AJKD

In Practice

Pain Management in CKD: A Guide for Nephrology Providers

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In Practice

Sleep Disorders, Restless Legs Syndrome, and Uremic Pruritus: Diagnosis and Treatment of Common Symptoms in Dialysis Patients

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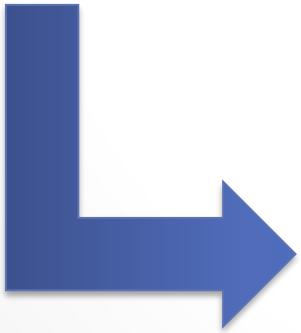
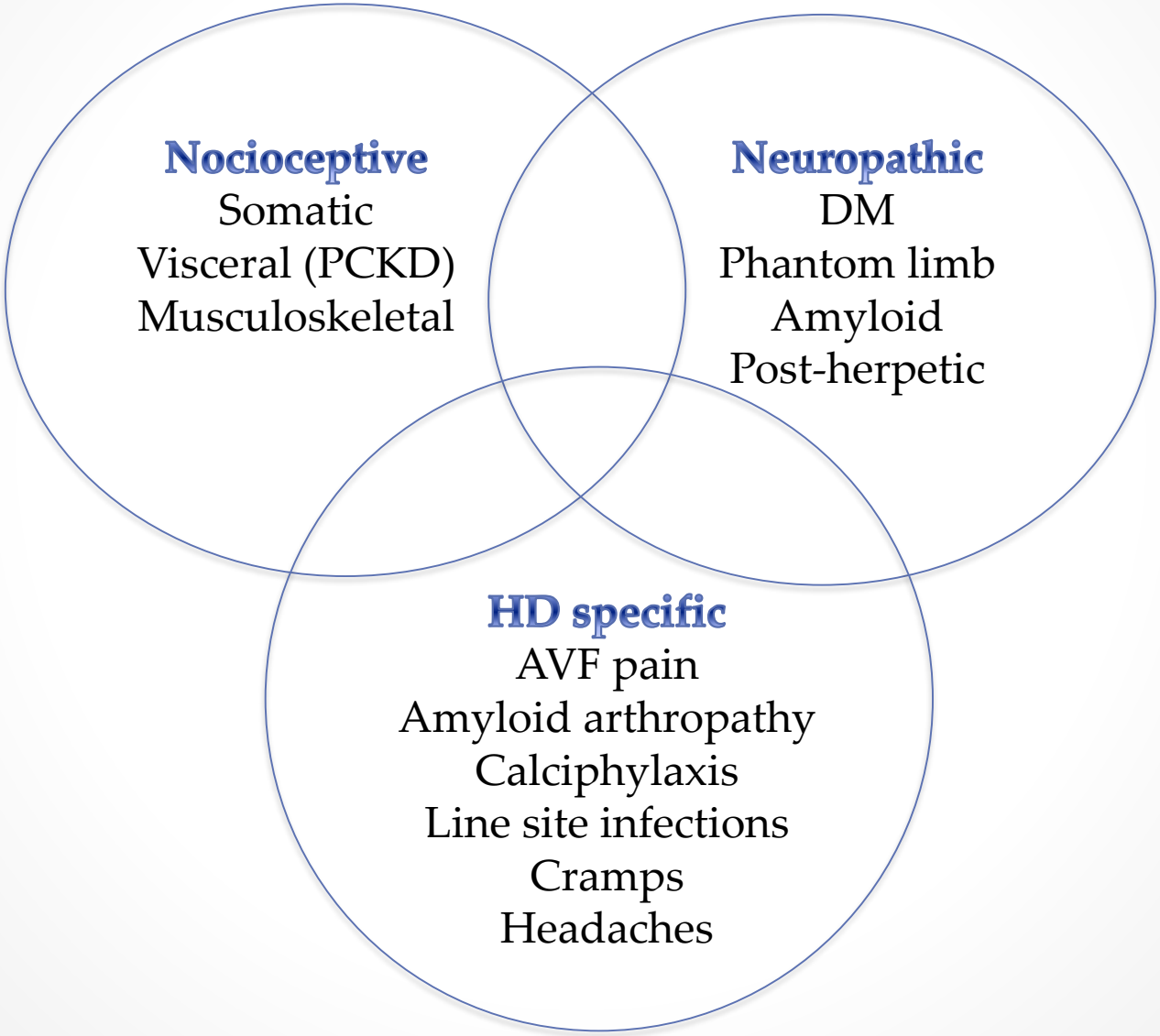
Incidence of pain in CKD

