

Symptom management in ESRD

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Why is symptom management an important aspect of patient care ?

Patients rate symptoms and their management very highly.

Patients' priorities for health research: focus group study of patients with chronic kidney disease

Tong A et al. *Nephrol Dial Transplant* 2008; 23: 3206-324.

Setting research priorities for patients on or nearing dialysis

Manns B et al. *CASN* 2014; 9: 1813-1824.

The 2 most frequent cited priorities by patients were:

1. The prevention of progression of CKD.
2. Symptoms and their management.

In 2016 the Kidney Health Initiative (KHI)
(a partnership between the ASN and the FDA)
conducted a study of US dialysis patients.

Flythe J et al. *CJASN* 2018; 13: 735-745.

Which symptoms would you give the highest priority in finding better treatments ?

Physical symptoms

- Fatigue
- Insomnia
- Cramps

Mood symptoms

- Anxiety
- Depression
- Frustration

- 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

Dialysis

FATIGUE/TIREDNESS	71%
PRURITUS	55%
CONSTIPATION	53%
ANOREXIA	49%
PAIN	47%
SLEEP DISTURBANCE	44%
ANXIETY	38 %
DYSPNEA	35 %
NAUSEA	33 %
RESTLESS LEGS	30 %
DEPRESSION	27 %

A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis = NFD 1

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

The symptoms of patients with CKD stage 5 managed without dialysis. = NFD 2

Brennan FP et al. *Progress in Palliative Care* 2015; 23 (5): 267-273.

SYMPTOM PREVALENCE

	NFD1	NFD2
FATIGUE/TIREDNESS	75%	88
PRURITUS	74%	69
CONSTIPATION		43
ANOREXIA	47%	62
PAIN	53%	45
SLEEP DISTURBANCE	42%	57
ANXIETY		43
DYSPNEA	61%	60
NAUSEA		
RESTLESS LEGS	48 %	
DEPRESSION		52

Between March 2009 and June 2019:

192 conservative and
126 renal replacement therapy patients
completed more than one POS

	NFD- First Visit (n=192)		RRT- First Visit (n=126)	
	Overall prevalence	Severe/ Overwhelming	Overall prevalence	Severe/ Overwhelming
Pain	58%	18%	69%	31%
Lack of Energy	83%	31%	86%	32%
Nausea	23%	1%	28%	6%
Poor appetite	47%	10%	48%	9%
Itch	60%	23%	60%	21%
Difficulty sleeping	56%	22%	66%	33%
Restless Legs	29%	7%	42%	12%

Symptom control is challenging

Symptoms interact and compound
each other

U.Pruritus

RLS



Insomnia



Fatigue

Pain

Symptoms may derive from
the co-morbidities.

ESRD constrains the use of medication

Pharmacology in the context of CKD
is complex

Gaps in knowledge

Recommendations in published data occasionally conflict on the specific doses of medications to be used.

Principles of symptom management

1. Think of the cause(s).
2. Be meticulous
3. Principle of non-abandonment

Symptom measurement instruments

I-POS – Renal

IPOS-Renal Patient Version



Patient name :

Date (dd/mm/yyyy) :

Patient number : (for staff use)

www.pos-pal.org

Q1. What have been your main problems or concerns over the past week??

1.
2.
3.

Q2. Below is a list of symptoms, which you may or may not have experienced. For each symptom, please tick the box that best describes how it has **affected you over the past week?**

	Not at all	Slightly	Moderately	Severely	Overwhelmingly
Pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weakness or lack of energy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea (feeling like you are going to be sick)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vomiting (being sick)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Poor appetite	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sore or dry mouth	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Drowsiness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Poor mobility	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Itching	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Difficulty Sleeping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Restless legs or difficulty keeping legs still	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Changes in skin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diarrhoea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Please list any other symptoms not mentioned above, and tick the box to show how they have affected you over the past week?

1.
2.
3.

Over the past week:

	Not at all	Occasionally	Sometimes	Most of the time	Always
Q3. Have you been feeling anxious or worried about your illness or treatment?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q4. Have any of your family or friends been anxious or worried about you?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q5. Have you been feeling depressed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Always	Most of the time	Sometimes	Occasionally	Not at all
Q6. Have you felt at peace?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q7. Have you been able to share how you are feeling with your family or friends as much as you wanted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Q8. Have you had as much information as you wanted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Problems addressed/ No problems	Problems mostly addressed	Problems partly addressed	Problems hardly addressed	Problems not addressed
Q9. Have any practical problems resulting from your illness been addressed? (such as financial or personal)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	None at all	Up to half a day wasted	More than half a day wasted		
Q10. How much time do you feel has been wasted on appointments relating to your healthcare, e.g. waiting around for transport or repeating tests	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	On my own	With help from a friend or relative	With help from a member of staff		
Q11. How did you complete this questionnaire?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

If you are worried about any of the issues raised on this questionnaire then please speak to your doctor or nurse

FATIGUE

Patient Perspectives on the Meaning and Impact of Fatigue in Hemodialysis: A Systematic Review and Thematic Analysis of Qualitative Studies

Jacobsen J et al. *Am J Kid Dis* 2019.

For patients undergoing dialysis who experience fatigue, fatigue is a profound and relentless exhaustion that pervades the entire body and encompasses weakness.

The fatigue drains vitality in patients and constrains their ability to do usual activities and fulfil their roles and meet personal aspirations.

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

- QOL
- ADLs
- Need for transport assistance
- Frustration

Mechanism is complex and multifactorial.

