

Acute Pain Management

Difficult Cases at the extremes of life

Jeremy Cashman



Declaration:

- **The following cases are real patients who have been under the care of the St George's Hospital In patient Pain Management Service**
- **What follows are my reflections on the issues involved and not necessarily a comprehensive overview**

Case 1. Tom Thumb

Case 1. TT

9 year old, ~30 kg boy.

Diagnosis of rapidly progressing, refractory non-Hodgkins lymphoma with mediastinal and pleural disease. Under joint care of RMH Outreach Service and Paediatric Oncology. Admitted mid December 2013 with large left pleural effusion

Case 1. TT

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Diagnosis of rapidly progressing, refractory non-Hodgkins lymphoma with mediastinal and pleural disease. Under joint care of RMH Outreach Service and Paediatric Oncology. Admitted mid December 2013 with large left pleural effusion

Recent septic shock, pulmonary embolus and mucositis due to chemotherapy. TPN because of poor oral absorption.

Complex psycho-social history; out of region, parents separated, mother pregnant

Pain as a result of mucositis, massive pleural effusion, and chemotherapy-induced neuropathy

Initial management in addition to ongoing chemotherapy included surgical thoracoscopy for insertion of chest drain and commenced iv paracetamol and morphine infusion for mucositis.

Admitted to PICU as high doses of morphine required for pain control. Morphine infusion converted to PCA with background infusion (5mg/h limit). Patient discharged to the paediatric oncology ward.

Case 1. TT

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Referred to Pain Team 3 weeks post admission and 1 day post PICU discharge with continuing, severe pain around chest drain. PCA alarming as hourly limit exceeded.

?Recommendation

Case 1. TT

Issues

Non-Hodgkin lymphoma

Complications of chemotherapy

Non-Hodgkin lymphoma

- **Rare; annual incidence ~9/million children
80 children <15 years of age, develop non-Hodgkin lymphoma (NHL) in the UK each year**
- **Commoner in boys than girls**
- **Two main types of NHL**
 - B-cell; usually involves lymph nodes in the abdomen**
 - T-cell; usually involves lymph nodes in the chest**
- **Treatment includes chemotherapy, radiotherapy, biological therapy or a combination**
- **>80% of children who get NHL recover completely**