- Equivalent reporting as in cancer patients
- Affects>58% of CKD patients
- 50% rate pain as moderate or severe
- Not limited to HD- also PD and CKD5 not on dialysis
- No association of chronic pain with sex, age, race or ethnicity



Reduced QOL
Depression
Insomnia
Irritability
Shortened/missed HD sessions
Increased hospital admissions

Types of pain in CKD



Barriers to CKD Pain management

- Only 37% nephrologists regularly treat pain
- Inadequate training (8 validated pain symptom assessment tools in CKD!)
- Perceived as Primary care responsibility
- Hesitancy over pharmacological interactions/renal drug handling
- Potential for drug abuse/dependence

Treatment options

Non-pharmacological

- Exercise
- Massage
- Acupuncture
- CBT

Box 1. An Approach to General Pain Management

1. Pain assessment
2. Use the WHO 3-step analgesic ladder for nociceptive pain
   a. Consider decreased clearance and potential adverse effects in patients with advanced kidney disease
   b. Start with lowest dose of medication and uptitrate slowly
   c. Dose medications orally if possible and on a scheduled basis
   d. Extra or "breakthrough" doses should be available for pain uncontrolled by scheduled medications or for incidental pain
3. Set expectations of treatment with patient
   a. Goal should not be of being pain free, but rather a reduction in pain with the goal to improve functional status and quality of life
4. Follow-up
   a. Schedule close evaluation of adequacy of pain relief and assessment of total daily dosage of medication used titration of scheduled dose based on patient use
5. Monitor for potential side effects
   a. If other side effects are experienced that make it intolerable for a patient, another medication on the same "step" can be trialed

Suggested Pain Ladder (Modified WHO)

WHO Step	Recommended	Use with Caution	Avoid
1	Paracetamol		NSAIDS
2		Tramadol	Codeine*
3	Fentanyl, Buprenorphine, Hydromorphine+, (Methadone- pall care)	Oxycodone	Morphine+ Propoxyphene
Adjuvant	Gabapentin Pregabalin	TCAs	

*Codeine half life in non-CKD= 2.5-4hrs, in HD= 13 to 19hrs, not dialysed

Tramadol significantly dialyzed, so dose after HD (max 50mg bd), half normal dose in CKD4. Uraemic states may lower seizure threshold

+Morphine-6-glucoronide can reach 15x concentration in CSF as non-CKD. Hydromorphone active metabolite (H3G) much better tolerated

Do NSAIDS ever have a role?

- No dose of NSAID considered "safe" in CKD
- CKD (HD) patients at greater baseline risk of extra-renal S/E of NSAIDS
- Topical NSAIDs more acceptable (limited reports of AKI)
- High patient use of NSAIDS in CKD
- Even higher use in HD group
- Few (older) trials state NSAIDS can be used in HD patients for time limited trials under close supervision for s/e (HTN, ↑K, GI bleed loss of RRF, water retention)
- Consider risk:benefit on individual level