Anaemia -

1. If on dialysis Hb best kept at 10-12.
2. If not on dialysis – treat according to symptoms.

Dialysis-related issues

Insomnia → Daytime somnolence

- Nutritional deficiency
- Depression
- Medications
- Pain → deconditioning

Electrolyte imbalance :

Hyper K

Hyper Ca

Hypo K

Hypo Ca

Hypo Mg

Hypo Na

Hypo PO₄

Management

- Optimise Dialysis
- Correct reversible causes
- Exercise
- Sleep Hygiene
- Social Supports

Fatigue in CKD

has been the subject of a growing international focus.

International Fatigue Consensus Workshop was held in 2016.

Standardized Outcomes in Nephrology-Hemodialysis (SONG-HD)

They found there was no satisfactory renal-specific fatigue instrument.

They called for a core outcome measure on fatigue in CKD.

That such an instrument must be:
“simple,
short and
include a focus on the severity of the impact
of fatigue on life participation.”

Ju A et al. *Am J Kid Dis* 2018; 72(1): 104-112.

URAEMIC PRURITUS

Not every patient with ESKD
reporting itch
has uraemic pruritus.

At the point of assessment always consider a differential diagnosis of the pruritus.

Associations

- Poor sleep quality
- Depression
- QOL
- Mortality

Pisoni RL, Wikstrom B et al. *Neprol Dial Transplant* 2006; 21: 3495-3505.

The pathogenesis of pruritus
remains elusive.

There are a plethora of suggested treatments

Pathogenesis

Management

Too often the literature concentrates on one or the other but rarely both

The pathogenesis of pruritus

C Fibres

5- 10 % of the C fibres
are dedicated to itch

For many years the assumption was :

Histamine → C Fibres → Spinal Cord

Of the C Fibres that are itch-sensitive :

10 % are Histamine-dependent

90 % are Histamine-independent

Davidson S. *J Neuroscience* 2007;27: 10007-14

Nainer B. *J Neurophysiology* 2008;100: 2062-9.

Myth 1

That all itch is histamine mediated

Myth 2

That the best first line medication for pruritus of whatever cause are Anti-Histamines

Pathogenesis of UP

Multiple theories, conflicting findings

Adequacy of dialysis

Dialysis adequacy (as measured by Kt/V)
did not correlate with the frequency of UP
in large epidemiological studies

Pisoni RL, Wikstrom B et al. *Neprol Dial Transplant*
2006; 21: 3495-3505.

Narita et al. *Kidney Int* 2006;69; 1626-32.

Duque et al. *Clin Nephrology* 2006; 66: 184-191.

Xerosis

Dry skin is an association
and exacerbating factor
but not a primary cause

Szepietowski JC. *Nephrol Dial Transplant* 2004; 19: 2709-2712.

HyperParathyroidism

- There is no correlation between PTH levels and UP
- PTH itself is not pruritogenic

Calcium

Inconsistent findings on s.Calcium and UP

Two studies found increased extracellular calcium ions in the deepest layer of the epidermis in patients on HD with UP

Momose A et al. *Neprol Dial Transplant* 2004 ; 19; 2061-2066.

Momose et al. *Nephron* 2017; 136(2): 103-110.

Phosphate

Inconsistent findings on Phosphate and UP

s. Calcium x s. Phosphate

In the DOPPS II study
only at a very high Calcium-Phosphate
product (ie. $> 80 \text{ mg}^2/\text{dL}^2$)
was there a correlation with UP frequency

Pisoni RL, Wikstrom B et al. Nephrol Dial Transplant
2006; 21: 3495-3505.

“Despite this vast array of possible explanations, none consistently have been demonstrated to be the underlying cause of pruritus associated with CKD. Large epidemiological studies ultimately may facilitate our understanding of the elusive pathophysiological process of this distressing symptom.”

Patel TS et al. *Am J Kidney* 2007; 50(1): 11-20.

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

- Topical preparations
- Oral medications
- UV- B Therapy

Topical preparations

Moisturisers

Capsaicin cream

There are three RCT studies showing efficacy for Capsaicin cream in UP

Major side effect –
transient “burning” feeling on the skin

Breneman DL et al. *J Am Acad Dermatol* 1992; 26: 91-94. Tarng D-C et al. *Nephron* 1996; 72: 617-622; Maklough A. *Iranian J Kid Dis* 2010;4(2): 137-140.

Over the past two years,
especially in intractable cases,
we have been trialling novel combinations of
creams

guided by the emerging understanding of
the pathophysiology of itch.

Novel creams

Capsaicin 0.025 % and
Menthol cream 3 %

Lignocaine 5 %

Menthol 3 %

Systemic therapies

Gabapentin

Gabapentin for uremic pruritus in hemodialysis patients : a qualitative systematic review.

Lau T et al. *Canadian J Kidney Health and Disease* 2016; 3: 14.

“Our review supports a trial of Gabapentin for the management of UP in hemodialysis patients refractory to antihistamines and/or emollients. The results should be interpreted cautiously due to the lower quality of included studies. We recommend a starting dose of 100mg after hemodialysis to minimize adverse events...”

Treatment of Uremic Pruritus : A Systematic Review.

Simonsen E et al. *Am J Kid Dis* 2017. Article in Press.

“The main finding...is that with exception of the evidence for gabapentin, there remains considerable uncertainty about effective treatments for this important and burdensome symptom...”

On Dialysis

Gabapentin 100 mg after each Dialysis

Titrate to effect

On conservative management

eGFR < 15

Gabapentin 100mg every 2nd night

Titrate to effect

On conservative management

eGFR > 15

Gabapentin 100mg nocte

Titrate to effect

Pregabalin

Several prospective cohort studies showed efficacy.

Aperis. *J Renal Care* 2010; 36(4): 180-185; Shavit L. *J Pain Symptom Management* 2013; 45(4): 776-781.