Chemotherapy induced neuropathic pain

Mainly sensory symptoms: pain, tingling, numbness and temperature sensitivity

Affects 30%-40% patients undergoing chemotherapy

**American Society of Clinical Oncology guidelines (April 2014)
based on systematic review of 48 RCTs**

- **Prevention**

No approach exists that can be recommended

- **Treatment**

Only Duloxetine recommended

**Not unreasonable to try a tricyclic, gabapentin or even
topical baclofen/amitriptyline/ketamine**

Do not use lamotrigine

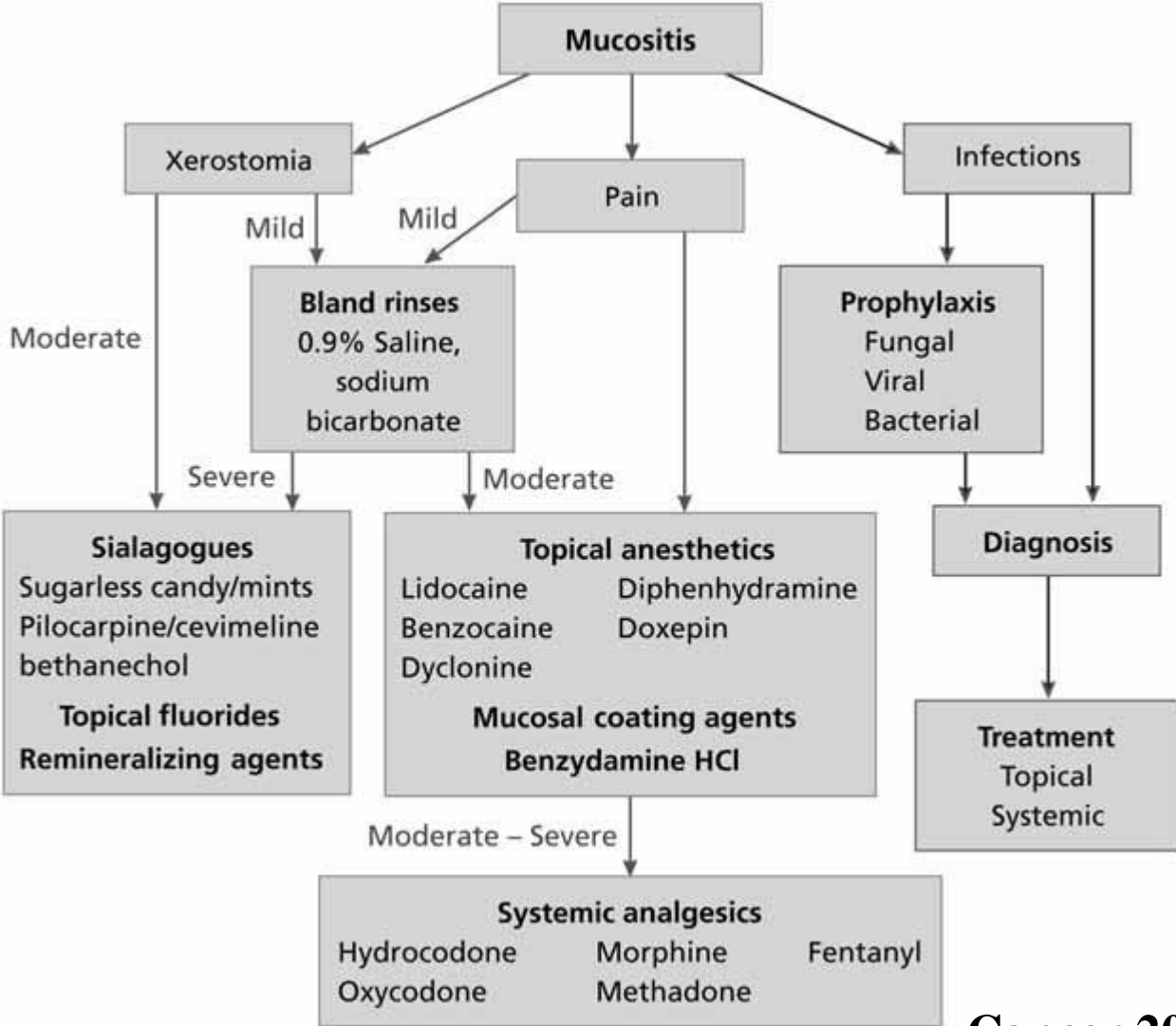
Chemotherapy induced mucositis

A review of toxicity data from 99 clinical trials found

- **Incidence of severe mucositis was <10%**
- **Patients with haematologic malignancies have an increased rate of oral mucositis compared with those with solid tumours**
- **Younger age is associated with more severe oral mucositis**

Cancer 2007;109:820-31

Management of chemotherapy induced mucositis



Day 1. **What we suggested**

- **Apply** lidocaine plaster (versatis TM) to chest drain site
- **Increase** PCA hourly limit to 7 mg/h
- **Consider** converting to MST if oral route becomes available, alternatively convert to fentanyl patch.

Parents (especially mum) concerned that this would result in suboptimal pain control ***

- **Consider** commencing an NSAID; vetoed by Oncologists

Case 1. TT

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Day 2. Versatis removed; only tolerated for 2 hour

**Increased pain over praecordium, eased by cold flannel.
Agreed that RMH PATCH team will lead on pain management. PATCH team recommend 25 mcg fentanyl patch alongside PCA morphine**

Weekend!

Issues

Paediatric Palliative Care

Paediatric Palliative Medicine (PPM) is a new subspecialty, recognised in 2009

In UK recommended that each region should have a tertiary consultant in PPM and each locality should have a paediatrician with a special interest (PWSI). In 2011 there were 10 tertiary consultants and 50 PWSI

Skills include complex pain and symptom control, so PPM overlaps with many clinical areas including acute and chronic pain medicine

Little evidence base for PPM and effectiveness is hard to prove

Adult palliative care improves quality of care and prolongs life but children tend to receive this care late in their illness trajectory because clinicians wait until they are certain that the child is “beginning to die”

Establish realistic goals of care and ensure all team members understand and work towards them. Discrepancies in treatment goals is one of the commonest barriers to optimal end-of-life care

Evidence of negative experiences by families of provision of medical care particularly in relation to information giving

Arch Dis Child 2011. doi 10.1136/archdischild-2011-300432

Clin Med Insights Pediatr 2012;6:75-88

Palliat Med 2010;24:796-806

Case 1. TT

Day 6. PATCH team recommend increasing fentanyl patch to 50 mcg and increase PCA hourly limit to 12 mg/h; vetoed by pain team clinical lead pending consultant-to-consultant discussion.

Pain team clinical lead requests MDT

Pain and PATCH team clinical leads discuss management

Day 7. Severe pain overnight.

Joint oncology/pain team review; mother upset by conflicting views from different parties.

Fentanyl patch and PCA hourly limit increased as agreed

Versatis re-instituted

Sublingual midazolam 1 mg BD commenced

Reduce buscopan dose to 10 mg TDS (cholinergic s/e)

Case 1. TT

Issues

Palliative sedation of terminally ill patients

Controversial!