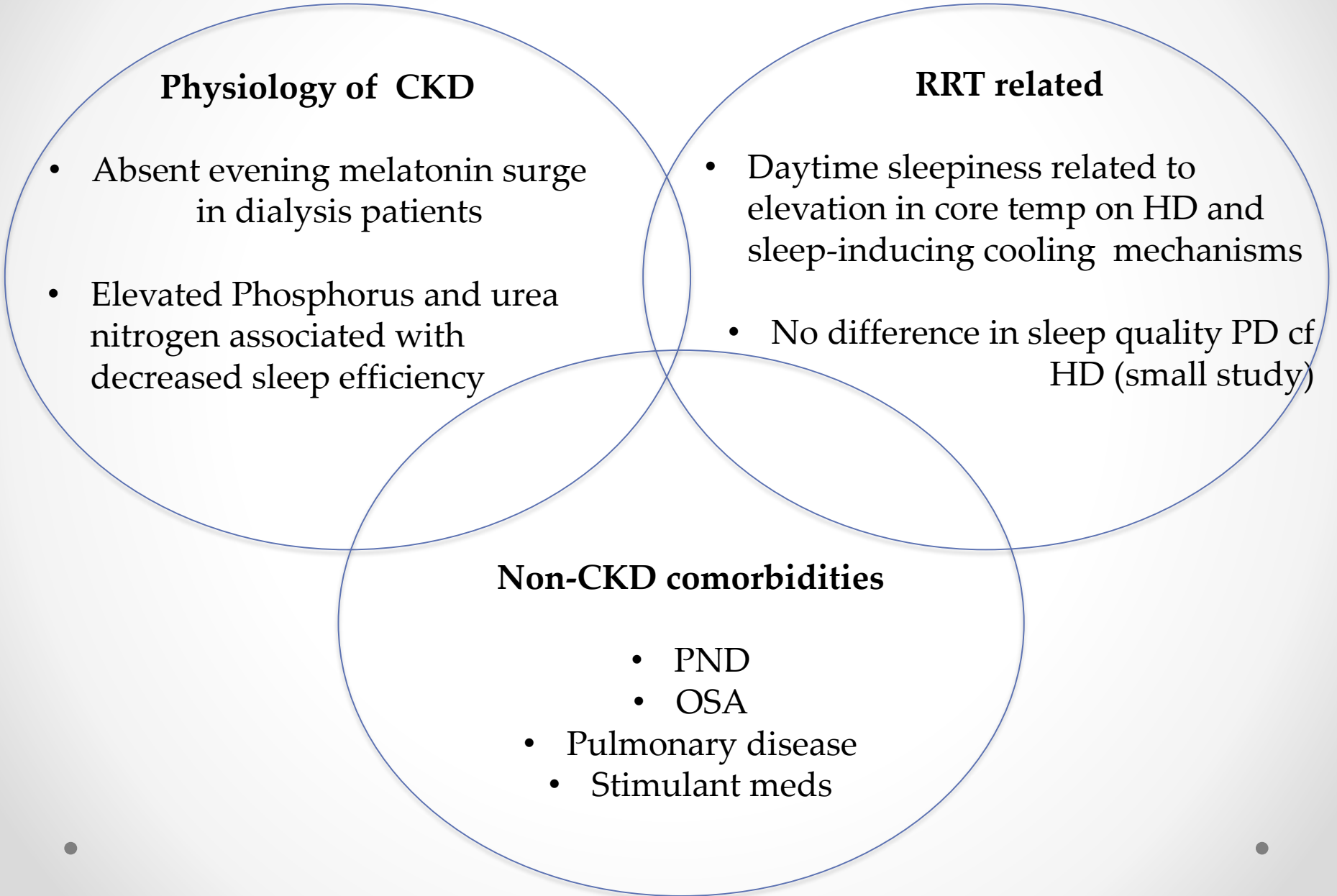
Common CKD ailments

Table 1. Prevalence of Symptoms Associated With Chronic Kidney Disease

Symptom	Prevalence
Uremic pruritus	40.6%
Sleep disorders	60.1%
Restless legs syndrome	10%-20%
Anorexia	56%
Nausea	46%
Pain	58%
Depression	21%-23%

Source: Davison et al.[7]

Insomnia


Physiology of CKD
• Absent evening melatonin surge in dialysis patients
• Elevated Phosphorus and urea nitrogen associated with decreased sleep efficiency
RRT related
• Daytime sleepiness related to elevation in core temp on HD and sleep-inducing cooling mechanisms
• No difference in sleep quality PD cf HD (small study)
Non-CKD comorbidities
• PND
• OSA
• Pulmonary disease
• Stimulant meds

Treatment of insomnia

- Manage reversible causes (RLS, pruritus, PND etc)
- Basic "sleep hygiene"
  - No caffeine, alcohol, daytime naps
  - Exercise more in the day
  - Quiet dark room with positive sleep associations
- CBT
  - Internet based options show positive results in 11 RCTs (general population)
- Non-benzodiazepine BDZ receptor agonists (Zopiclone)- no dose adjustment required
- Melatonin 3mg (only effective in short term)
- General lack of evidenced based treatments

