multimodal Analgesia



Multimodal Analgesia for Controlling Acute Postoperative Pain

Askkumar Buvanendra and Jeffrey S Kroin.
Current Opinion in Anaesthesiology 2009, 22;588-593

- Conclusions on multimodal analgesia shows variable degree of success even using the same adjuvant medication.
- Advantages:
  - Reduce consumption of opioid and related side effects
  - Enhance recovery
  - Good for ambulatory surgery

Conclusion

Continuing Need to Explore New Drug Combinations to Achieve the Goals of Multimodal Analgesia.

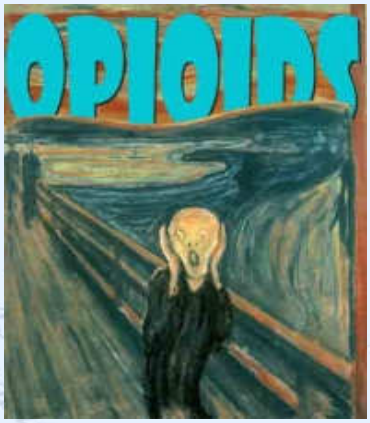
PROSPECT: a practical method for formulating evidence-based expert recommendations for the management of postoperative pain

E.A.M. Neugebauer, R.C. Wilkinsonm, H. Kehlet, S.A. Schug (PROSPECT Working Group).
Surf Endosc (2007) 21: 1047-1053

- The Procedure-specific Postoperative Pain Management (PROSPECT) Working Group
- Recommendations for postoperative pain management
- Supporting evidence from systematic literature reviews and related procedures
- Different combinations for different surgeries

Old Drugs

Chronic Opioids Therapy (COT) on Chronic Non Cancer Pain Patients (CNCP)



Concerns of using COT

- ✓Labeling effect;
- ✓Cultural belief;
- ✓Efficacy of opioids;
- ✓Side effect of opioids;
- ✓Addiction and tolerance;
- ✓Diversion of prescribed opioids;
- ✓**Legal issues (inappropriate prescription of opioids or inadequate pain control)**

- COT is more common in western countries than in Hong Kong.
- COT can be useful for a selected group of CNCP patients.
- Guidelines are present at different regions.
- Opioid consent/ contrast

Future Direction in Hong Kong??

Cannabinoids

- Act via neuronal pre-synaptic CB_1R to ↓ neurotransmitter release
  - Potent analgesics in animal models
  - May mediate a physiological anti-nociceptive 'tone'
  - Microglial activation and peripheral inflammation may be down-regulated
  - Synergism with opioid analgesics

- Psychoactivity may be avoided by using combinations of CB_2R agonists and peripheral CB_1R agonists which do not cross the blood-brain barrier
- Many clinical trials have provided negative or equivocal results
- Strongest evidence of benefit is for central neuropathic pain in MS

Ketamine

- Inexpensive
- Invaluable in developing/ developed world
- Phencyclidine derivative described in 1965
- NMDA antagonist
- Inhibits hyperalgesia and allodynia

- Racemic mixture: S(+) and R(-)
- S (+):
  - 4 times more affinity for the NMDA receptors
  - Binds to mu and kappa opioid receptors
  - Higher potency, fewer side effects and shorter recovery time

Perioperative Ketamine for Acute Postoperative Pain (Review)

Bell RF, Dahl JB, Moore RA, Kalso E.
Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004603. Review.

- Sub-anaesthetic dose of ketamine for acute postoperative pain:
  - Reduce rescue analgesic requirement
  - Reduce pain intensity
  - Reduce 24 hour PCA morphine consumption
  - Reduce postoperative nausea and vomiting
- Longer infusion and optimal dose?
- Anti-inflammatory effect

Ketamine for Chronic Non-cancer Pain

Rae Frances Bell. Pain 2009; 141:210-214

- Sub-anaesthetic ketamine can improve short term relief to refractory neuropathic pain in some patients
- No evidence to support for long term use in chronic pain patients
- Long term safety issues
- Use only after careful evaulation of risk/ benefit of individual patient

- Rapid acting routes should be avoided
- Future Clinical Trials:
  - Long term treatment
  - Benefit of oral route
  - Low dose ketamine as adjuvant
  - Optimal dose, route of administration and duration of treatment

Drugs in New Routes

Patient Controlled Analgesia

- Patient controlled analgesia
  - Effective for cancer pain control
  - Portable pump available
  - Good for incident pain, breakthrough pain, pain related to movement

- New technique of patient controlled transdermal analgesic administration:

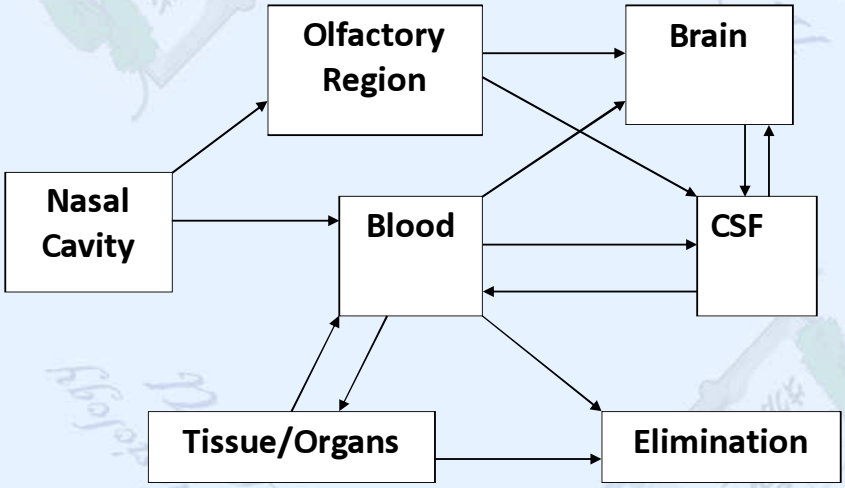
Inotophoresis

- Withdrawn from market recently

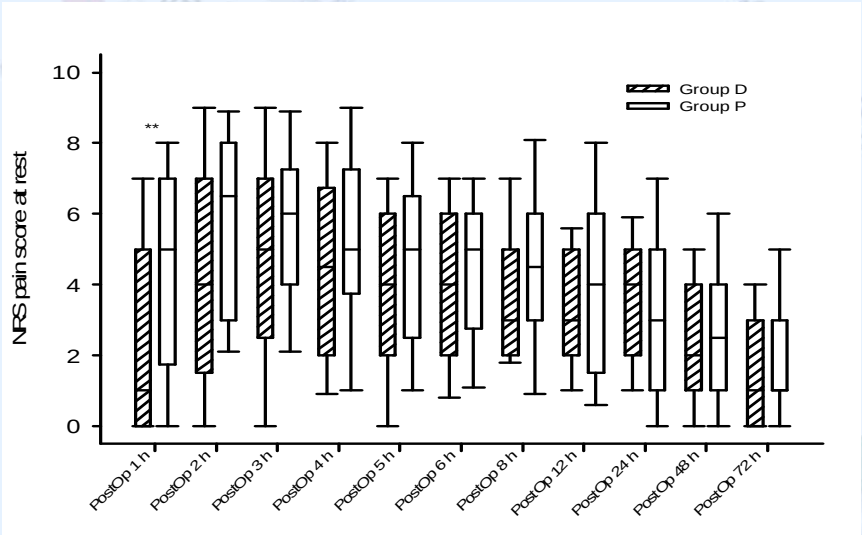
Dexmedetomidine

- Use primarily in hypertension
- Recently used in anaesthesia and pain management
- Alpha 2: alpha 1 receptor ratio: 1600:1
- Sedative effect and analgesic effect from action on locus ceruleus
- Pain relief not conclusive
- Opioid sparing effect

Intranasal Dexmedetomidine



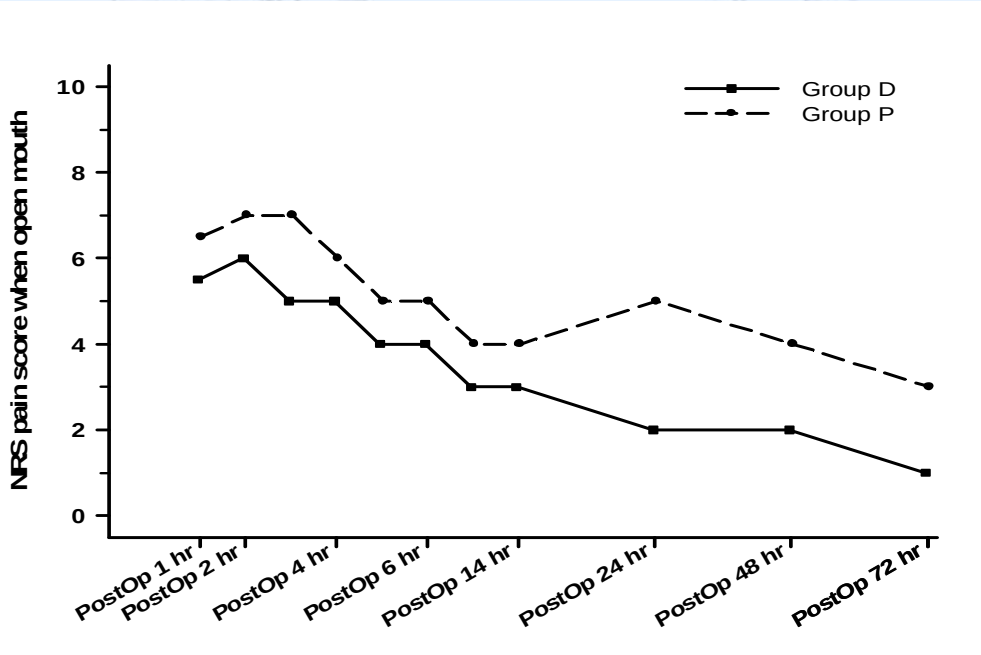
Analgesic effect of Intranasal Dexmedetomidine in Third Molar Surgery Under Local Anaestheisa