Definition

Use of sedative drugs to relieve symptoms that are unbearable and refractory to other treatments

Classified according to degree

Indications

At least 2 refractory symptoms; pain, fatigue, depression, tiredness, suffering, distress, malaise

Drugs

Benzodiazepines (commonest), opioids, neuroleptics, other

Midazolam for palliative sedation

Uses

Breakthrough anxiety

Agitation at end of life

Routes

Buccal, intranasal, oral

Dose

Oral; 100 mcg/kg to max 5 mg po; onset 5-10 mins

Sc/iv infusion; up to 3000 mcg/kg/24hr

Association Paediatric Palliative Medicine Master Formulary 2012

No evidence that initiation of treatment, or increases in dose of opioids or sedatives, is associated with precipitation of death

In a case note review of 237 consecutive adult palliative care patients sedation was given to 48% of patients whilst 56% commenced sedative use only in the last 48 hours of life

Sedative dose increases in the last hours of life were not associated with shortened survival overall,

Lancet Oncol 2003;4:312-8

Arch Intern Med 2003;163:341-4

Day 8. Pain scores recorded as 0 overnight, but patient and dad report paroxysmal severe pain. PCA usage ~4 mg/h, only partially effective.

Increase PCA bolus to 1.5 mg

Increase fentanyl patch to 62 mcg

Adjust timing of BD midazolam

Joint oncology/pain team review to discuss pain management strategy in event of further deterioration; use of NCA agreed with head of nursing

Case 1. TT

Day 9. Chest drain blocked overnight resulting in increased pain; iv morphine 5 mg effective

MDT meeting (oncology, pain, PATCH teams) to discuss overall management strategy including pain

Increase PCA hourly limit to 16 mg/h

Increase fentanyl patch as necessary

Increase midazolam frequency to TDS

Dad fully involved in discussions

Weekend

Day 12. Over weekend

Error in reprogramming PCA resulted in 1 mg boluses!

PCA usage 30 mg/24 hr

Fentanyl patch **increased to 75 mcg**

Pain generally well controlled but severe episodic pain at drain site

****Increase** PCA bolus to 2 mg**

Day 13. Pain generally better

PCA usage 34 mg/24 hr

Discussion regarding deterioration strategy

Day 14. CXR shows significant disease progression

Fentanyl patch dislodged needed 34 mg morphine in 4 hr

****Dad reports increasing night terrors****

Case 1. TT

Day 18. Significant deterioration over weekend

Parents pressing PCA

**Plans for terminal care agreed including use of iv
midazolam infusion**

Day 20. Passed away

Case 1. TT

Day 18. Significant deterioration over weekend

Parents pressing PCA

**Plans for terminal care agreed including use of iv
midazolam infusion**

Day 20. Passed away

**One month later video-linked multi disciplinary governance
meeting to review management**

Case 3. Doris Day

88 year old, ~45 kg lady.

Admitted with right neck of femur fracture following fall whilst recovering from left THR. Also wedge compression fractures of T12 (new) and L1 (old), fracture of right iliac wing and sacrum at S2.

Chronic anaemia, hyponatraemia and weight loss ~10 kg

Dynamic Hip Screw fixation of femur following which care transferred to Orthogeriatric team.

Postoperative mobilisation hampered by pain but family insist patient cannot take any opioids as they blame Butrans for causing confusion which led to her fall

What would you do?

Issues

Buprenorphine and confusion in the elderly

Risk of fracture with opioids

Medications causing delirium/confusion in the elderly

MEDLINE search “buprenorphine AND confusion AND elderly” identified only 2 case reports

- **56 year old, male with rare chromosomal abnormality developed delirium following epidural buprenorphine**
- **82 year old, female, developed delirium following buprenorphine patch dose increase**

Both occurred in Japanese patients (!)

Both resolved on discontinuation of buprenorphine

Masui 1995:44:282-5

Psychogeriatrics 2013; 13: 118–23

Patients >60 have increased risk of falls and fractures

A meta-analysis of 6 studies found a 38% increased risk of osteoporotic fractures in elderly patients taking opioids

A recent observational trial found increased rates of falls and of composite fractures with opioids but was unsure whether this was true causation or due to confounding factors.

Risk increases further with higher doses; >50 mg morphine equivalent associated with 2-fold increased risk

Am J Geriatr Pharmacother 2006;4: 219-26

Drug Saf 2007;30:171-84

Arch Intern Med 2010;170:1968-76

Systematic review comparing opioids

6 studies, 1078 patients

3 RCTs (Level II), 3 observational studies (Level III)

Only 4 studies enrolled mainly elderly patients

Discordance when more than one neuropsychological assessment was used!