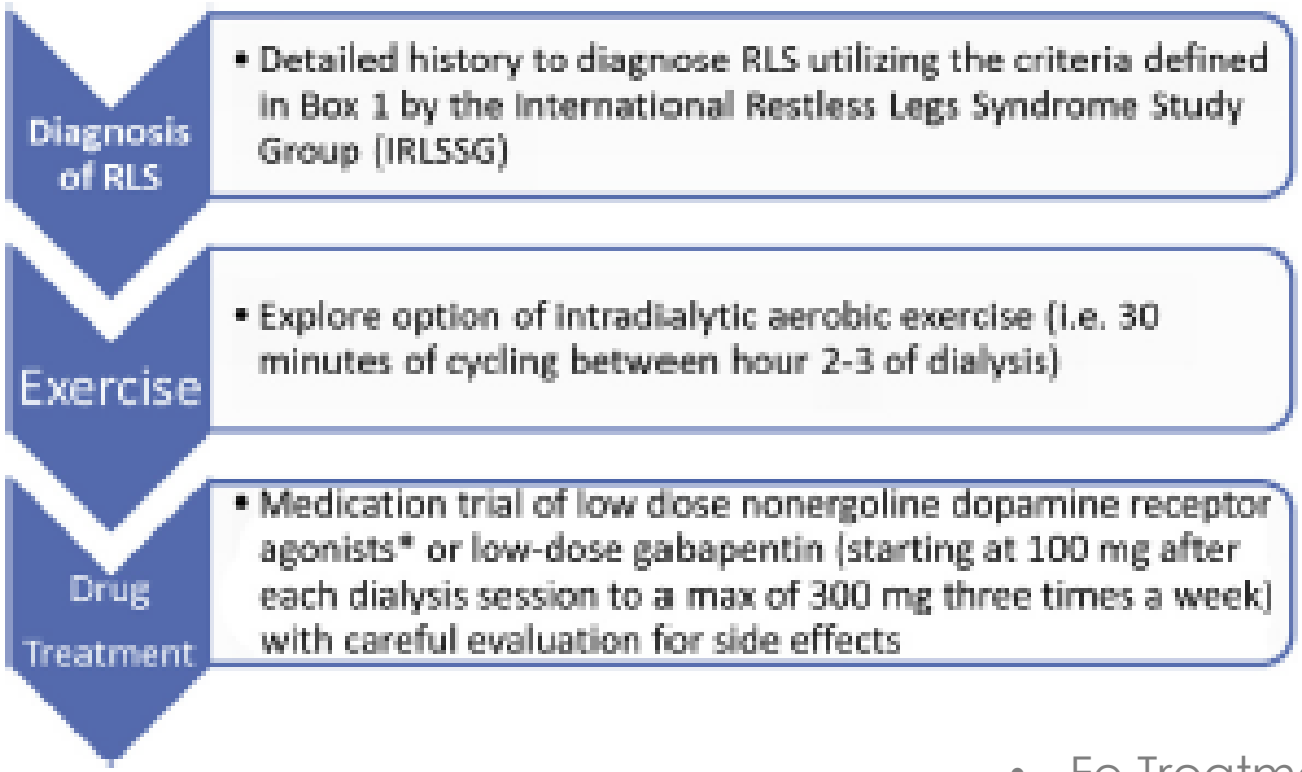
Restless Legs Syndrome (RLS)

- Neurologic sensorimotor disorder occurs in 12-25% HD patients
- May be a genetic association (BTBD9)
- Low (cerebral) Fe, low dopamine and high glutamate
- Decreased opioid receptors in HD
- Kidney disease itself (reduction after transplant)
- Associated with premature stopping of HD, decreased QOL, incresaed mortality, anxiety daytime somnolence….

Box 1. Diagnosis Criteria of Restless Legs Syndrome by International Restless Legs Syndrome Study Group

1. An irresistible impulse to move one's legs, often accompanied by unpleasant sensations in lower limbs
2. Such urges or sensations start or are made worse by periods of inactivity
3. Such urges or sensations are partly or completely relieved with movement
4. Such urges or sensations are more severe in the evening or at night than during daytime
5. The clinical criteria are not caused by any other medical or behavioral condition that can possibly mimic restless legs syndrome (myalgia, venous stasis, leg cramps)

Treatment of RLS



- Fe Treatment?- IV dextran improved RLS at 1 and 2/52 but this did not persist past 4/52 (single study)
- Opioids?- No studies in HD patients

Uraemic itch

- 42% of HD patients rate as mod/severe (DOPPS)
- 24.5% “extreme "among 16,672 dialysis patients in 7 studies

- Immunohypothesis- systemic inflammatory response
- Opioid hypothesis- increased mu:kappa receptor imbalance
- Hyperparathyroidism, Elevated CaxPO4 product
- Sweat gland atrophy-dry skin
- High Mg and Al
- Anaemia
- High Vit A
- HLA-B35
- High B2M
- Male, age, smoking history

Inconsistent evidence, small studies

Treatment options for uraemic itch

Established

- Optimize biochemistry
  - Effective dialysis, normal adequacy targets
  - Switch to biocompatible membrane and high flux dialyzer
  - Usual CKD-MBD targets
  - Treat anaemia (scanty evidence for EPO)
- Skin Hydration
  - Aqueous cream/baby oil
- Antihistamine
  - Conflicting, sedating properties may play biggest part (hydroxyzine 25mg qds)
- Gabapentin
  - 100mg post HD, 300mg off
  - Pregabalin 25mg-75mg ON if intolerant

Experimental/Limited use

- (Narrow band) UV-B
- Topical Capsaicin 0.025% cream bd to qds double blinded, placebo controlled studies
- Tacrolimus 0.03% ointment (prospective study only) but increased risk of skin malignancies in animal studies
- Kappa-opoid receptor agonist (nalfurarfin) shows promise
- SSRIS sertraline used often for general itch in non-CKD population but no RCTS
- Transplant!