Incident / procedural pain management without an iv

Patient controlled analgesia with inhaled Methoxyflurane

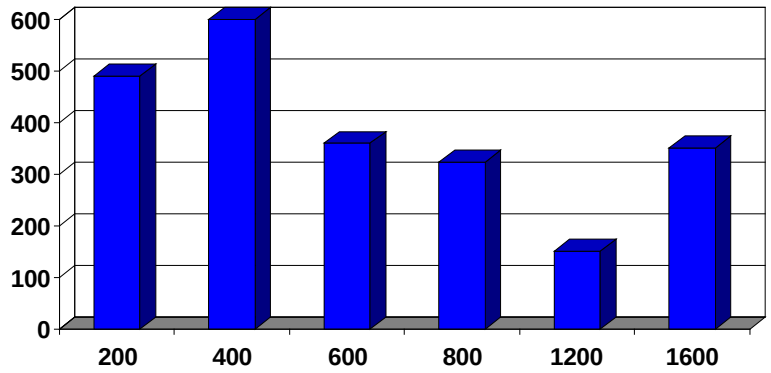
Dr Odette Spruyt

Pain and Palliative Care, Peter MacCallum

17October 2009 FPM Duelling with Pain

OTFC@petermac

- Increased use since PBS April 2008
- No. patients =50
  - from Jan 07-Sept 09
  - 3 patients before April 08
- Age range 20 – 80 yr
- F 28
- Mode (dose) =400ug
  - (600 x doses dispensed)



- Dose range prescribed
  - 200ug - 1600ug
  - No.on 1600ug = 4pts
- range of Rx duration from
  - single prescription to >12/12
- Clinically useful for some
- Concerns re abuse
  - Eg “thumb sucking” replaced with lozenge sucking

OTFC-general comments

- meets criteria for I/P pain therapy
- Useful for some
  - Renal impairment
  - Fentanyl patch BT
  - Predictable I/P pain -dressings
  - Less constipation if frequent use -RC
- Need for selected non-malignant procedural pain also
  - eg renal dialysis- associated pain
- Slow absorption if dry mucosa
- Dose titration in one-off procedures is a clinical problem

Main points

- Incident pain and procedural pain accounts for approximately half the pain reported by patients with cancer and is not well treated
- Effective incident pain therapy needs to be potent, patient controlled and easy to use
- Penthrox™ Inhaler fulfills several of the desirable characteristics of a therapy for predictable incident or procedural pain

ECS-CP - Incident Pain

- classification
  - Io – No incident pain
  - I i – Incident pain present
  - Ix – Insufficient information to classify
- **Guidelines for Use**
  - There are six key characteristics of *incident pain*, as defined in the ECS-CP:

    - *Relationship with background pain:* The intensity of incident pain is significantly greater than background pain.
    - *Severity:* The intensity of incident pain is moderate to severe.
    - *Predictability:* The trigger is often known, such as movement, defecation, urination, swallowing and dressing change. However, clinically significant episodic pain (i.e. no predictable trigger) can be included (e.g. bladder or bowel spasm).
    - *Onset:* Its onset is rapid, with intensity often peaking within 5 minutes.
    - *Transiency:* Incident pain is transient, and may return to baseline shortly after the trigger is stopped or removed.
    - *Recurrence:* It is intermittent, recurring when the trigger is reinitiated or reapplied.

Transitory pain - unpredictability

- 39% of 243 consecutive cancer pain pts admitted to MD pain clinic Germany
- **Only half movement-related TP was predictable**
  - Petzke F et al JPSM 1999
- **Unpredictable in 78.2%**
  - Portenoy RK et al Pain 1999

Impact

- 84 (51.2%) had BTP previous day
  - Median number episodes = 6 (1-60)
  - Median interval to peak = 3mins (1s to 30min)
  - 61.7% identified precipitants
- More intense (P<0.001) and more frequent (P<0.01) background pain than patients without breakthrough pain
- > pain-related functional impairment, worse mood, more anxiety
- Independently contributed to impaired functioning and psychological distress
  - Portenoy RK et al Pain 1999

ECS-CP and incident pain

- International validation study (in press)
- 944 patients referred to palliative care services
- 48% had incident pain

- Incident pain was associated with :
  - > time to stable pain $p<0.001$
  - > MEDD $p<0.001$
  - > adjuvants $p<0.001$

ideal BTP therapy

- P atient controlled
- E asy to use -Rapid dose determination
- E ffective in majority of patients
- P otent

- C ompatible with opioids
- A dverse effects few
- R apid onset
- S hort duration <30mins

methoxyflurane

- Most potent volatile anaesthetic
- No longer used in anaesthesia
- Profound analgesia (*sub*anaesthetic)
- Muscle relaxation
- Use limited by:
  - Hepatic metabolism 50-70%
  - Dose-dependent renal toxicity
  - Idiosyncratic hepatic necrosis
- Prominent use by Vic/NSW ambulance

Penthrox™ Inhaler

MEDICAL DEVELOPMENTS INTERNATIONAL LIMITED

Methoxyflurane:Registered Indications Aust.

