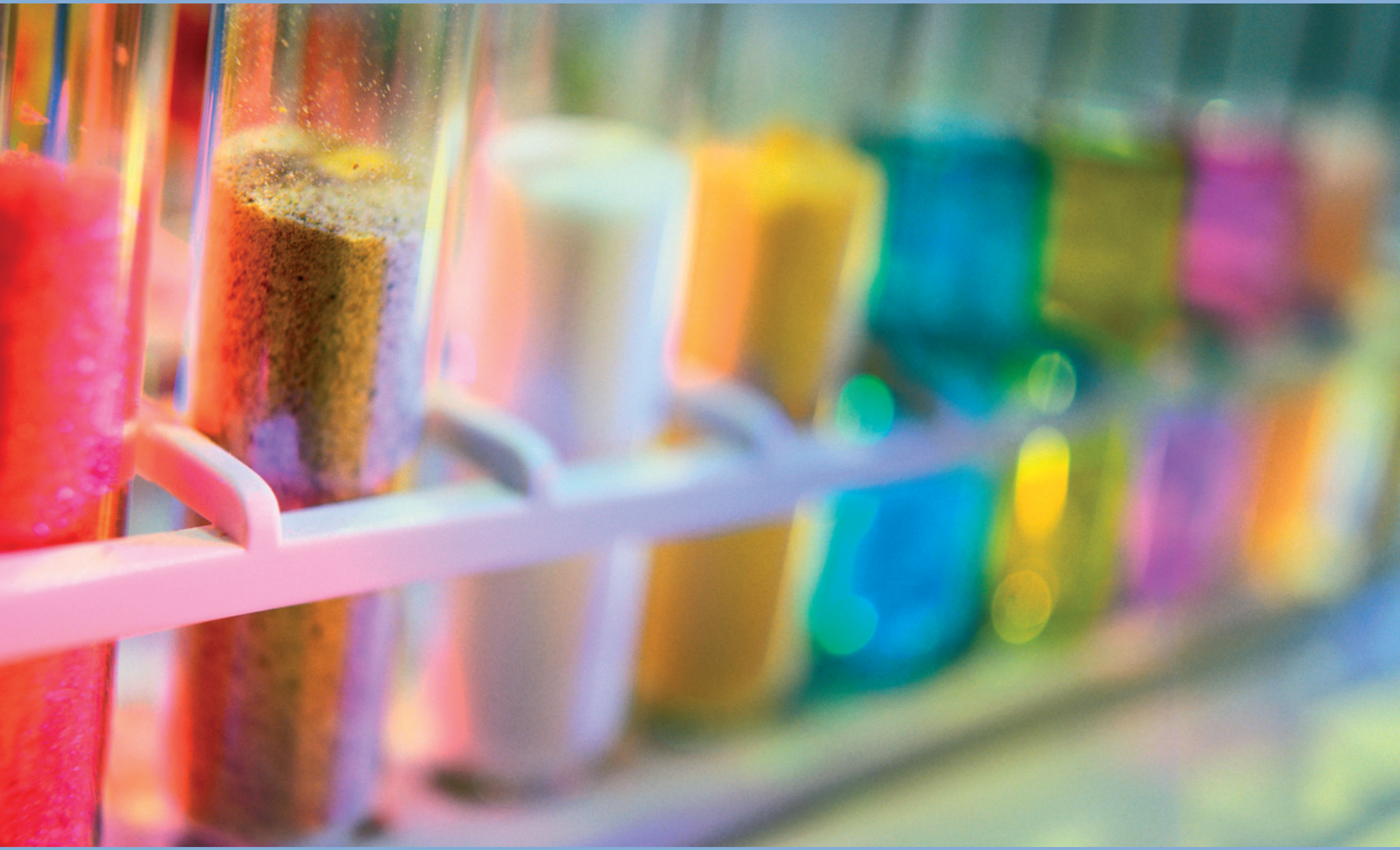
VERSION 1.1: NOVEMBER 2003

DATE OF REVIEW: JULY 2005

Palliative Care

GUIDELINES FOR MANAGING COMMON SYMPTOMS



South London Palliative and Supportive Care Network *and* Surrey West Sussex Hampshire (SWSH) Cancer Network *in conjunction with the* South East and South West London Cancer Networks

contents

ONE

Local contact details

Hospital Palliative Care Team Members:

Telephone number:

Bleep:

Fax:

Email:

Availability:

Out of hours palliative care contact details:

Additional Information:

TWO

Introduction

These hospital palliative care guidelines aim to give clear advice on the management of common symptoms for healthcare professionals caring for patients with palliative care needs in the generalist setting.

Throughout the document, indication is given concerning when to refer for specialist palliative care advice. However specialist advice may be sought at any stage and local contact details are given at the front of the guidelines.

These network wide hospital palliative care guidelines are designed to complement the Drug Formulary agreed by the South West London, South East London and Surrey, West Sussex and Hampshire (SWSH) Cancer Network Palliative Care working groups.

These guidelines will be audited and reviewed by the cancer networks to represent changes in clinical practice and research findings.

Comments regarding the hospital guidelines can be made by completing the form at the back of the document and returning to the address stated.

Last updated 23rd April 2003 to include all comments from network formulary/ guideline committees.

THREE

Prescribing guidelines in palliative care[1]

The aim of treatment for patients with terminal disease is to keep them as comfortable, alert and free from symptoms as possible.

The number of drugs should be as few as possible as taking medicine(s) may be an effort.

Oral medications are usually satisfactory unless there is severe nausea and vomiting, dysphagia, weakness, or coma, in which case parenteral medications may be necessary.

If the parenteral route is necessary, repeated administration of injections can be difficult in a cachectic patient. This has lead to the use of portable subcutaneous syringe drivers, which give a continuous infusion over 24 hours. This can provide good control of many symptoms with little discomfort or inconvenience to the patient.

The following guidelines are aimed at giving suggestions for appropriate prescribing for adult patients in the palliative care setting, based on an accurate assessment of the clinical situation.

Several recommendations in these prescribing guidelines involve off-label indications or routes. Where this is the case there is clinical evidence to support the indication for use.

[1] British National Formulary, September 2002

3.1 GUIDELINES FOR PRESCRIBING CONTROLLED DRUGS

Preparations which are subject to the prescription requirements of the Misuse of Drugs Regulations 1985, outlined below, are distinguished throughout the BNF by the symbol CD (controlled drug).

