Symptom management in ESRD

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Why is this an important aspect of patient management ?

- Symptoms are prevalent
- Symptoms are multiple
- Symptoms are burdensome

What are the common symptoms associated with ESRD ?

The Prevalence of Symptoms in End-stage Renal Disease : A systematic Review

Murtagh FE et al. *Advances in Chronic Kidney Disease*

Vol 14, No 1 (January) 2007; pp 82-99

SYMPTOM PREVALENCE

- 59 studies in dialysis patients
- 1 in dialysis discontinuation
- None in patients without dialysis

SYMPTOM PREVALENCE

FATIGUE/TIREDNESS	71%
PRURITIS	55%
CONSTIPATION	53%
ANOREXIA	49%
PAIN	47%
SLEEP DISTURBANCE	44%

SYMPTOM PREVALENCE

ANXIETY	38%
DYSPNOEA	35%
NAUSEA	33%
RESTLESS LEGS	30%
DEPRESSION	27%

Patients who are treated conservatively and who never receive dialysis

A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis

Murtagh FEM et al. J Pall Med (2007) 10;6:1266-1276

- Longitudinal data collection
- Symptoms assessed within one month of entry into trial using Memorial Symptom Assessment Scale (MSAS-SF) plus 7 common renal symptoms.

- Fatigue 75 %
- Pruritis 74 %
- Dyspnea 61 %
- Pain 53 %
- Restless legs 48 %
- Anorexia 47 %
- Insomnia 42 %

		A little/ somewhat	Quite a lot/ very much
Fatigue	75 %	39 %	36 %
Pruritis	74 %	42 %	32 %
Dyspnea	61 %	38 %	23 %
Pain	53 %	21 %	32 %
Restless legs	48 %	38 %	11 %
Anorexia	47 %	36 %	11 %
Insomnia	41 %	20 %	21 %

Symptom control is challenging

Symptoms interact and compound each other

U.Pruritis

RLS → Insomnia → Fatigue

Pain

Symptoms may derive from the co-morbidities

ESRD constrains the use of medication

Principles of symptom management

1. Think of the cause(s).

2. Be meticulous

3. Principle of non-abandonment

Background of symptoms

ESRD

and its treatment

Co-morbidities

FATIGUE

Complex and multifactorial

- Anaemia - Hb best kept at 11-12
- Electrolyte imbalance

Hyper K	Hypo K
Hyper Ca	Hypo Ca
	Hypo Mg
	Hypo Na
	Hypo PO_4

- Nutritional deficiency
- Depression
- Insomnia > Daytime somnolence
- Pain > deconditioning

Fatigue will have an effect on multiple other aspects for the patient :

- QOL
- ADLs
- Need for transport assistance
- Frustration

Management

- Optimize Dialysis
- Correct reversible causes
- Physiotherapy
- Sleep Hygiene
- Social Supports

- If profound – consider Ritalin 10mg mane

PAIN

Impact on QOL

Davison (2002)

69 dialysis patients

62% stated that pain interfered with their ability to participate and enjoy recreational activities.

51 % stated that pain caused them "extreme suffering"

41 % stated that pain caused them to consider ceasing Dialysis

Positive correlation with depression

Davison S, Jhangri GS. J Pain Symptom Management 2005; 30(5): 465-473

Causes of Pain

ESRD
and its treatment

Co-morbidities

ESRD and treatment

Disease related :

- Polycystic Kidney Disease
- Renal Bone Disease
- Amyloid

Dialysis-related pain :

- PD pts with recurrent abdominal pain
- AV Fistulae > ‘Steal syndrome’
- Cramps

Co-morbidities

- OA
- Diabetic neuropathy
- PVD

Pain etiquette

- ENQUIRE REGULARLY
- RESPOND COMPASSIONATELY
- TREAT COMPETENTLY
- REFER WISELY

Principles of pain management

1. Always enquire about pain.
2. Treat the underlying cause of the pain.
3. Treat the pain meticulously.
4. Treat the pain proportionately.
5. Constantly reassess.