Evening Primrose Oil

Chen YC et al. *Am J Kid Dis* 2006; 48: 69-76

Gamma Linolenic Acid (GLA)

Essential Fatty Acids (EFA) in the epidermis

n- 6 EFA

Linolenic Acid (LA)



Gamma -Linolenic Acid (GLA)



DGLA



Arachidonic Acid



Adrenic Acid



Docosapentaenoic Acid

n-EFA

Linolenic Acid (LA)



Gamma-Linolenic Acid (GLA)



DGLA



Arachidonic Acid (AA)

PGE2



Leukotriene B4



Adrenic Acid



Docosapentaenoic Acid

Supplementing the Gamma-Linolenic Acid (GLA) has an anti-inflammatory/ anti-itch effect

n-EFA

Linolenic Acid (LA)



Gamma -Linolenic Acid (GLA)



DGLA

PGE1



15 OH DGLA



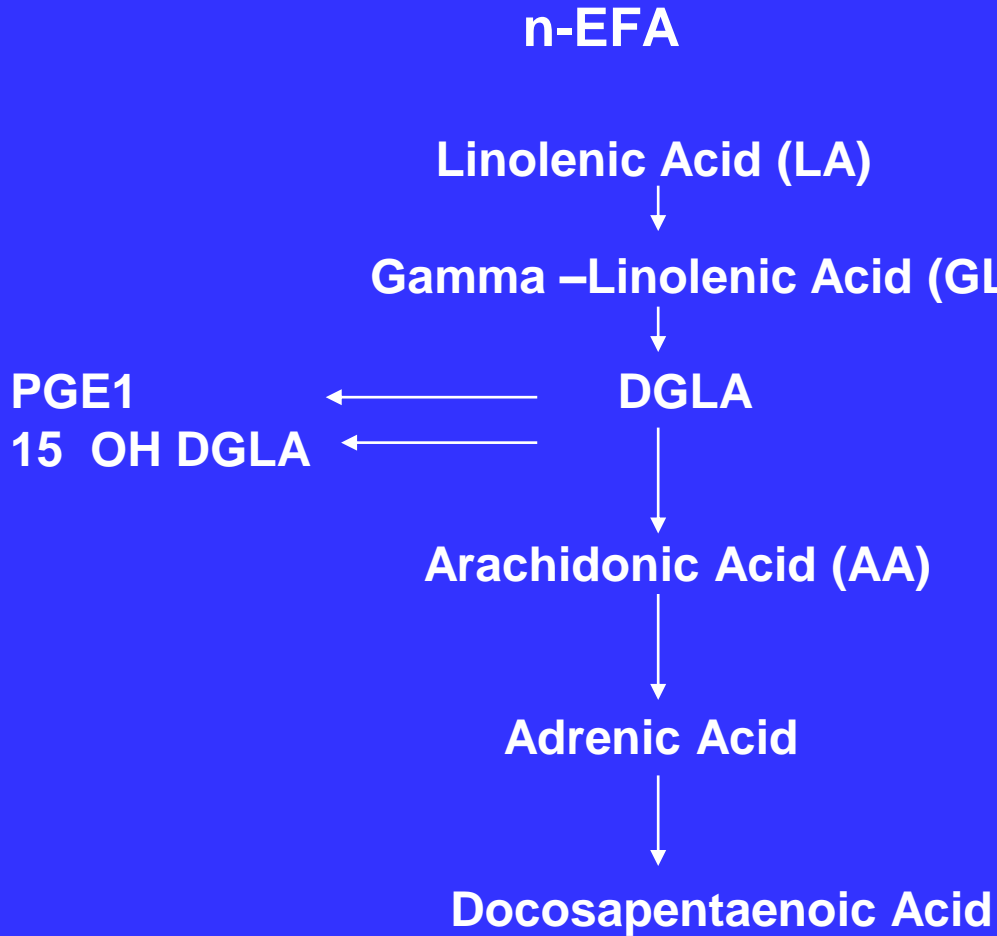
Arachidonic Acid (AA)



Adrenic Acid



Docosapentaenoic Acid



100- 200mg bd

= Super Evening Primrose Oil
contains 200mg GLA per capsule

Sertraline (SSRI)

Shakiba M et al. *Int J Nephrology* 2012;
Article ID 363901; 1-5

- Before and after trial of 19 HD patients.
- 50mg daily for 4 months.
- The difference in the grade of pruritus before and after sertraline was significant.

Thalidomide 100mg nocte

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

Kappa – receptor agonists

Wikstrom B et al. *J Am So Nephrol* 2005; 16: 3742-3747;

Kumagai H et al. *Nephrol Dial Transplant* 2010; 25: 1251-1257.

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. To THM et al. *J Pain Symptom Management* 2012;44: 725-730.

UV B Therapy

Acupuncture

Che-yi et al. *Nephrol Dial Transplant* 2005; 20: 912-915

Uraemic pruritus summary

Moisturisers plus

1. Gabapentin/Pregabalin

2. Evening Primrose Oil

3. UV – B therapy

4. Others.

Note - Anti-histamines do not help

PAIN

Epidemiology of pain in CKD

Haemodialysis patients – 68.9 %

Pooled mean weighted prevalence of 19 studies since 2000

Davison S, Brennan F. Pain in CKD. In : *Evidence Based Nephrology*. In Press.

40.4 % reported the pain as moderate to severe.

Davison S, Brennan F. Pain in CKD. In : *Evidence Based Nephrology*. In Press.

Data on conservatively managed patients
is more limited
but shows similar prevalence and severity
figures.

Murtagh FEM et al. A Cross-sectional Survey of Symptom Prevalence in Stage 5 CKD managed without Dialysis. *J Pall Med* (2007) 10;6:1266-1276.
Brennan FP. et al. Symptoms in patients with CKD managed without dialysis. *Progress in Palliative Care* 2015; 23 (5): 267-273.