No difference between codeine, fentanyl, fentanyl, hydromorphone, morphine or oxycodone

Pethidine associated with significantly increased risk

Systematic review comparing mode of delivery of opioids

5 studies, 436 patients

4 RCTs (Level II), 1 case controlled study (Level III)

Only 3 studies enrolled mainly elderly patients

No difference between iv and epidural opioids wrt delirium

**Case controlled study found significant increase in delirium
associated with epidural pethidine**

**Less pain in patients receiving epidural analgesia was not
associated with improvement in rate of delirium**

Which medications to avoid in people at risk of delirium

Systematic review of 14 studies, 4652 patients

6 surgical studies, ~1,700 patients; only 1 RCT (Level II)

Average age of patients ~80 yr

Most recent study 2005

Found only moderate quality evidence that:

**Opioids associated with 2-fold increased risk of delirium
in surgical patients**

**Oxycodone (OR 0.7) has most favourable profile, followed by
codeine (OR 1.1), morphine (OR 1.2), and fentanyl (OR 1.5)**

**Inverse dose–response relationship in patients recovering
from hip fracture; lower dose greater risk than higher
doses (morphine equivalent dose <10> mg)**

Age and Ageing 2011; 40: 23–29

Which medications to avoid in people at risk of delirium

Systematic review of 14 studies, 4652 patients

6 surgical studies, ~2,800 patients; only 1 RCT (Level II)

Average age of patients ~80 yr

Most recent study 2005

“Acute severe pain is an important contributing factor for delirium, withholding opioids for fear of risk of delirium is inappropriate”

Age and Ageing 2011; 40: 23–29

Postoperative mobilisation hampered by pain but family insist patient cannot take any opioids as they blame Butrans for causing confusion which led to her fall

Day 0

In-patient pain team contacted on 5th postoperative day.

Palliative care team had already been contacted regarding difficulty with physiotherapy; they advised ibuprofen 200 mg TDS and lidocaine plaster.

Case 2. DD

Postoperative mobilisation hampered by pain but family insist patient cannot take any opioids as they blame Butrans for causing confusion which led to her fall.

Day 0

In-patient pain team contacted on 5th postoperative day.

Palliative care team had already been contacted regarding difficulty with physiotherapy; they advised ibuprofen 200 mg TDS and lidocaine plaster.

Day 2. Long discussion with Care of the Elderly team **we suggested**

- **Commence** dihydrocodeines initially 10 mg OD but increasing dose/frequency as tolerated
- **Consider** pregabalin
- **Ibuprofen not ideal but continue *pro tem***

Issues

Analgesic medicines in older people

Pharmacological response

Age associated decline in drug metabolism

Current guidelines advocate a '*Start low, go slow*' approach

NB not '*Start low, stay low*'!

Chronological age is a poor determinant of response

Frailty may be an independent predictor

Pain Pract 2008;8:287-313

J Am Geriatr Soc 2009;57:1331-46

Br J Clin Pharm 2011; 71: 351-64

Paracetamol

Clearance reduced in older people (?clinical significance)

Frailty is associated with significant decrease in clearance ~30% frail older vs fit older

FDA advisory panel has suggested reducing maximum single dose to 650 mg and total dose to 3.25 gm in elderly

Br J Clin Pharm 2011; 71: 351–64

NSAIDs

Diclofenac and possibly ibuprofen are comparable to coxibs for vascular risk whereas naproxen is lower risk

A systematic review of only 6 studies found risk of ischaemic stroke does not increase with age whereas a longitudinal study of Australian veterans found increase in all-cause mortality with NSAIDs

Lancet 2013; 382: 769-79

Pharmacoepidemiol Drug Saf 2010;19:490-8

Br J Clin Pharm 2011; 71: 936–42

Opioids

Morphine is the standard against which other analgesics are judged. In older patients dose adjustment and careful monitoring are essential

However, according to an International Expert Panel consensus statement on management of chronic severe pain in the elderly buprenorphine is the “*top-line choice for opioid treatment in the elderly*”

Oxycodone is also recommended in hospitalised older people because of relatively fewer ‘pharmacological complexities’

Pain Pract 2008;8:287-313

Br J Clin Pharm 2011;71:351-64

Advantages of buprenorphine in the elderly

No dosage adjustment required

Unaffected by renal impairment, minimal effect of hepatic impairment

Ease of use and greater compliance with patches also no peak/trough effect

Low incidence of adverse events

Disadvantages of buprenorphine in the elderly

**Specific inhibitors of CYP450 may inhibit breakdown
e.g. ketoconazole, nifedipine, norfluoxetine**

Patches not licensed for the treatment of acute pain

Clin Interv Aging 2008;3:421-30

Pain Pract 2008;8:287-313

Day 6

After witnessing Physiotherapy session family agree pain relief is problematic and agree to trial of oramorph

- **Commence** oramorph 2.5 mg BD with same dose for breakthrough pain

Day 7

- Oramorph now 2.5 mg TDS
- Duloxetine

Pain control and engagement with physiotherapy much better

Day 10

Transferred to Rehab unit

Thank you!



 @StGManageMyPain

 @StGPainTeam