Pain Assessment

- Location
- Intensity
- Quality
- Duration

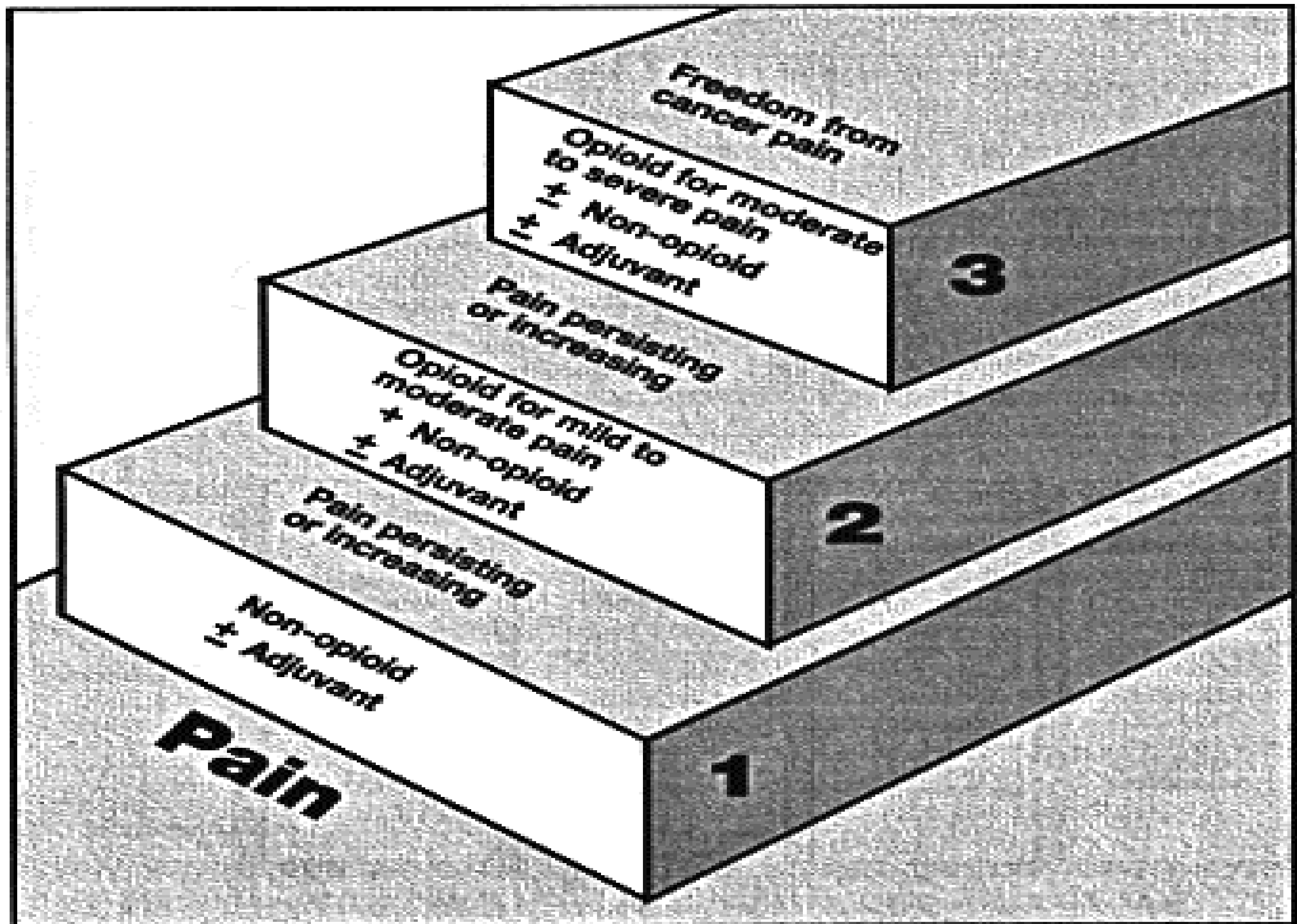
WHO - Pain

WHO method for pain relief

- Right drug
- Right dose
- Right time intervals

WHO method for pain control

- By the mouth
- By the clock
- By the ladder


The WHO three-step analgesic ladder
Freedom from cancer pain
Opioid for moderate to severe pain
± Non-opioid
± Adjuvant
3
Pain persisting or increasing
Opioid for mild to moderate pain
± Non-opioid
± Adjuvant
2
Pain persisting or increasing
Non-opioid
± Adjuvant
1
Pain
Source: World Health Organization, 1990. Used with permission.

Step 1

Paracetamol

“It is considered the non-narcotic analgesic of choice for mild-moderate pain in CKD patients.”

Davison S, Ferro CJ. Management of Pain in CKD. *Progress in Palliative Care* 2009; 17: 186-195.

Step 2

Tramadol “is the least problematic of the Step 2 Analgesics for ESRD patients”

Nevertheless use with caution – use a bd dose.

If on Dialysis or
on Conservative pathway eGFR 15-30

Commence 50mg bd

Maximum 100mg bd

If on a Conservative pathway

eGFR < 15

Tramadol 50mg bd (maximum)

Step 3

Hydromorphone

- Commence low and qid.
- If tolerated – q4hours
- Titrate up dose carefully – once pain well controlled aim to convert to Fentanyl patch

Fentanyl

Methadone

The hand that writes the opioid must also write the laxative

NEUROPATHY

- Uraemic peripheral neuropathy

- Diabetic peripheral neuropathy

Uraemic peripheral neuropathy

- Mixed motor/sensory polyneuropathy
- Distal, symmetrical
- Sensory earlier than motor

Management

- Adequate Dialysis - Kt/V at least 1.2
- High flux membrane to ensure good middle molecule clearance
- Check Thiamine
- Meds – TCA, Gabapentin

NAUSEA

Look for the cause (s)

- Uraemia → CTZ zone
- Delayed Gastric emptying
- Concurrent medications
- Constipation

Treat the symptom :