3.1.2 In Patient Administration

The following details are required:

- Hospital approved drug chart
- Patient name, hospital number and ward
- Approved drug name written in CAPITALS
- The dose to be given specified in milligrams/micrograms
- The route, frequency and intended times of administration of the drug. Try to coincide with routine drug rounds where possible.
- For 'as required' drugs it is essential to specify how often the dose may be repeated or the maximum dose to be given in 24 hours and the reason to be given.
- The prescription must be signed and dated
- If dose changes are required the existing prescription must be cancelled with a line through it, signed and dated and a new prescription written

3.1.2 Out Patient Prescriptions

FP 10 PRESCRIPTIONS

Prescriptions ordering controlled drugs must be:

- Signed and dated by the prescriber
- Specify the prescriber's address
- Prescription must ALWAYS be in the prescriber's own handwriting in indelible ink and include:
- The name and address of the patient
- The TOTAL quantity of the preparation, or the number of dose units, in both words and figures
- The dosage form (e.g. tablets) must be included on a controlled drugs prescription, IRRESPECTIVE of whether it is implicit in the proprietary name (i.e. MST Continus) or whether only one form is available
- The total quantity needs to be in words and figures.

FOUR

Guidelines for prescribing analgesics in palliative care

4.1 PRINCIPLES OF PAIN MANAGEMENT

- Promptly assess each pain and diagnose cause.
- Acknowledge psychological and spiritual components of pain.
- Prescribe analgesics according to WHO ladder.
- The preferred method of administration is the oral route.
- Assess frequently and regularly
- Anticipate and treat likely drug side-effects
- Pain not responding to the above regimen may need the use of co-analgesics or specialist advice.

WHO ANALGESIC LADDER[2]

STEP 1	STEP 2	STEP 3
		STRONG OPIOID
		+ NON OPIOID
		+/- COANALGESICS
	WEAK OPIOID	
	NON OPIOID	
	+/- COANALGESICS	
	*	
+ NON OPIOID		
+/- COANALGESICS		
MILD PAIN	**MODERATE PAIN**	**SEVERE PAIN**

*** Do not exceed total daily dose of paracetamol (4g), if e.g. compound weak opioid is combined with paracetamol.**

[2] World Health Organisation. Cancer Pain Relief. Geneva: WHO, 1996

4.2 ANALGESICS FOR USE WITH WHO LADDER

4.2.1 Non Opioid Analgesia

Drug group	Drug name	Dose	Frequency	Route
Non-opioid Analgesia	Paracetamol	500mg-1000mg	q.d.s	PO

4.2.2 Weak Opioid Analgesia

Drug group	Drug name	Dose	Frequency	Route
Weak Opioid Analgesics	*Co-proxamol*	2 tablets	q.d.s	PO
	Co-codamol 30/500mg	2 tablets	q.d.s	PO
	Dihydrocodeine Immediate release 30mg Modified release 60mg	Immediate release 30-60mg Modified release 120mg	4-6 hourly 12 hourly	PO PO
	Tramadol Immediate release 50mg Modified release 100mg	Immediate release 50 – 100mg Modified release 100 – 200mg	Immediate release 4-6 hourly Modified release b.d Max dose 400mg daily	PO PO

4.2.3 Strong Opioid Analgesia

Drug group	Drug name	Frequency	Route	Preparations
Immediate release morphine preparation	*Sevredol tablets*	PRN or regularly 4 hourly	PO	10mg, 20mg, 50mg
	Oramorph / Sevredol oral solution	PRN or regularly 4 hourly	PO	10mg/5mL, 100mg/5mL

Sustained release morphine preparations	*MST Continus (tablets) / Zomorph capsules*	12 hourly	PO	5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg
	MST Continus (suspension)	12 hourly	PO	20mg, 30mg, 60mg, 100mg, 200mg
	MXL / Morcap SR	Daily	PO	Capsules 30mg, 60mg, 90mg, 120mg, 150mg, 200mg
Parenteral Preparations	*Diamorphine Hydrochloride*	PRN or Continuous infusion	SC	Injection 5mg, 10mg, 30mg, 100mg, 500mg

4.2.4 Alternative Strong Opioids

Drug name	Preparation	Trade name	Regular prescribing interval
Oxycodone	Immediate release capsules 5mg, 10mg, 20mg	Oxynorm	4 hourly
Oxycodone	Immediate release solution 5mg/5mL, 10mg/m L	Oxynorm	4 hourly
Oxycodone	Slow release capsules 5mg, 10mg, 20mg, 40mg, 80mg	Oxycontin	12 hourly
Oxycodone	Parenteral solution 10mg/mL	Oxynorm	PRN injection or continuous infusion SC
Fentanyl	Transdermal patches 25micrograms/hr, 50micrograms/hr, 75micrograms/hr, 100micrograms/hr	Durogesic	72 hourly

Oral transmucosal fentanyl citrate	200mcg, 400mcg, 600mcg, 800mcg, 1200mcg, 1600mcg	Actiq	Max 6 hourly
Methadone	5mg tablets 1mg/1mL, 2mg/5mL	Physeptone	8 – 24 hourly
Hydromorphone	Immediate release capsules 1.3mg, 2.6mg	Palladone	4 hourly
Hydromorphone	Slow release capsules 2mg, 4mg, 8mg, 16mg, 24mg	Palladone	12 hourly

4.3 PRESCRIBING STRONG OPIOIDS FOR CANCER PAIN[3 4]

4.3.1 Dose titration with immediate release morphine

- Oral immediate release morphine is the drug of choice
- Dose titration of immediate release morphine is usually required to determine the optimal dose for the patient.
- Morphine has NO ceiling dose pharmacologically
- Prescribe immediate release morphine 4 hourly
  e.g. at 6am, 10am, 2pm, 6pm, 10pm and 2am
- The starting dose is usually 5 -10mg every 4 hours, but depends on the severity of pain, previous analgesic requirements and age - reduced dose (e.g. half) in frail and/or elderly patients.
- Breakthrough doses of immediate release morphine should be equivalent to the current 4 hourly dose and clearly prescribed, “as needed” not 4 hourly. Caution no more than 2 doses in any 4 hours
- Reassess pain control regularly. If still in pain, increase dose by 30-50%,
  e.g. 5mg→7.5mg→10mg→15mg→20mg→30mg etc. 4 hourly.

NB: Be cautious of the incremental change in the higher dose ranges of morphine.
SEEK SPECIALIST ADVICE.

4.3.2 Converting to modified, sustained or slow release morphine

- To convert 4 hourly immediate release morphine to sustained release morphine, the equivalent dose should be given:

[3] Hanks G & Cherny C. Opioid Analgesic Therapy. In Doyle D, Hanks G, MacDonald N (eds). Oxford textbook of Palliative Medicine, 2nd Ed. Oxford University Press 1998, 331-355

[4] Working Party on Clinical Guidelines in Palliative Care. Guidelines for Managing Cancer Pain in Adults. National Hospice Council for Hospices and Specialist Palliative Care Services (2nd Ed.) 1998.

Example
Immediate release morphine: 10mg/4 hourly = 60mg/24hours
To convert slow release morphine: MST 30mg/12 hours or MXL/Morcap 60mg daily

• Appropriate breakthrough doses of immediate release morphine must be prescribed and should be equivalent to the 4 hourly dose.