Impact on function and QOL

Data from 9 studies representing approximately 2100 HD patients found that pain was associated with lower HR-QOL.

Table 2 in Davison S, Koncicki H, Brennan F. Pain in Chronic Kidney Disease : A Scoping Review. *Seminars in Dialysis* 2014; 27(2): 188-204.

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

Independently associated with:

- Missed or shortened dialysis sessions
- A+E presentations
- Hospitalisations.

Weisbord SD et al. *Clin J Am Soc Nephrol* 2014; 9(9): 1594-1602.

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

1. Pain related to the disease:

- Polycystic Kidney Disease
- Renal Bone Disease
- Amyloid – including Carpal Tunnel Syndrome
- Calciphylaxis

2. Pain secondary to treatment :

- PD pts with recurrent abdominal pain
- AV Fistulae > 'Steal syndrome'
- Cramps
- Intradialytic headaches

3. Pain related to co-morbidities

- OA
- Diabetic peripheral neuropathy
- PVD / IHD

Pain etiquette

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

Pain management in patients with CKD

The traditional approach to the pharmacological management of pain has been to use the WHO Analgesic Ladder.

Certainly, the WHO Ladder
has been validated in the context of ESKD
and it remains a very useful construct.

Is an approach based on the WHO
Analgesic Ladder the most appropriate
approach in the specific context of CKD ?

Towards a strategic approach to pain management in patients with CKD

1. There are few studies
examining pain management
in the specific context of CKD

2. There are international evidence based guidelines and consensus statements on pain management of specific pain syndromes for the whole population.

- Osteoarthritis
- Painful diabetic peripheral neuropathy
- Post herpetic neuralgia
- Cancer pain

3. There is an increasing, although not complete, understanding of the pharmacology of analgesic medications in the context of CKD and their dialysability

These recommendations could be filtered through the known pharmacology of medications in the context CKD and their dialysability

Pain syndrome



Evidence based Guidelines and Consensus Statements



Pharmacokinetics/Pharmacodynamics



Pain management for patients in the context of CKD

An example...

Painful diabetic peripheral neuropathy

1. Currently there are no evidence-based or consensus guidelines on the management of painful DPN in patients with CKD.

“Clinical evidence regarding the effects of [analgesic agents] to treat DPN in patients on dialysis therapy and those with CKD Stage 4-5 is virtually non-existent.”

Pop- Busui R et al. The Management of Diabetic Neuropathy in CKD. *Am J Kid Dis* 2010; 55(2): 365-385.

2. There is a significant body of literature on the management of painful DPN.

That literature includes several international evidence based guidelines.

Evidence-based guideline : Treatment of painful diabetic neuropathy. Report of the American Association of Neurology et al.

Bril V et al. *Neurology* 2011; 76: 1758-1765.

Level A Evidence - Pregabalin

Novel combination creams

1. Capsaicin 0.025 % and
Menthol cream 3 %

2. Lignocaine 4%
Prilocaine 1.5 %
Tetracaine 4%

Role of Pain Services

Pain management in patients with ESKD

A one day Symposium - 2016

St George Hospital, Sydney

Cramps

Prevalence: 33- 78 % in HD

Associated with premature cessation of dialysis sessions → inadequate dialysis.

Causes:

1. Fluid-electrolyte shifts during dialysis.
2. Muscle fatigue → inhibits the mechanism that blocks muscle contraction.

Management:

1. Magnesium -- Crampeze 1-2 bd
2. Quinine -- Tonic water
3. Stimulation of the oropharyngeal reflex that inhibits α - motor neurons leading to muscle relaxation...Pickle juice / vinegar / yellow mustard / ginger.

RESTLESS LEGS SYNDROME

Definition

1. An urge to move the limbs, usually associated with paresthesia/dysaesthesia
2. Motor Restlessness
3. Symptoms exclusively while at rest, with relief (completely or partially) with movement.
4. Symptoms worse at night.
5. Cannot be solely attributed to another cause.

Not all ESKD patients
with a disturbance of their legs
have Restless Legs Syndrome.