- Self administration to conscious, haemodynamically stable, patients with trauma and associated pain, under supervision by personnel trained in its use.
- Monitored conscious patients who require analgesia for the relief of pain in short surgical procedures such as the change of dressings.
- The total maximum dose must not be exceeded.
  - Up to 6 mL/day of Penthrox™ (methoxyflurane)
  - The total weekly dose should not exceed 15 mL.
  - The lowest effective dosage should be used.
  - Administration on consecutive days is not recommended.

safety

- below 2 MAC Hours, renal toxicity does not occur (Cousins 1972)
- the inhalation of 6mL via the Penthrox™ inhaler lasts less than 1 hour.
- assuming neither re-distribution nor losses, the maximum MAC level that can be achieved is approximately 0.3 to 0.6 MAC Hours, ie about 25% of renal toxicity level (Komesaroff)

Penthrox™ Inhaler & Oxygen

@petermac

- Pilot study
- Pain during radiotherapy
- Pain during lymphoscintigraphy
- Pain during bone marrow biopsy

PMCC Pilot study 2005

- 28 patients
- 13 on maintenance opioids
- 18 no oral/sc analgesia (9 of these had local anaesthetic)
- 10 received standard breakthrough analgesia +MEOF
- Loading dose of 10 breaths
- Median total time 9 min, 29 secs (23sc – 39m,47s)

Indication for Analgesia	***n (%)***
Bathing / toileting	1 (3.5)
Bone marrow biopsy	9 (32)
Change of dressing	5 (18)
Diagnostic procedure-change of stent	1 (3.5)
Transfer to and/or positioning for diagnostic imaging	3 (11)
Transfer to and/or positioning for radiotherapy	6 (21)
Sentinel lymphoscintigraphy node biopsy	3 (11)

Efficacy

	All	MEOF alone	MEOF+
Mod - highly effective	89%	88%	90%

	All	MEOF alone	MEOF+
Helpful during worst pain	86%	89%	80%

Patient preference for MEOF n=18

- Instant pain relief 86%
- Better personal control 27%
- More at ease, calm 7%
- Min. side effects 13%
- Rapid onset & short-acting 13%

Pain during Radiotherapy

- 2006-7-No patients recruited
- Continue to use Penthrox™ Inhaler for relief of pain associated with radiotherapy transfers