4.3.3 Parenteral route

• Diamorphine is the drug of choice due to its greater solubility.
• The preferred route of administration is subcutaneously either PRN or by continuous infusion via a syringe driver.
• Parenteral diamorphine is 3 times more potent than oral morphine. In order to convert a 24 hour dose of oral morphine to an equivalent dose of SC diamorphine, use calculation as shown:

$$\frac{\text{Total dose oral morphine in 24 hours}}{3} = \text{24 hour SC dose diamorphine}$$

Example
MXL 90mg o.d = 30mg SC diamorphine in 24 hours
MST or Zomorph 60mg b.d = 40mg SC diamorphine in 24 hours

• Appropriate breakthrough doses should be treated with a subcutaneous injection of the equivalent 4 hourly dose of diamorphine.

4.3.4 Transdermal route

Fentanyl is a synthetic opioid that is available as a transdermal preparation. The patch delivers fentanyl over a 72-hour delivery period. Active drug is absorbed through the skin and forms a subcutaneous depot, from which it is absorbed into the systemic circulation. It takes approximately 12 hours for the depot to build up after application of the first patch and up to 24 hours for the depot to disperse after the patch is removed. For this reason, transdermal fentanyl is not as flexible as morphine for patients with rapidly changing opioid requirements.

• Transdermal fentanyl may be less constipating than oral morphine.
• The transdermal preparation may be considered for patients with stable opioid requirements but where there are problems with:
  - Constipation
  - Mood disturbance

- Nausea & vomiting
- Number of tablets
- Unable to swallow

- Transdermal fentanyl is unsuitable for patients with:
    - Rapidly changing opioid requirements
    - New renal or hepatic Impairment
    - Chronic skin disorders
    - Patients with limited dexterity

- Fentanyl patches should not be put on very oedematous areas or on patients with poor circulation

<u>Starting transdermal fentanyl.</u>

The conversions from oral morphine to transdermal fentanyl is as follows:

Total oral morphine (mg/day)	Approx 4 hourly IR morphine dose (mg)	Transdermal fentanyl (mcg/hr)
50-134	⇠20	25
135-224	25-35	50
225-314	40-50	75
315-404	55-65	100
405-494	70-80	125
495-584	85-95	150
585-674	100-110	175
675-764	115-125	200
765-854	130-140	225
855-944	145-155	250

- The first fentanyl patch needs to be applied at the same time as the last dose of MST. When converting to patches from immediate release morphine patients will usually require three 4 hourly doses until the subcutaneous depot has built up.
- Breakthrough immediate release morphine should be prescribed with transdermal fentanyl (see chart above for dose). The breakthrough dose of diamorphine is equal to 1/5 of the patch strength expressed in mg.

4.3.5 Side-effects and toxicity of opioid analgesics

- Common side effects
  - Constipation - prescribe regular laxative e.g. codanthramer
  - Nausea and vomiting (usually wears off after a few days) - prescribe PRN antiemetic, eg haloperidol
  - Drowsiness and confusion
  - Dry mouth

- Opioid Toxicity
  Can occur with:
  - Too rapid dose escalation
  - Pain that is partially or not morphine responsive
  - Renal impairment/failure
  - Can occur with successful therapeutic intervention to relieve pain, e.g. chemotherapy, radiotherapy or nerve block

Warning signs include:

- Drowsiness
- Confusion
- Pin-Point pupils
- Myoclonic jerks
- Hallucinations (auditory and visual)
- Vomiting

If toxicity occurs, reduce opioid daily dose (the patient may need to miss one or several 4 hourly doses, then restart at a lower dose) or stop opioid and convert to a weak opioid.

FOR FURTHER ADVICE CONTACT YOUR PALLIATIVE CARE TEAM

FIVE Guidelines for prescribing co-analgesics in palliative care[5]

Co - analgesics are drugs that, when used concurrently with analgesics, may contribute significantly to pain relief

5.1 PRINCIPLES OF USE OF CO-ANALGESICS

- All principles of pain management apply for the use of co-analgesics.
- Note that many of the drugs classified as co-analgesics were developed and released for clinical indications other than pain.
- Ensure the first line co-analgesic is at its pharmacologically effective dose level and interval before changing to/adding second line drugs
- Several co-analgesics may be used concurrently for different indications
- For parenteral co-analgesic administration, refer to the prescribing guidelines for Syringe Drivers

[5] Portenoy R.K. Adjuvant analgesics in Pain Management. In Doyle D, Hanks G, MacDonald N, (eds) Oxford textbook of Palliative Medicine, 2nd Ed. Oxford University Press 1998, 361-380

5.2 EXAMPLES OF CLINICAL USE OF CO-ANALGESICS

Co-analgesic	Main Indication	Drug name	Typical dose range	Frequency	Route
NSAID	Bone	*Ibuprofen*	200-400mg	t.d.s-q.d.s	PO
		Naproxen	250-500mg	b.d-t.d.s	PO/pr
		Diclofenac	25-50mg	b.d-t.d.s (max 150mg/24 h)	PO/SC
		Ketorolac	10mg	q.d.s	PO/SC
COX2 Inhibitor		*Rofecoxib*	12.5-25mg	o.d	PO
Steroids	Nerve compression	*Dexamethasone*	2-16mg	o.d-b.d	PO/SC
Anti-depressants	Neuropathic	*Amitriptyline*	10-150mg	o.d	PO
		Dothiepin	25-150mg	o.d	PO
Anti-convulsants	Neuropathic	*Carbamazepine*	100-400mg	b.d-t.d.s	PO
		Sodium valproate	200-500mg	b.d-t.d.s	PO
		Clonazepam	0.5-2mg	o.d	PO/SC
		Gabapentin	200-600mg	t.d.s	PO
Anti-spasmodics	1. Muscle spasm	*Baclofen*	10-20mg	t.d.s	PO
		Diazepam	2-10mg	t.d.s	PO
	2. Colic	*Hyoscine butylbromide*	20mg	hourly	SC
Psychotropic	Co existing anxiety with pain	*Diazepam*	5-20mg	o.d	PO
		Levomepromazine	25-200mg	o.d	PO/SC
NMDA Receptor antagonist	Neuropathic	*Ketamine*	Seek Specialist Advice		

5.2.1 Non-steroidal anti-inflammatory drugs

Indication: Bone pain, local inflammation

- Characteristics of bone pain can change with the site involved.
- The clinical benefits of long-term use must be carefully balanced against adverse effects.

Most common side effects

- Gastric irritation, fluid retention, renal impairment, exacerbation of asthma/bronchitis.

5.2.2 Steroids

Indication: Nerve compression pain, pressure pain from tumour, oedema or inflammation, e.g. liver capsule pain, bone pain

- Dexamethasone is the first line choice.
- It has high glucocorticoid action, which reduces the prevalence of water retention as opposed to prednisolone and has a long duration of action.
- A starting high dose of 8 to 16mg daily is frequently used and the dose then titrated to the lowest possible level.
- Usually given in a single daily morning dose to minimise side effects.
- The clinical benefit of high dose or long term use must be carefully balanced against adverse effects

Most common side effects

- Oral thrush, facial swelling, ankle oedema, dyspepsia, diabetes, proximal myopathy, agitation, insomnia or psychiatric disturbance.