Differential diagnosis

- Leg cramps
- Peripheral neuropathy
- Osteoarthritis
- Pruritus
- Akathisia

Associations

Sleep disturbance

Daytime somnolence

Premature cessation of dialysis sessions

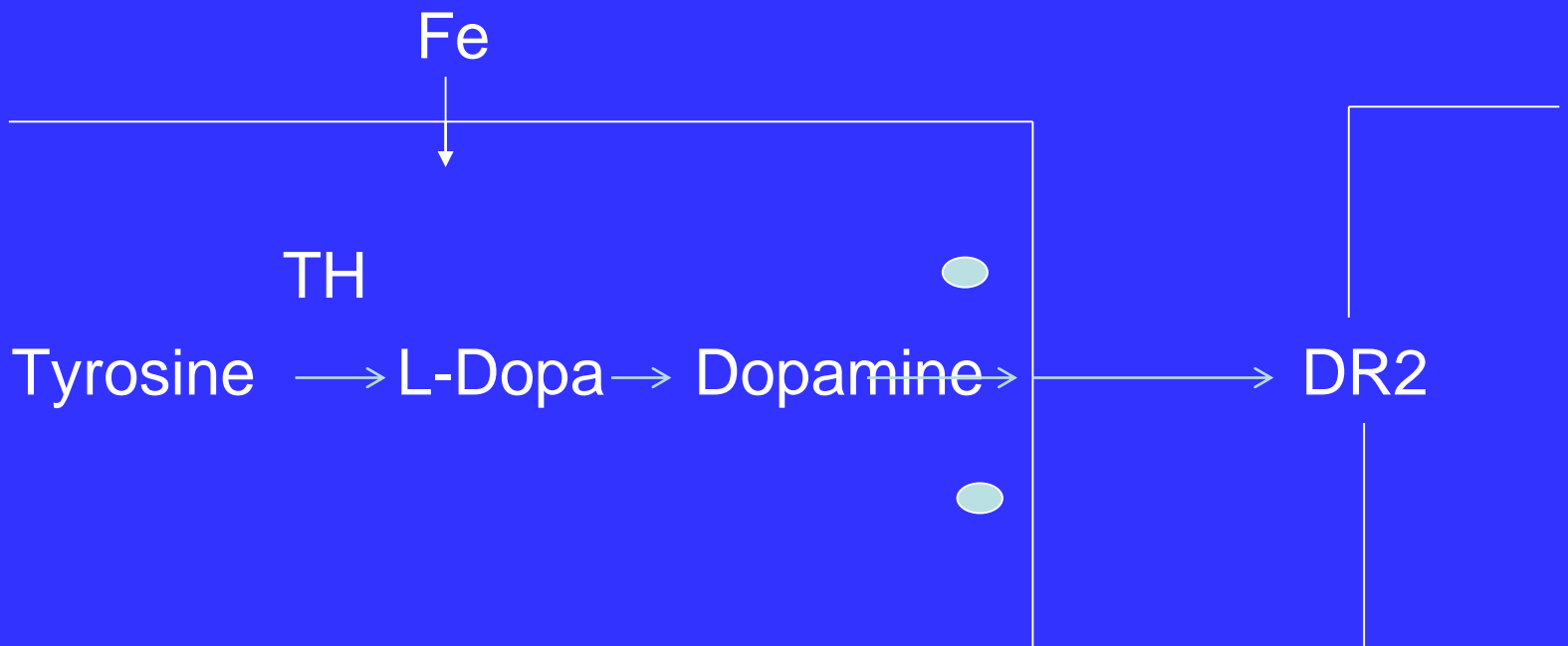
- Reduced QOL
- Hypertension
- New CVS events
- Mortality

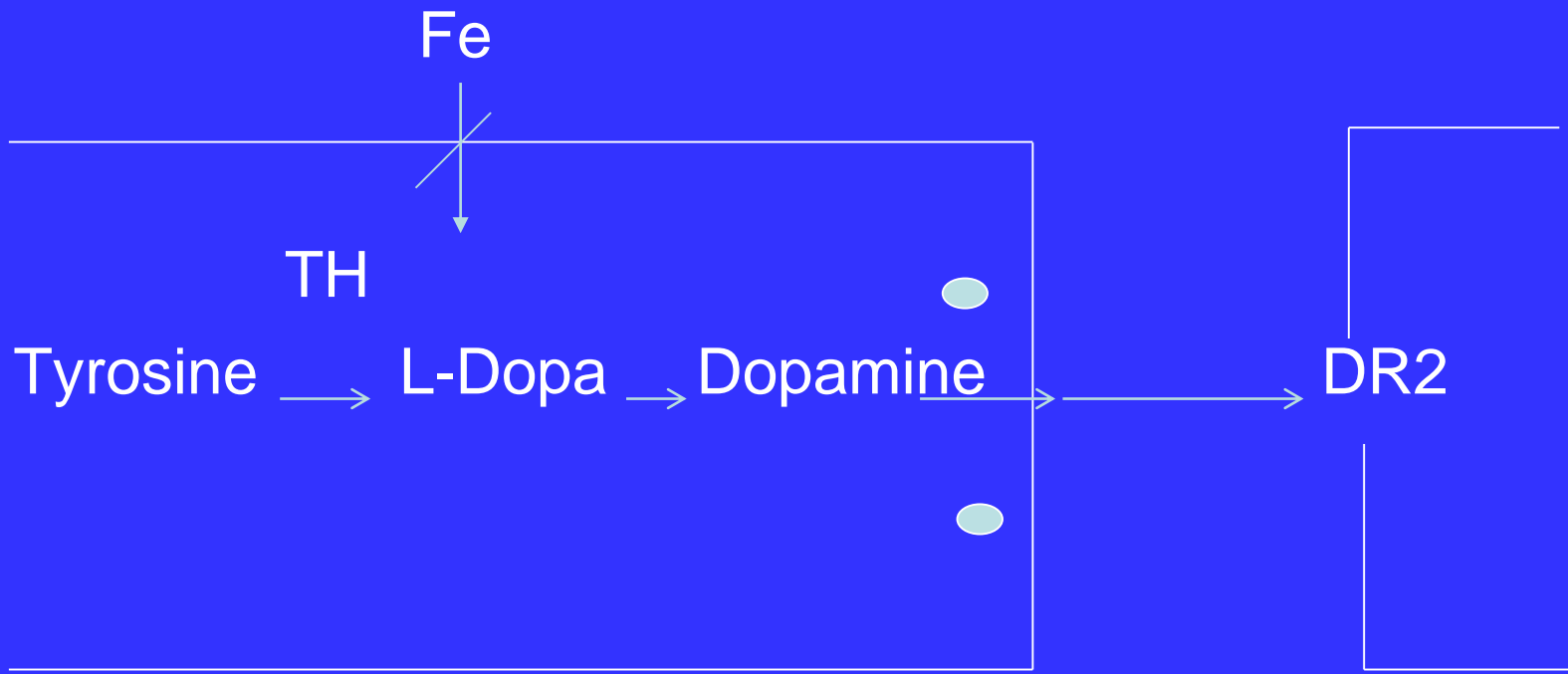
Novak M et al.

Restless Legs Syndrome in Patients with CKD.

Sem. in Nephrology 2015; 35(4): 347-358.

Mechanism is not completely understood





Management

Dopamine agonists

- **Non-Ergot Dopamine Agonists (Pramipexole, Ropinirole, Rotigotine)**
- Ergot-Dopamine Agonists (Pergolide, Cabergoline) – not used.