Pain during Lymphoscintigraphy

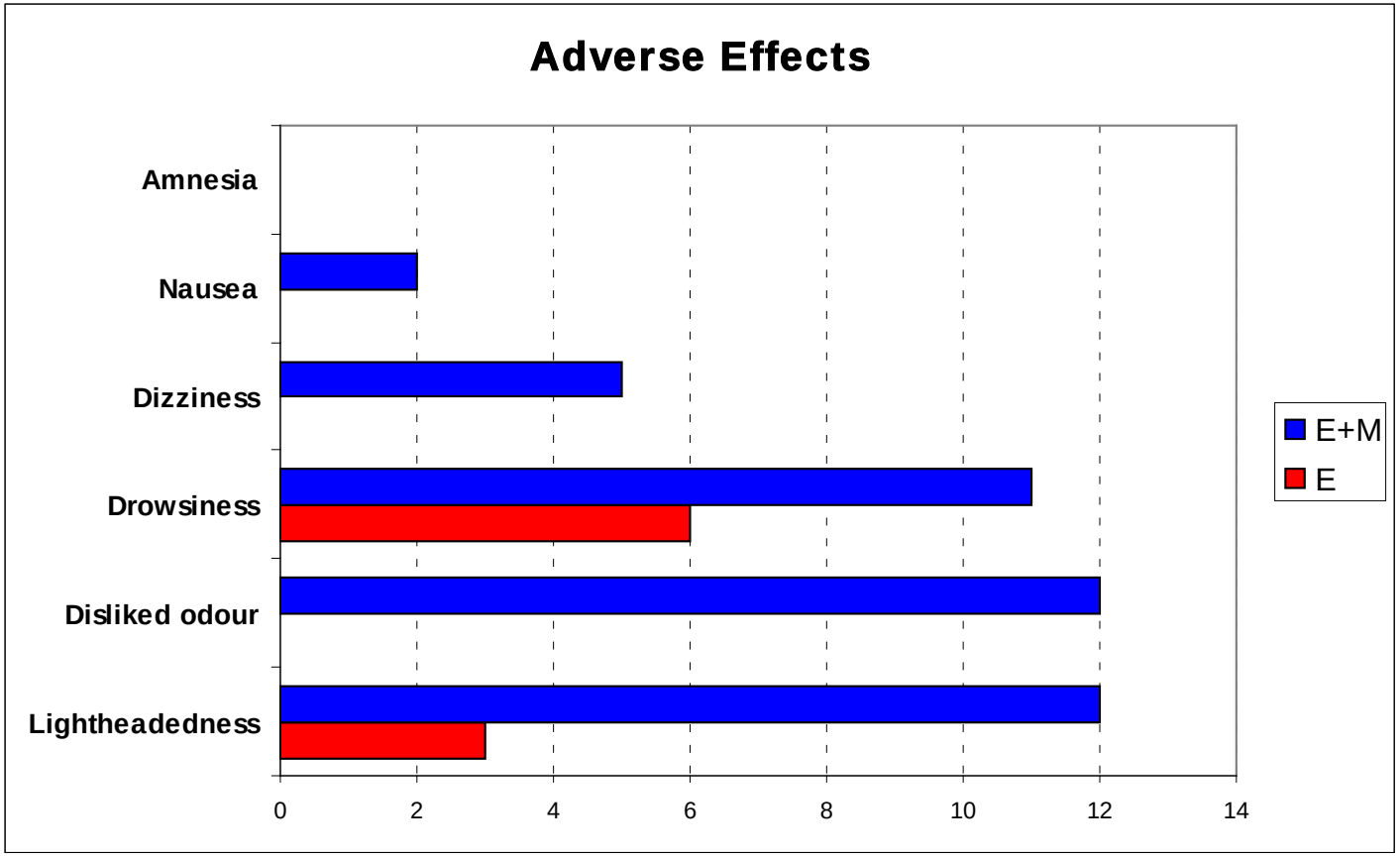
Fleming J et al Peter Mac 2007

- Patients report lymphoscintigraphy to be the worst experience during admission for sentinel node surgery
- No literature relates to lymphoscintigraphy and pain
- Pain is brief but intense
- Patients are unpremedicated other than topical EMLA

ANXIETY ($VAS_{0\text{-}100mm}$) n=60

no anxiety — *worst anxiety*

	E + M *median (range)*	**E** *median (range)*	***p*** ***Mann Whitney***
baseline	34 (0-99)	30 (0-88)	***0.55***
during injection (recalled @ T1)	17 (0-88)	38 (0-99)	***0.18***
DVAS (injection – baseline)	-5 (-75-69)*	8.5 (-78-54)*	***0.025****
post-injection anxiety	4 (0-42)*	11 (0-99)*	***0.020****
DVAS (post-inj'n – baseline)	-23 (-84-21)*	-5 (-80-51)*	***0.004****
post-scan anxiety	1 (0-49)	1 (0-73)	*?*


Adverse Effects
Amnesia
Nausea
Dizziness
Drowsiness
Disliked odour
Lightheadedness
0
2
4
6
8
10
12
14
E+M
E

Pain during Bone marrow biopsy

- 86% report moderate to severe pain during bone marrow biopsy Vanhelleputte P et al JPSM 2003

- @PeterMac, conducted a DB, placebo controlled study
  - MEOF vs standard treatment with local anaesthesia.

- Primary outcome: worst pain during BMB
  - determined from highest pain score recorded at two time points: pain during aspirate and pain during core biopsy

BMB study

-introducing MEOF to patient prior to biopsy

Demographics to date n=50

- F : M 13 : 37
- mean age 56.9yr
  - (48-82)
- ECOG
  - 0 33
  - 1 13
  - 2 4

STAI state anxiety score

Timepoint	Mean	Range	N
Pre-procedure	27.3	20-48	50
End of BMB	25.9	20-47	50
30-45 min postBMB	23.8	19-44	49

Penthrox™ Inhaler

- Benefit for cancer patients, including those on opioids
- Technique important and requires coaching
- Ongoing interest in role in procedural and incident pain
- Collaboration with others to investigate efficacy and safety further