5.2.3 Antidepressants

Indication: Neuropathic pain

- Have a specific analgesic role in neuropathic pain, which is independent of their antidepressant action.
- Start at a low dose and titrate upwards every 3-5 days according to response and adverse effects.
- Studies have shown increased analgesic benefit with doses of amitripyline up to 150mg.
- Partial relief may occur within 2-4 days, but the full benefit can require 3-4 weeks.

Possible side effects

- Dry mouth, blurred vision, dizziness due to hypotension, and difficulty with micturition.

5.2.4 Anticonvulsants

Indication: Neuropathic pain

- These drugs are thought to act by suppressing spontaneous activity in traumatised nerve fibres and may require 2-5 days to assess their benefit.
- Start at the low dose and titrate up every 3-5 days according to response and adverse effects.

Possible side effects

- Nausea, dizziness, confusion and ataxia

5.2.5 Antispasmodics

Indication: 1. Muscle Spasm
2. Colic

- Titration of dose level of baclofen, diazepam and hyoscine butylbromide should be slow to minimise adverse effects.

Possible side effects:

- Drowsiness, light headedness, confusion, ataxia

5.2.6 Psychotropics

Indication: Co-existing anxiety and distress

- The dose of psychotropic drugs should be titrated against the patient's level of anxiety, with particular attention to minimising adverse effects.

Possible side effects.

- Diazepam: drowsiness, confusion

SIX

Guidelines for prescribing antiemetics in palliative care[6 7]

6.1 POTENTIALLY REVERSIBLE CAUSES.

Prior to instituting drug treatment, exclude or actively treat any potentially reversible causes such as:

- Drugs
- Chemotherapy
- Radiotherapy
- Constipation
- Raised intracranial pressure
- Hypercalcaemia
- Renal or hepatic failure
- Gastric outflow obstruction, e.g. Hepatomegaly / upper GI tumour
- Small/large bowel obstruction
- Gastritis
- Cough
- Pain
- Anxiety

6.2 MANAGEMENT

Treat the underlying cause wherever possible, otherwise manage symptomatically. Antiemetics should be used in accordance with the likely aetiology of the nausea and/or vomiting.

[6] Mannix K.A. Palliation of nausea and vomiting. In Doyle D, Hanks G, MacDonald N,. (eds) Oxford textbook of Palliative Medicine, 2nd Ed. Oxford University Press 1998, 489-498

[7] ABPI Data Sheet Compendium. Datapharm Publications, London Ltd. 1999-2000

Recommended Antiemetics by Aetiology

Suspected aetiology	Drug of choice	Dose PO	Dose SC
Drug Induced	*Haloperidol*	1.5-3mg b.d	1.5mg PRN 3-5mg/24 hrs
	Cyclizine	50mg t.d.s	50mg PRN 150mg/24hrs
Metabolic e.g. renal failure	*Haloperidol*	1.5-3mg b.d	1.5mg PRN 3-5mg/24hrs
Partial gastric outflow obstruction/ gastric stasis	*Metoclopramide* N.B. Do not use in small/ large bowel obstruction with colic	10-20mg t.d.s-q.d.s	10-20mg PRN 30-120mg/24 hrs
Gastric irritation	*Stop NSAID* *Lansoprazole* *Omeprazole*	 30mg o.d 20mg o.d	
Raised intracranial pressure	*Dexamethasone* *+/- Cyclizine*	16mg o.d 50mg t.d.s	8 -16mg o.d 150mg / 24hrs
Vestibular disorders	*Cyclizine* *Prochlorperazine* *Betahistine*	150mg t.d.s 5-10mg t.d.s 8-16mg t.d.s	150mg/24hrs
Bowel obstruction	*Cyclizine* *Haloperidol* *Buscopan* *Octreotide* *(For specialist use only)*	50mg t.d.s 1.5-3mg b.d 20mg t.d.s	150mg / 24hrs 3-5mg / 24hrs 60 – 120mg / 24hr 300ug – 600ug / 24hr
Intractable, unknown or mixed aetiology	*Levomepromazine* *Dexamethasone*	6.25-12.5mg o.d 8-12mg o.d	5-12.5mg/24hrs 8-12mg as stat dose

N.B. do not use cyclizine and metoclopramide concurrently, as anticholinergic effects of cyclizine will negate cholinergic activity of metoclopramide

SEVEN

Guidelines for prescribing laxatives in palliative care[8 9]

7.1 CONTRIBUTING FACTORS

In most patients there are multiple contributing factors:

- Immobility
- Poor intake and debility
- Weakness
- Drugs (opioids and anticholinergics)
- Hypercalcaemia
- Dehydration
- Bowel obstruction / pseudo-obstruction
- Cord Compression / cauda equina syndrome

7.2 MANAGEMENT

- Treat underlying cause where appropriate / possible
- Encourage good oral intake and increased mobility

8 Sykes N. Constipation and Diarrhoea. In Doyle S, Hanks G, MacDonald N. (eds) Oxford Textbook of Palliative Medicine, 2nd Ed. Oxford University Press 1998, 513-521

9 Sykes N. Constipation. Tutorials in Palliative Medicine 1997, 12:250-268

7.2.1 Recommended oral laxatives for constipation

Clinical effect	Preparation	Dose	Comments
Combined Stimulant and Softeners	Codanthramer 1 capsule = 5mL suspension Codanthramer Forte 2 capsules = 5 mL suspension Codanthrusate	5mL-30mL b.d. 1-6 capsules b.d. 5mL-20mL b.d. 2-4 capsules b.d. 5ml-30mL b.d. 1-6 capsules b.d.	May cause danthron burns – avoid in patients with bypassing catheters or who are incontinent.
Softener	Docusate Sodium Liquid Paraffin & Magnesium Hydroxide Mixture (Milpar)	100-200mg b.d. – t.d.s. up to 600mg/day 10mL-30mL b.d.	
Stimulant	Senna Bisacodyl	10mL-20mL nocte/b.d. 2-4tablets nocte/b.d. 5-10mg nocte/b.d.	May cause colic. Avoid in patients with malignant intestinal obstruction
Osmotic	Lactulose	10mL-20mL b.d. / t.d.s.	Patients require good oral fluid intake for efficacy

Laxatives that could be considered for resistant cases include:
- Macrogols (Movicol)
- Magnesium Sulphate

Anticipate that a quicker escalation of the laxative dose is required when:
- Activity/mobility is reduced
- Oral intake is reduced

7.2.2 Treatment of faecal impaction

The treatment of faecal impaction is usually managed in stages. Generally, only one stage should be implemented in each 24 hours period.

