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

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue/Tiredness</td>
<td>71%</td>
</tr>
<tr>
<td>Pruritis</td>
<td>55%</td>
</tr>
<tr>
<td>Constipation</td>
<td>53%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>49%</td>
</tr>
<tr>
<td>Pain</td>
<td>47%</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>44%</td>
</tr>
<tr>
<td>Symptom</td>
<td>Prevalence</td>
</tr>
<tr>
<td>---------------------</td>
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</tr>
<tr>
<td>Anxiety</td>
<td>38%</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>35%</td>
</tr>
<tr>
<td>Nausea</td>
<td>33%</td>
</tr>
<tr>
<td>Restless Legs</td>
<td>30%</td>
</tr>
<tr>
<td>Depression</td>
<td>27%</td>
</tr>
</tbody>
</table>
Patients who are treated conservatively and who never receive dialysis
A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis

• 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 %
<table>
<thead>
<tr>
<th>Symptom</th>
<th>A little/ somewhat</th>
<th>Quite a lot/ very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>75 %</td>
<td>39 %</td>
</tr>
<tr>
<td>Pruritis</td>
<td>74 %</td>
<td>42 %</td>
</tr>
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<td>61 %</td>
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</tr>
<tr>
<td>Insomnia</td>
<td>41 %</td>
<td>20 %</td>
</tr>
</tbody>
</table>
Symptom control is challenging
Symptoms interact and compound each other
U. Pruritis
RLS → Insomnia → Fatigue
Pain
Symptoms may derive from the comorbidities
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 PO4
- 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

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

1. Pain
   - Non-opioid + Adjuvant

2. Pain persisting or increasing
   - Opioid for mild to moderate pain + Non-opioid + Adjuvant

3. Pain persisting or increasing
   - Opioid for moderate to severe pain + Non-opioid + Adjuvant
   - Freedom from cancer pain

Step 1

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

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 parasthseias/dysthesias
2. Motor Restlessness
3. Symptoms exclusively while at rest, with relief (completely or partially) with movement.
4. Symptoms worse at night.

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 Levodopa – Micozkadioglu et al (2004)
On Dialysis

Gabapentin 300mg after each Dialysis

On conservative management

Gabapentin 100-300mg every 2\textsuperscript{nd} night
“In Stage 5 CKD without dialysis it is preferable not to use.”

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

Dialyse 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

Naini et al (2007)
Razeghi et al (2009)
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.”

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.

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. Coloxyll) 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

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