Maxalon 5mg – 10mg tds

Haloperidol 0.5mg bd

Cyclizine 25- 50mg tds

Ondansetron 4mg bd

CRAMPS

In Dialysis patients :

Secondary to removal of fluid/solutes

Treat by :

Adjusting the Dialysis Na/K

Quinine prior to dialysis

Carnitine 1-2 g IVI during dialysis

Cramps in patients not on Dialysis :

Quinine

INSOMNIA

This may be the product of multiple other symptoms

- Pain
- Uraemic Pruritis
- Cramps
- RLS
- Periodic Leg Movement Disorder
- Sleep Apnea

- Treat the cause

- Treat the symptom

General measures

- No caffeine after lunchtime
- No alcohol at night
- No smoking at night
- Temazepam 10-20mg nocte

Specific measures

If suspicious of Sleep Apnea –

Formal Sleep Study

RESTLESS LEGS SYNDROME

Definition

1. An urge to move the limbs, usually associated with parasthesias/dysthesias
2. Motor Restlessness
3. Symptoms exclusively while at rest, with relief (completely or partially) with movement.
4. Symptoms worse at night.

International RLS Study Group – Definition of RLS (1995)

Incidence in the general population :
2-15 %

Incidence in ESRD : 20-30 %

Mechanism is not completely understood

- Dopaminergic dysfunction
- Fe metabolism
- Supraspinal inhibition

Management

Clonazapem

0.5mg – 1mg nocte

Dopamine agonists

- Ergot-Dopamine Agonists (Pergolide, Cabergoline)

- Non-Ergot Dopamine Agonists (Pramipexole, Ropinirole, Rotigotine)

- Augmentation

- Rebound

Gabapentin

Two Level 1 studies have shown efficacy for Gabapentin in the treatment of RLS in Dialysis patients

- Study A – Placebo controlled – Thorp et al (2001)
- Study B – Gabapentin compared to Levo-dopa – Micozkadioglu et al (2004)

On Dialysis

Gabapentin 300mg after each Dialysis

On conservative management

Gabapentin 100-300mg every 2nd night

“In Stage 5 CKD without dialysis it is preferable not to use.”

Murtagh FEM, Weisbord D . Symptom management in renal failure. In : Chambers EJ et al (eds). *Supportive Care for the Renal Patient*. 2nd ed. 2010. OUP, p. 123.

URAEMIC PRURITIS

Mechanism not understood

C Fibres

- Histamine – sensitive fibres

- Histamine – insensitive fibres

In the dermal layer a complex interaction between :

Mast Cells

Lymphocytes

Keratinocytes

Large number of therapies described

Correct Calcium/Phosphate

Dialyise efficiently

What therapies have the strongest foundation in evidence – based practice ?

- Oral medications
- Topical preparations
- UV Therapy

Gabapentin

There are 3 (three) Level 1 studies showing that Gabapentin has significant efficacy in treating uraemic pruritis

Gunal et al (2004)

Naini et al (2007)

Razeghi et al (2009)

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Thalidomide 100mg nocte

Silva SR. *Nephron* 1994; 67(3): 270-273

Other oral medications

- Anti-Histamines – evidence does not support use.
- Ondansetron – conflicting results. Not recommended.
- Cimetidine – not recommended
- Naltrexone – conflicting results. Not recommended.

Murtagh FEM, Weisbord D . Symptom management in renal failure. In : Chambers EJ et al (eds). *Supportive Care for the Renal Patient*. 2nd ed. 2010. OUP. p. 120

Topical preparations

UV Therapy

CONSTIPATION

Multifactorial

- Reduced mobility
- Reduced fluid intake
- Medication – oral Fe, PO4 binders, opioids
- Poor diet
- More common on CAPD

- General measures – Increased fluids, high fibre diet, increased mobility

- Specific – combination of softener (eg. Coloxyl) and stimulant (eg. Senna)

ANOREXIA

Multifactorial

- Nausea
- Dry mouth
- Altered taste
- Delayed gastric emptying
- Depression
- Uraemia
- Inadequate dialysis
- Abdominal discomfort and swelling from CAPD

- Patients on Dialysis require 2 x protein of the non-dialysis patient.
- Chronic Protein Energy Malnutrition is common

Management

- Attempt to reverse the reversible causes
- Renal Dietician Review
- Megace 160mg bd

ANXIETY

Psychosocial support

BZ have a prolonged half-life

Lorazepam (Ativan) sublingually useful for panic attacks

DEPRESSION

Incidence – 5-22 % of patients

O’Donnell K, Chung Y. The diagnosis of major depression in end-stage renal disease. Psychother Psychsom (1997) 66:38-43.

Difficult to accurately diagnose with multiple neuro-vegetative symptoms already present with the ESRD –

Fatigue, anorexia, insomnia

Do you feel depressed ?

1. SSRIs that can be used without dose adjustment are :

   Citalopram, Fluoxetine, Sertraline

2. TCA

Conclusion

- Symptom management is an important arm of management.

- Symptoms are prevalent and multiple

- Be meticulous

- Symptom relief may have a significant impact of patients’ Hr QOL