These are suggested stages but assessment of patients' individual needs and their normal bowel habit should be taken into consideration first.

Soft faeces palpable in rectum
- Bisacodyl suppositories
- Microlette enema
- Microlette enema and increase oral laxatives

Hard faeces palpable in rectum
- Bisacodyl and glycerine suppositories
- Microlette and increase oral laxatives
- Microlette enema and consider manual evacuation

Rectum empty but ballooned.
- Stage 1 Microlette enema
- Stage 2 Microlette enema and increase oral laxatives
- Stage 3 Arachis oil enema
- Stage 4 Phosphate enema

Movicol is also licensed for use in faecal impaction

EIGHT

Guidelines for management of anorexia and cachexia in palliative care[10]

8.1. CONTRIBUTING FACTORS:

Whilst many patients will have the anorexia-cachexia syndrome, potentially reversible factors should be sought and actively treated, including:

- Dry mouth
- Oral infection, e.g. candidiasis
- Oral ulceration
- Ill-fitting dentures
- Nausea and vomiting
- Gastric stasis
- Constipation

8.2 MANAGEMENT STRATEGIES:

8.2.1 Nutritional supplements

Refer to the dietician for exposure to the full range of supplements available. However Pro –Sure (EPA enriched Ensure) has a demonstrated benefit on cachectic patients with pancreatic cancer.

8.2.2 Drug treatment

Corticosteroids

- The optimal dose, type of steroid and length of treatment has yet to be evaluated
- Known to improve appetite and well-being, but does not result in weight gain. The effect is short lived (weeks).
- A trial of corticosteroids is indicated for 1 week, against a clear endpoint e.g. improved appetite. If there has been no benefit after this, they should be stopped.

dexamethasone	4mg o.d
prednisolone	30 mg o.d

[10] Bruera E, Fainsinger RL. Clinical management of cachexia and anorexia. In: Doyle D, Hanks G, MacDonald N (eds). Oxford textbook of Palliative Medicine, 2nd Ed. Oxford University Press 1998, 548-557

- In responding patients, the steroid dose should be reduced gradually to avoid toxicity. e.g. by 2 mg/week for dexamethasone and 5 mg/week for prednisolone

Progestogens

- Increased appetite and weight gain have been shown with megestrol acetate and medroxyprogesterone acetate, but only in high dose (i.e. 800-1600 mg/day)
- More durable effect than with corticosteroids - effect seen over months rather than weeks, but it may take a few weeks for therapeutic effect

megestrol acetate	80-160mg b.d
medroxyprogesterone	400mg o.d

NINE

Guidelines for the management of symptoms in a dying patient[11]

9.1 SIGNS THAT ARE COMMONLY SEEN IN THE LAST 2-5 DAYS OF LIFE

- More rapid deterioration, often day-by-day
- Increasing weakness, bed-bound and requiring help with personal care
- Barely able to take even liquids and unable to take medicines by mouth
- Impaired concentration, possible muddled thinking, and difficulty sustaining even the briefest conversation
- Increasing drowsiness

9.2 COMMON SYMPTOMS IN DYING PATIENTS

- Pain
- Nausea and vomiting
- Breathlessness
- Restlessness / agitation
- Retained chest secretions

9.3 ETHICAL CONSIDERATIONS IN DYING PATIENTS [12]

Guidelines for Withholding and Withdrawing Life-Prolonging Medical Treatment

- Examples of life-prolonging medical treatments include IV fluids, enteral or parenteral feeding, antibiotics, CPR, ventilation.
- The primary goal of any medical treatment is to benefit the patient by restoring or maintaining health, maximising benefit and minimising harm.
- Treatment that does not provide net benefit to the patient may, ethically and legally, be withdrawn and the goal should shift to the palliation of symptoms.
- A voluntary refusal of life-prolonging treatment by a competent adult must be respected; advance directives must be respected if the patient has lost the capacity to make a decision.
- Decisions to withhold or withdraw treatment should be made by the clinician in overall charge of a patient's care following discussion with the health care team and where appropriate, patient and/or those close to the patient.

[11] National Council for Hospice and Specialist Palliative Care Services. Changing Gear-The Last 48 Hours. 1999.

[12] British Medical Association. Withholding and Withdrawing Life Prolonging Medical Treatment. Guidance for decision-making. 2nd edition, 2001.

9.4 DRUG MANAGEMENT OF SYMPTOMS IN THE DYING PATIENT

9.4.1 Reduce medication to the minimum necessary:

Only medications, which are essential to control symptoms, should be used at this time, and many drugs can be stopped including:

- Antihypertensives
- Lipid-lowering drugs
- Diuretics
- Iron Preparations
- Vitamins

Consider whether it is still appropriate to use intravenous fluids, artificial nutrition or antibiotics - each decision should be individualised

9.4.2 Review route of administration of drugs:

- As patients become unable to take medication by mouth, give essential medications subcutaneously.
- If symptoms are continuous e.g. pain or nausea, then drug administration should be continuous. In practice, the most effective way of doing this is by continuous subcutaneous infusion via the syringe driver.

Please refer to section 10 on use of a syringe driver

9.4.3 PRN Medication

All dying patients should be prescribed ‘as required’ medication for common symptoms:

Symptom	Drug and suggested dose
Pain	Diamorphine 2.5mg SC In patients previously taking morphine or other strong opioid, calculate the PRN dose by dividing the total dose required in 24 hours by 6
Agitation/ Breathlessness	Midazolam 2.5 to 10mg SC
Chest Secretions	Glycopyrronium 0.2mg SC Hyoscine butylbromide 20mg SC Hyoscine hydrobromide 0.4mg SC
Nausea/Vomiting	Haloperidol 1.5mg SC

9.4.4 Drugs commonly used in a syringe driver for dying patients

Indication	Drug	Dose	Comments
Pain	*Diamorphine*	- 5-20mg if no previous opioid. - For patients on morphine divide **total** dose of oral morphine by 3 for 24-hour SC diamorphine dose. e.g. MXL 90mg = 30mg diamorphine	Diamorphine is better absorbed SC than morphine. No maximum dose
Sedation	*Midazolam*	10-30mg/24 hours	Max dose 200mg /24 hours
	Levomepromazine	25-200mg/24 hours	Not in patients with cerebral metastases or a history of fits
Antiemetic	*Haloperidol*	3-5mg/24hours	Can be sedating
	Cyclizine	150mg/24hours	Can precipitate in syringe drivers
	Levomepromazine	6.25-25mg/24 hours	Sedating in increased doses
Retained oropharyngeal/ chest secretions[13]	*Glycopyrronium*	0.6–2.0mg/24 hours	More potent than hyoscine hydrobromide, does not cross the blood brain barrier (BBB)
	Hyoscine butylbromide	60-180mg/24 hours	Does not cross (BBB)
	Hyoscine hydrobromide	1.2-2.4mg/24 hours	More expensive, and may cross BBB - theoretical risk of agitation or confusion

[13] Bennett M et al. Using anti-muscarinic drugs in the management of death rattle: evidence-based guidelines for palliative care. Palliative Medicine 2002;16:369-374

9.5 GENERAL MANAGEMENT STRATEGIES

9.5.1 Management of breathlessness

The following measures allow the frightened breathless patient to feel less distressed:

- A calm member of staff can improve patient confidence
- An electric fan at the bedside
- Simple breathing exercises encourages the patient to use their diaphragm
- Positioning - avoid lying the patient flat. A semi-recumbent position allows greater movement of the diaphragm than sitting bolt upright

9.5.2 Management of restlessness and agitation

Exclude potentially reversible causes for example:

- A full bladder
- Musculoskeletal pain/stiffness
- Fear, feelings of isolation
- Pain through inadequate analgesia

If it is necessary for the patient's comfort to administer sedating medication, explain why this is necessary both to the patient if possible, and to family members.