PostOperative 12-hour AUC	3.6 ± 1.9	4.8 ± 1.9	0.017^{**}

Peripheral Dexmedetomidine

- Mechanism of actions:
  - Dorsal horn of spinal cord
  - Depress nerve fiber action potential
  - Reduce the release of nor-adrenaline at the nerve endings



Analgesic effect of Peripheral Dexmedetomidine in Third Molar Surgery Under General Anaestheisa

	Group D (n=33)	Group P (n=33)	*p* value
NRS pain at rest			
AUC NRS 1-72 h	168.2±133.7 (0–482.6)	212.2±136.1 (7.0–457.8)	0.1455
NRS pain during mouth opening			
AUC NRS 1-72 h	198.2±145.9 (0–491.5)	272.8±135.0 (43.5–580)	0.0278**

Traditional Chinese Medicine

SCHOOL OF CHINESE MEDICINE
The University of Hong Kong
香港大學中醫藥學院

香港中文大學中醫學院
School of Chinese Medicine
The Chinese University of Hong Kong

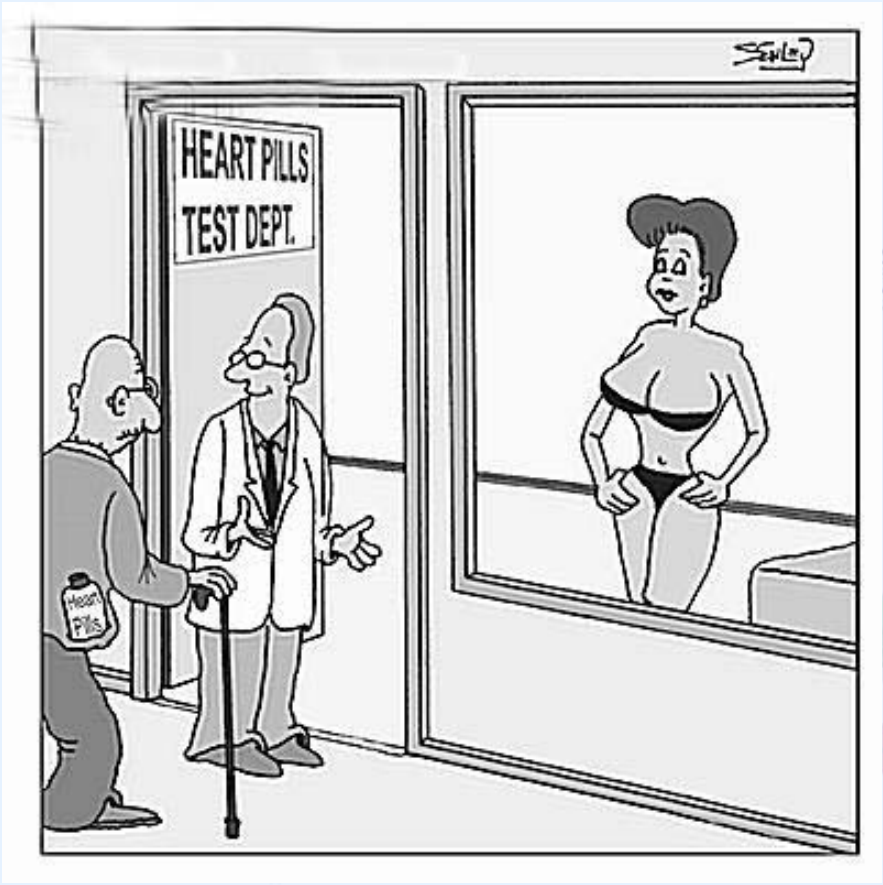
School of 中醫藥學院
Chinese Medicine

Welcome Message

Chinese Medicine Council of Hong Kong

Pharmaceutical Support

"Here's how it works. First we discover the drug and identify the market, then we invent the disease."



"Do a double-blind test. Give the new drug to rich patients and a placebo to the poor. No sense getting their hopes up. They couldn't afford it even if it works."

Find a new drug again if there is money left!


Goodbye mate!
I may reappear in the future...

Thank You


Seeking the Dragon Pearl
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