- Augmentation

- Rebound

Gabapentinoids

Two RCTs have shown efficacy for Gabapentin in the treatment of RLS in Dialysis patients

1. Placebo controlled – Thorp et al (2001)
2. Gabapentin compared to Levo-dopa – Micozkadioglu et al (2004)

Three RCT comparing Pregabalin, Pramipexole and placebo.

Heuber et al. *Neurology* 2013; 80: 738-742

Allen RP et al. *N Eng J Med* 2014; 370; 621-632

Garcia-Borroguero MD. *Sleep* 2014; 37(4): 635-643.

Two found that Pregabalin was significantly more efficacious than Pramipexole and placebo in treating uraemic RLS.

Heuber et al. *Neurology* 2013; 80: 738-742

Garcia-Borroguero MD. *Sleep* 2014; 37(4): 635-643.

One found Pregabalin provided significantly improved treatment over placebo but not Pramipexole. Also Pregabalin caused statistically less augmentation.

Allen RP et al. *N Eng J Med* 2014; 370; 621-632

Opioids

Opioids have a protective effect on dopamine cells that have been subject to Fe deficit.

Trenkwalder C et al. *Lancet Neurol* 2013; 12 : 1141-1150.

Fe infusions

IVI 1000mg Iron Dextran

Statistically improved RLS over placebo.
Effect faded at 4 weeks.

Sloand JA et al. *Am J Kid Dis* 2004; 43: 663-670.

Intradialytic exercise

Giannaki CD et al. *BMC Nephrol* 2013; 14: 194.

International Guidelines

European Federation of Neurological Societies (2012)

International RLS Study Group (2013)

“The use of a dopamine-receptor agonist or a [Gabapentinoid] is recommended as the first line treatment of RLS...for most patients...”

Garcia-Borreguero D et al. International RLS Study Group.
Sleep Medicine 2013; 14: 675-684.

INSOMNIA

Prevalence: 40-85 % of HD patients.

In a large study of HD patients:

1/2 had trouble falling asleep

1/2 woke at night

1/2 early morning waking

Anand S et al. *Hemodial Int* 2013; 17: 50-58.

Associated with:

- Reduced QOL
- Higher mortality

Causes

1. This may be the product of multiple symptoms

- Pain
- Uraemic Pruritus
- Cramps
- RLS
- Periodic Leg Movement Disorder
- Nocturia
- Obstructive Sleep Apnea (OSA)

In a study of 254 HD patients
there was a 57 % prevalence of moderate to
severe OSA.

Nicholl DD et al. *Chest* 2012; 141: 1422-1430.

2. Emotional causes

Worry/concerns/anxiety

Causes of insomnia

3. The evening surge of melatonin that controls the circadian sleep-wake cycle is absent in dialysis patients.

Koch BC et al. *Nature Reviews. Nephrology* 2009; 5 : 407-416.

4. Poor sleep hygiene

Management

1. Manage the underlying symptoms.

[That may include organising a formal sleep study.]

2. Address underlying emotional issues.

3. Trial of melatonin.

Russcher M et al. *Brit J Pharmacol* 2013; 76: 668-679. [The MELODY Study]

4. Sleep hygiene.

General measures

- No caffeine after lunchtime
- No alcohol at night
- No smoking at night
- No artificial light from devices.

Gastrointestinal symptoms

Taste disturbances

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 Dietitian Review

NAUSEA

Look for the cause (s)

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

Treat the symptom :