9.5.3 Management of retained secretions

Many dying patients develop noisy moist breathing, sometimes known as the 'death rattle'. It is often due to aspirated oropharyngeal secretions and retained bronchial secretions although in some patients there will be underlying hypostatic pneumonia.

Explanation

- Explain to patient's family what is causing the secretions/noise, and if the patient is unconscious, reassure them that it should not distress the patient.

Repositioning

- Simply turning the patient on his side may stop the oral secretions pooling in the pharynx, and reduce the rattling sound.

TEN

Guidelines for syringe driver use and prescribing in palliative care

10.1 AVAILABILITY OF SYRINGE DRIVER PUMPS

Syringe driver pumps are available:

During working hours

Out of hours

10.2 INDICATIONS FOR USE OF A SYRINGE DRIVER

- Persistent nausea & vomiting
- Severe dysphagia
- Intestinal obstruction / malabsorption
- Semi / unconscious patient

10.3 ANALGESIA VIA THE SUBCUTANEOUS ROUTE

- For patients who have previously been prescribed oral morphine the conversion factor to parenteral diamorphine is 3:1 *(see Analgesia section 4)*
- The equivalent 4 hourly dose of drugs used should also be prescribed PRN for breakthrough symptoms.

10.4 GENERAL PRINCIPLES

- Care should be taken when mixing more than two drugs in a syringe and in ensuring that the diluent used is compatible with the drugs. The diluent of choice is water for injection except in the following where sodium chloride for injection should be used: Diclofenac, Granisetron, Ketamine, Ketorolac, Octreotide and Ondansetron.
- If requiring more than three drugs in one syringe driver, re-assessment of treatment aims is required.
- With combinations of two or three drugs in one syringe, a larger volume of diluent may be needed, e.g. in a 20mL or 30mL syringe.

10.5 EXAMPLE OF A WRITTEN PRESCRIPTION

Using a MS26 "GREEN " Syringe Driver

Name of Drug(s) Dose in milligrams or micrograms /24 hours subcutaneous infusion via syringe driver.

Mixed with diluent (Water for Injection) to a length of 48mm in syringe, set at
48mm/24hours.

NB: It is the distance travelled (mm) that is important to prescribe **not** *the volume (mLs), as the pump measures* **mm/24hours.**

Using a MS16A "BLUE" Syringe Driver

Name of Drug(s) Dose in milligrams or micrograms /24 hours subcutaneous infusion via syringe driver

Mixed with diluent (Water for Injection) to a length of 48mm, set at 2mm/hr

NB: It is the distance travelled (mm) that is important to prescribe **not** *the volume (mLs), as the pump measures* **mm/hr**.

All Prescriptions

- Alterations to the dose should not be made. If doses need to be changed the prescription should be cancelled as stated and a new prescription written
- A label should be attached to the giving set with the information
- Name of patient
- Length of starting volume in mm
- Names and dosages of drugs
- Date and time started.

10.6 SETTING UP THE SYRINGE DRIVER

Nurses setting up the syringe driver are required to be competent in the use of the pump in line with local 'Use of Medical Devices Policies'.

Any uncertainty in how the syringe driver is set up then contact the Palliative Care Team.

A monitoring form should be used for every patient with a syringe driver in use (contact local Palliative Care Team for details).

10.7 GUIDELINES FOR COMMON DRUGS, DOSES AND RANGES FOR PALLIATIVE CARE USE WITH A 24-HOUR SYRINGE DRIVER[14 15 16]

The following is a guide to drugs that may be used in a 24-hour subcutaneous driver. They may be used alone or in combinations.
Advise should be sought when combining drugs or in exceptional circumstances

All drugs should be mixed with WATER unless otherwise indicated.

14 Twycross, R. et al (1998) Palliative Care Formulary. Oxford, Radcliffe Medical Press

15 Kaye, P. (1994) A - Z Pocketbook of symptom control, Northampton, EPL

16 Dickman A, Littlewood C and Varga J (2002) The Syringe Driver, Oxford University Press

Guidelines for Common Drugs, Doses and Ranges for Palliative Care use with a 24-hour Syringe Driver

Drug / Class of drug/ (ampoule size)	Indications	Compatibility	Contra indications	Possible Side effects	PRN dose Onset of action	24 hr infusion dose ranges
Diamorphine Opioid analgesic (5mg, 10mg, 30mg, 100mg, 500mg)	- Pain, - Dyspnoea, - Cough, - Diarrhoea	With most drugs	None if titrated carefully against patients' symptoms. Modify dose in renal failure	Nausea, drowsiness, dry mouth, constipation, confusion, twitching	One sixth of total 24 hour infusion dose *Within 10-30mins*	Variable depending on total oral intake of morphine. Conversion of oral morphine to subcutaneous diamorphine is 1:3
Metoclopramide Prokinetic antiemetic (10mg/2mL)	- Nausea and vomiting caused by gastric irritation, - Delayed gastric emptying, - Stimulation of the CTZ, - Obstructive bowel symptoms without colic. - Non sedating	With most drugs	Concurrent administration with antimuscarinic drugs. Concurrent iv administration of 5HT3 receptor antagonists Do not give in bowel obstruction if colic present	Dizziness, diarrhoea, depression, extra pyramidal effects	10mg-30mg IM/SC every 8 hours *Within 10-15 mins*	60mg-120mg
Cyclizine Antihistaminic, antimuscarinic antiemetic (50mg/1mL)	- Nausea and vomiting associated with motion sickness, - Anticipatory nausea - Pharyngeal stimulation, - Mechanical bowel obstruction, - Raised intracranial - Pressure	Can precipitate with dexamethasone, diamorphine (in higher doses), metoclopramide, midazolam and saline	No absolute ones in patients with advanced cancer Do not give with metoclopramide Do not give with Levomepromazine Do not give with Buscopan	Drowsiness, dry mouth, blurred vision, sedation and hypotension. Injection can be painful. If syringe driver site is irritating, try to dilute further.	50mg IM / SC every 8 hours *Within 2 hours*	50mg-150mg usual dose

Haloperidol Butyrophenone Antipsychotic (5mg/mL)	- Nausea & vomiting - Psychotic symptoms - Agitated delirium - Intractable hiccup	With most drugs	Parkinson's disease. Possible CNS depression with anxiolytics & alcohol	Extra pyramidal symptoms, dry mouth, sedation, drowsiness, difficulty in micturition, hypotension, blurred vision	1.5mg– 3mg SC daily to every 8 hours *Within 10-15mins*	2.5mg – 5mg usual dose for nausea & vomiting
Levomepromazine Antiemetic, phenothiazine antipsychotic (25mg/1 mL)	- Nausea & vomiting - Insomnia - Terminal agitation - Intractable pain. - Useful as antiemetic and sedation - Can be very sedating	Precipitates with dexamethasone Do not use with cyclizine	Parkinson's disease, postural hypotension, antihypertensive therapy, epilepsy, hypothyroidism, myasthenia gravis	Sedation, dose dependent postural hypotension	6.25mg - 12.5mg IM/SC every 4 - 6 hours usual dose *Within 30 minutes*	6.25mg - 25mg usual dose for nausea & vomiting 25mg-150mg usual dose terminal agitation
Midazolam Benzodiazepine (10mg/2mL) Anxiolytic	- Sedation for terminal agitation, - Multifocal myoclonus - Epilepsy - Intractable hiccup - Muscle spasm	With most drugs	Drowsiness, hypotension	Dizziness, drowsiness	2.5mg - 10mg IM/SC every 4 hours *Within 5-10 mins*	10mg – 60 mg usual dose

Guidelines for Common Drugs, Doses and Ranges for Palliative Care use with a 24-hour Syringe Driver (continued)

Drug / Class of drug/ (ampoule size)	Indications	Compatibility	Contra indications	Possible Side effects	PRN dose Onset of action	24 hr infusion dose ranges
Glycopyrronium Bromide Quarternary ammonium antimuscarinic (0.2mg/mL, 0.6 mg / 3mL)	- Death rattle, - Colic in inoperable bowel obstruction, - Reduction of secretion - May be effective if no response to hyoscine's anti secretory effect - Does not cross the blood brain barrier so does not cause drowsiness	With most drugs	2-5 times more potent than hyoscine hydrobromide	Tachycardia, dry mouth	0.2mg SC every 6-8 hrs *Within 20-40 mins*	0.6mg - 1.2 mg usual dose
Hyoscine butylbromide Antimuscarinic antispasmodic antisecretory (20mg/mL)	- Obstructive symptoms with colic and antisecretory effects, - Death rattle	With most drugs, except cyclizine	Narrow angle glaucoma (unless moribund), myasthenia gravis.	Does not cross blood brain barrier so does not cause drowsiness	10mg – 20 mg IM every 8 hours *Within 3 - 5 mins*	Bowel obstruction with colic: 20mg - 120 mg usual dose Death rattle: 20 - 40mg usual dose
Hyoscine hydrobromide	- Reduction of secretions, e.g. death rattle	With most common drugs	Narrow angle glaucoma (unless moribund), myasthenia gravis.	Crosses blood brain barrier; ,risk of increased drowsiness/ agitation	0.4mg SC every 6-8 hours *Within 3-5 mins*	Secretions: 1.2-2.4mg/24 hours usual dose

Octreotide Somatostatin analogues FOR SPECIALIST USE ONLY (50mg/mL 100mg/mL 200mg/mL 500mg/mL)	- Intestinal obstruction associated with vomiting, - Intractable diarrhoea, symptoms associated with hormone secreting tumours, bowel fistulae - Injection can be painful (gently hand warm the vial)	Precipitates with dexamethasone	Caution in diabetes mellitus as may potentiate hypoglycaemia	Dry mouth, nausea, vomiting anorexia, abdominal pain, flatulence	50mcg -100 mcg SC every 8 hours *Within 30 mins*	Intestinal obstruction: 300ug - 600ug usual dose
Diclofenac NSAID Non opioid analgesic (75mg/3mL)	- Pain (particularly associated with tissue inflammation or bone pain/ movement related pain)	Incompatible with most drugs. Give in a separate syringe driver Use 0.9% Saline for dilution **Do not mix**	Active peptic ulceration, urticaria, rhinitis, asthma, angioedema	Skin ulceration especially with prolonged use (SC)	75mg SC every 12 hours (do not give as well as the infusion) *Within 20-30 mins*	75mg-150mg - usual dose
Dexamethasone Corticosteroid (4mg/mL)	- Antiemetic - Pain relief - Raised intracranial pressure - Spinal cord compression - Intestinal obstruction	Mixes with metoclopramide, precipitates with cyclizine, midazolam, haloperidol, and vomepromazine. Advisable to put in a separate syringe but can mix with diamorphine	Diabetes - may need supervision	Gastrointestinal side effects, impaired healing, weight gain, hirsutism, and increased appetite.	Discuss with oncology / palliative care team Not usually needed	4mg -16 mg usual dose

ELEVEN Guidelines for palliative care emergencies

11.1 HYPERCALCAEMIA

11.1.1 Tumours that commonly cause hypercalcaemia

The most common tumours are breast, myeloma, lung, head and neck, prostate and kidney. However most tumours have been implicated and calcium levels should be checked if a patient presents with symptoms.

N.B. Patients do not have to have bone metastases to have a raised calcium.

11.1.2 Common symptoms

- Confusion
- Nausea +/- vomiting
- Constipation
- Drowsiness
- Anorexia
- Lethargy
- Polyuria and Polydipsia
- Exacerbation of bone pain

11.1.3 Management[17]

- Treatment is required for symptomatic patients and those with a corrected calcium of greater than 3.0mmol/L

- Normal calcium levels: 2.15 – 2.55 mmol/L (N.B some laboratory ranges vary)
    - Beware that not all calcium results have been corrected
    - Formula to calculate corrected calcium: (40 – serum albumin g/L) x 0.02 added to ionised calcium

[17] Saunders J, Ross JR, Edmonds PM, Patel S, Johnston SR, Broadley K. Systematic Review of the Role of bisphosphonates in Metastatic Disease: Hypercalcaemia. Oral Presentation. Palliative Care Congress 2002

Corrected Calcium mmol/L	Treatment
⇠ 3 mmol/L	IV hydration of at least 2 litres per day if clinically safe
⇢ 3 mmol/L	IV hydration of at least 2 litres per day is required, followed by IV disodium pamidronate 90mg in 500mLs N/Saline over 4 hours

- The maximum effect of disodium pamidronate is seen after 7 days and is usually effective for 2-3 weeks

- *Bloods*

Check U & E's daily to ensure adequate hydration
Check calcium levels every 3 days

- *An alternative bisphosphonate is zoledronic acid.*

For corrected calcium levels of greater than 3 mmol/L treat with Zoledronic Acid 4mg by a 15-minute infusion. Adequate hydration of the patient with at least 2 litres IV fluids per day is still essential.