Maxalon 5mg – 10mg tds

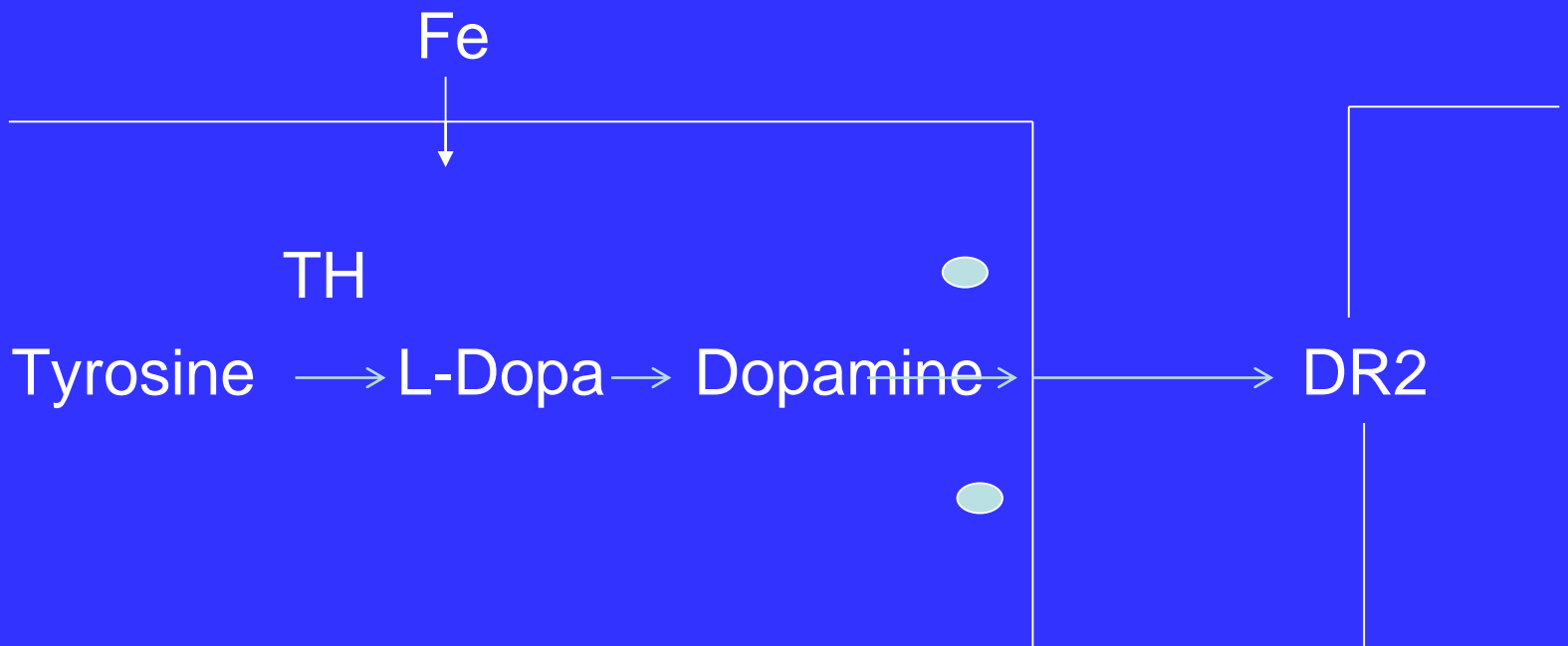
Haloperidol 0.5mg bd

Cyclizine 25- 50mg tds

Ondansetron – very constipating

A 72 y.o. man.

- ESKD – on Home HD
- Main symptom is nausea.
- Commenced on Metoclopramide 10mg tds.
- Two weeks later reports nausea well controlled.
- “By the way, doctor, my legs keep moving at night.” - Restless Legs ++



The experience of the Renal Supportive
Care Service, St George Hospital in
symptom management.

Of those who presented at first clinic visit with a symptom that was reported as “severe” or “overwhelming”...

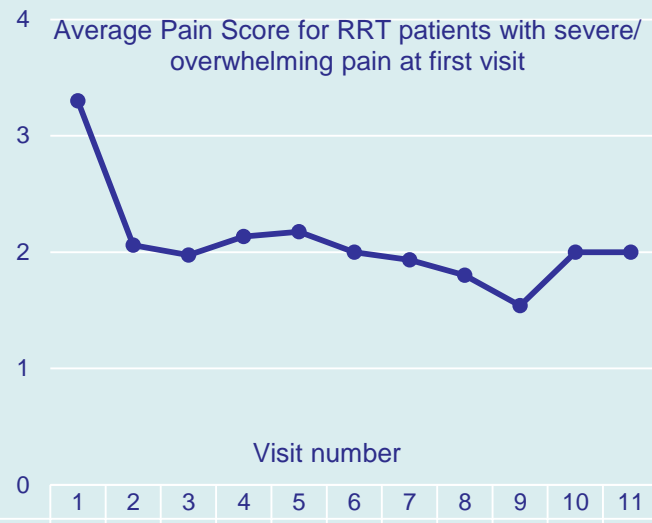
What happened over time ?

Average Pain Score for NFD patients with severe/overwhelming pain at first visit



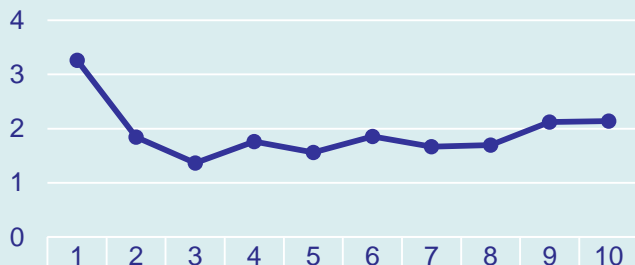
Average Score	3.2	1.8	2.0	2.1	1.9	2.0	1.9	1.7	2.1	2.3	1.7	1.6
Av weeks between visits		11	9	9	10	6	5	4	7	8	5	7
Number of patients	33	33	33	27	23	17	14	14	12	12	12	10

Average Pain Score for RRT patients with severe/overwhelming pain at first visit



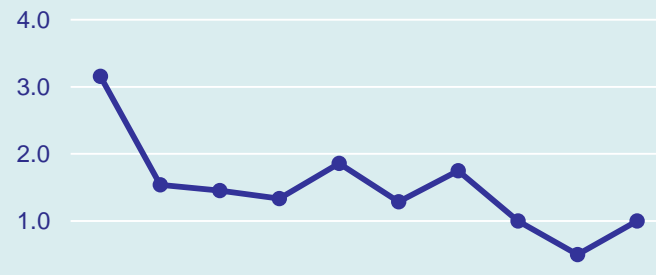
Average Score	3.3	2.1	2.0	2.1	2.2	2.0	1.9	1.8	1.5	2.0	2.0
Av weeks between visits		5	20	10	7	14	8	10	18	11	10
Number of patients	50	50	40	30	23	19	15	15	13	12	10

Average Poor Appetite Score for NFD patients with severe/overwhelming poor appetite at first visit

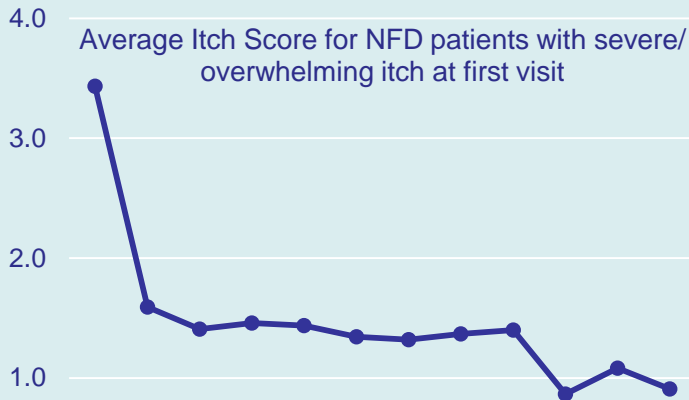


Average Score	3.3	1.8	1.4	1.8	1.6	1.9	1.7	1.7	2.1	2.1
Av weeks between visits		5	5	6	7	6	6	6	6	7
Number of patients	19	19	19	17	16	14	12	10	8	7

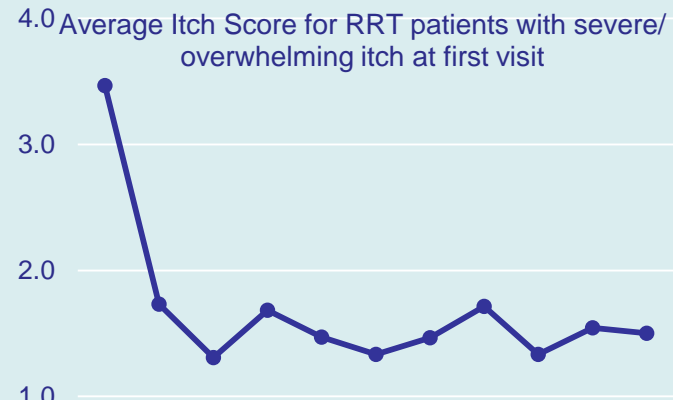
Average Poor Appetite Score for RRT patients with severe/overwhelming poor appetite at first visit



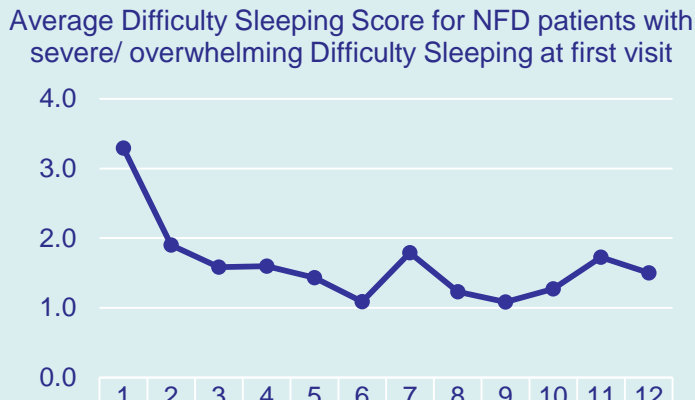
Average Score	3.2	1.5	1.5	1.3	1.9	1.3	1.8	1.0	0.5	1.0
Av weeks between visits		6	17	5	7	7	8	8	7	13
Number of patients	13	13	11	9	7	7	4	2	2	2



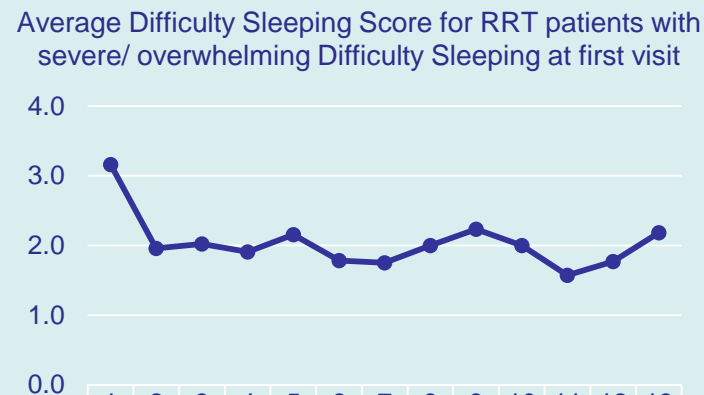
Visit number	1	2	3	4	5	6	7	8	9	10	11	12
Average Score	3.4	1.6	1.4	1.5	1.4	1.3	1.3	1.4	1.4	0.9	1.1	0.9
Av weeks between visits		10	10	6	8	5	5	5	7	6	5	6
Number of patients	44	44	44	37	32	29	25	19	15	15	12	11



Visit number	1	2	3	4	5	6	7	8	9	10	11
Average Score	3.5	1.7	1.3	1.7	1.5	1.3	1.5	1.7	1.3	1.5	1.5
Av weeks between visits		6	9	5	6	6	8	5	19	10	9
Number of patients	30	30	26	19	17	15	15	14	12	11	10



Visit number	1	2	3	4	5	6	7	8	9	10	11	12
Average Score	3.3	1.9	1.6	1.6	1.4	1.1	1.8	1.2	1.1	1.3	1.7	1.5
Av weeks between visits		11	7	6	7	7	5	5	7	6	6	6
Number of patients	41	41	41	35	30	23	19	13	12	11	11	10



Visit number	1	2	3	4	5	6	7	8	9	10	11	12	13
Average Score	3.2	2.0	2.0	1.9	2.2	1.8	1.8	2.0	2.2	2.0	1.6	1.8	2.2
Av weeks between visits		6	7	7	6	13	10	9	15	9	7	15	11
Number of patients	50	50	42	33	26	23	20	20	17	17	14	13	11

Conclusion

In terms of symptom control, the discipline of Palliative Care has several significant strengths.

1. A forensic interest in the pathophysiology of symptoms.

2. The principle of non-abandonment.

Conclusion

- Symptom management is an important arm of management.
- Symptoms are prevalent and multiple

Be curious and reactive
rather than passive and nihilistic

- Be meticulous
- Symptom relief may have a significant impact of patients' Hr QOL

Useful resources

Renal Supportive Care Symptom Guidelines:

ckmcare.com

Alberta, Canada

St George Renal Department Palliative Care tab.

1. Commonly used Palliative Care medications in the context of CKD (being revised).
2. End of Life medications.
3. Symptom management guidelines (in development)

Fostering Innovation in Symptom Management
among hemodialysis patients.

Paths forward for insomnia, fatigue and cramps.

Flyhte JE et al. *Clin J Am Soc Nephrol* 2019; 14: 150-160.

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