Seek advice from an oncologist or palliative care consultant

11.2 SPINAL CORD COMPRESSION[18] [19] [20]

11.2.1 Clinical signs and symptoms

Pain

- Localised pain in spine, radiating around chest / abdomen
- May be aggravated by coughing, sneezing, straining and lying supine
- Pain may be reproduced by percussion of the affected vertebral body or by forced neck or straight leg flexion
- Pain may be present for some time before onset of motor or sensory symptoms

Motor and sensory symptoms

- *The onset of sensory symptom*s may be sudden and rapidly progressive
- Sensory abnormalities vary from numbness and tingling to complete loss of sensation below level of damage to spinal cord
- Sphincter dysfunction
- Sudden unexplained reduction of pain in spine / legs
- Change in power – may be sudden or progressive

[18] Abraham JL Management of Pain and Spinal Cord Compression in Patients with Advanced Cancer. Annals of Internal Medicine 1999. Vol131 (1): 37-46

[19] Choudhury A, Gerrard G and Kumar S. Malignant Spinal Cord Compression. Geriatric Medicine 2002.:17-22

[20] Loblaw AD and Laperriere NJ. Emergency treatment of extradural spinal cord compression: An evidence-based guideline. Journal of Clinical Oncology 1998; 16 (4): 341-344

11.2.2 Investigation of choice

Urgent MRI of whole spine within 24 hours

11.2.3 Management

- Start high dose steroids e.g. dexamethasone 16mg/day
- Refer for radiotherapy
- Consider decompressive laminectomy if:
  - Very early presentation and solitary metastasis
  - Relapse after maximum radiotherapy
  - No history of malignancy
  - Diagnostic uncertainty
  - Progression in otherwise fit patient
  - Pain on movement
- Catheterise if sphincter involvement
- Consider:
  - Mattress
  - Pressure areas
  - Bowel function
- Do not use codanthrusate or codanthrumer as laxatives as the danthron can cause superficial burns in catheterised or incontinent patients
- Patient should be encouraged to remain mobile unless there is evidence of bony instability
- If instability exists, then stabilisation must precede mobilisation
- Input from the physiotherapist and occupational therapist should occur from the start

11.3 HAEMORRHAGE

This may be directly related to the underlying tumour, caused by treatment i.e. steroids or NSAIDs, or due to a generalised clotting deficiency.

11.3.1 Non acute haemorrhage

Treatment includes:

- Radiotherapy, for example to superficial tumours and those of bronchus and genitourinary tract
- Systemic treatment with Tranexamic Acid 1g t.d.s, however beware that clots may form in the bladder if used for haematuria.

NB Consider carefully if patient has a history of CVA or Ischaemic heart disease

- Local measures include topical tranexamic acid or adrenalin (1:1000) soaks. Also Sucralfate may stop stomach mucosal bleeding although will inhibit the absorption of proton pump inhibitors

11.3.2 Acute haemorrhage

- Erosion of a major artery can cause acute haemorrhage, which may be a rapidly terminal event.
- If it is possible to anticipate such an event appropriate medication should be readily available
- If the haemorrhage is not immediately fatal i.e. haematemesis, bleeding from rectum, vagina or superficially ulcerated wound, the aim of treatment is local control of bleeding and sedation of a shocked patient with rectal or sublingual diazepam 10mg or midazolam 5 – 10mg SC or buccally

Relatives will need a lot of support if they witness such a haemorrhage.

TWELVE Guidelines for mouthcare

12.1 CONTRIBUTING FACTORS

In most patients there are multiple contributing factors, eg:

- Poor fluid intake
- Poor nutritional state
- Medication which dries the secretions i.e. amitriptyline, morphine, hyoscine
- Radiotherapy to the facial area
- Reduced capacity for the patient to manage their own oral hygiene

12.2 MANAGEMENT

Mouth care should be given routinely to all patients with palliative care needs, paying particular attention to those who are unable to manage this themselves. Families may want to contribute to this role. This includes:

- Regular teeth brushing with toothpaste, after meals
- Regular cleaning of dentures
- Regular mouth washing with e.g. chlorhexidine mouthwash
- Keeping the mouth moist
- Regular inspection of the oral mucosa for potentially reversible causes or problems, such as infection, bleeding and pain.

12.2.1 Non-specific dry mouth

- Frequent sips of water
- Suck ice cubes
- Partly frozen drinks e.g. pineapple juice
- Sugar-free chewing gum
- Artificial saliva i.e. saliva orthana, salivix pastilles, SST tablets
- Effervescent vitamin C
- Pilocarpine 5mg t.d.s
- Petroleum jelly on lips

NB Avoid glycerin and lemon juice, which may dry the mouth further

12.2.2 Infection

• *Candida*:

- Fluconazole 150mg stat or 50mg daily for 7 – 14 days
- Nystatin 1-2mLs every 4 hours
- Amphoteracin gel or miconazole

• *Herpes simplex*:

- Aciclovir cream / tablets

• *Bacterial infection*:

- Appropriate antibiotic or tetracyline mouthwash
- Metronidazole orally, rectally or topically if foul smell

• *Bleeding*

This is often associated with local oral cancer or deficiencies in blood clotting.

- Consider giving platelets or vitamin K as appropriate
- Avoid over vigorous mouth hygiene
- Tranexamic acid mouthwash or try a gauze soaked in tranexamic acid
- Oral tranexamic acid

• *Pain*

Where there is a specific pain treat the cause, i.e. infection or candidiasis

Aphthous ulceration, treat with:

- Adcortyl in orabase
- Carbenoxolone sodium mouthwash
- Hydrocortisone pellets

Generalised mouth pain:

- Soluble paracetamol / co-codamol / aspirin as a mouthwash +/- swallow
- Opioids if the pain is severe
- Topical anaesthetics e.g. benzydamine mouthwash, benzocaine lozenges, choline salicylate, mucaine suspension

NB Sucralfate paste/mouthwash or Gelclair which coat the oral mucosal surfaces may provide extra comfort

SOUTH LONDON PALLIAIVE AND SUPPORTIVE CARE NETWORK
SURREY WEST SUSEX HAMPSHIRE CANCER (SWSH) NETWORK

Comments regarding the Hospital Guidelines for Palliative Care

Date:

1. Comment relates to section

2. Drugs not included within the guidelines that should be:

Section

Indications for use

3. Drugs to be removed form the guidelines:

Section

Reason

4. Any overall comment

Within the South East London Cancer Network please return comments to:

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Acknowledgments

The contributors would like to thank NAPP Pharmaceuticals and the South East London Cancer Network for generously supporting the production of these guidelines.

design: www.thiswayupdesign.co.uk