

MANAGEMENT OF MUSCLE CRAMPS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Assessment

- Assess for possible non renal causes of muscle cramps
 - Structural foot/leg disorders
 - Peripheral vascular disease
 - Poor glycemic control
 - Hypothyroidism, iron deficiency, hypomagnesemia
- Review medication profile and minimize/substitute medications associated with leg cramps¹

Non-pharmacological Strategies

Preventing muscle cramps:

- Daily stretching (hold stretch for 10-20 seconds and repeat 3-5 times).
- Get up and walk around if sitting for long periods.
- If leg cramps at night, stretch before bedtime. Light exercise (e.g. stationary bike) before going to bed might also help.
- Keep the bed covers at the foot of the bed loose and not tucked in.
- Drink plenty of fluids, if not on fluid restrictions.
- Avoid exercising in extreme heat.
- Limit alcohol and caffeine.
- Wear comfortable shoes with proper support.
- Avoid walking on concrete floors for long periods of time, if you can.

Easing the pain of muscle cramps:

- Massage and stretch the cramped muscle.
- Apply hot or cold to the tight muscle (e.g., warm towel or heating pad, hot shower or bath, massage muscle with ice). Be cautious with the use of hot or cold in patients with diabetes or peripheral neuropathy due to the potential for burns.

Avoiding/easing muscle cramps pain during dialysis:

- Low intensity exercise (e.g. stationary bike) during dialysis.
- Minimize intra-dialytic weight gain.
- Minimize dialysis related hypotension.
- Consider higher dialysate sodium concentration (sodium ramping).

See BCPRA patient teaching tool on “Muscle Cramps.”

¹ Examples of medications associated with muscle cramps: IV iron sucrose (up to 23% of patients), oral contraceptive (3.5-14%), nifedipine (2-8%), pyrazinamide (1-10%), statins (4-5%), long-acting β -agonists (2-3%), diuretics (especially potassium-sparing and thiazide-like diuretics), β -blocker intrinsic sympathomimetic, benzodiazepines.

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Pharmacologic Options (based on studies in the HD population)

- Vitamin E, 400 units po daily^{1,2,3}
- If Vitamin E not effective, try Gabapentin (Gabapentin is renally cleared).^{4,5}
 - 100mg po HS, titrate by 100mg Q7days. Maximum dose should be adjusted based on renal function and patient tolerance – see drug monograph.
 - Consider 50mg (compounded capsule) po HS as a starting dose in frail elderly and/or if eGFR <15mL/min.
 - Consider if concomitant indication (e.g. peripheral neuropathy, pruritus, RLS).
 - Daily dosage can be divided between supertime and bedtime.
- Go to www.bcrenalagency.ca (health professionals, CKD) for information on costs of medications and whether coverage may be available through BCPRA, Pharmacare or Palliative Care benefit plans.

Special note: Quinine

Avoid the use of quinine for the treatment of muscle cramps in patients who have CKD. Health Canada issued a black box warning because this drug has been associated with severe adverse events, e.g., arrhythmia, thrombocytopenia.

References

1. Roca AO, Jarjoura D, Blend D, et al. Dialysis leg cramps. Efficacy of quinine versus vitamin E. *ASAIO J* 1992; 38: M481.
 - In a randomized control trial of 29 HD patients, vitamin E 400 units/day was equally effective to quinine 325 mg/d and superior to a placebo in reducing the number and severity of leg cramps
2. Khajehdehi P, Mojerlou M, Behzadi S, Rais-Jalali GA. A randomized, double-blind, placebo-controlled trial of supplementary vitamin E, C and their combination for the treatment of haemodialysis cramps. *Nephrol Dial Transplant* 2001; 16: 1448.
 - One small trial (n=19) found that vitamin E 400 units/day + vitamin C 100 mg/day for 8 weeks was more effective than either option alone. Safety in non-dialysis CKD patients or for longer period is unknown.
3. El-Hennawy AS, Zaib S. A selected controlled trial of supplementary vitamin E for the treatment of muscle cramps in hemodialysis patients. *Am J Ther* 2010; 17: 455.
 - In a study including 19 HD patients, the number of muscle cramps decreased from 6.4 to 2.4 per week while taking vitamin E 400 units/day. No adverse events were reported.
4. Mousavi SSB, Zeraati A, Moradi S, Mousavi MB. The effect of gabapentin on muscle cramps during hemodialysis: a double-blind clinical trial. *Saudi J Kidney Dis Transpl* 2015; 26: 1142-8.
 - A small double blind cross-sectional

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placebo-controlled trial (n=15) assessed the efficacy of gabapentin 300 mg 5 minutes prior to each HD session for 1 month. Gabapentin helped reduce the incidence and intensity of HD-associated muscle cramps, without causing adverse drug reactions.

5. Serrao M, Rossi P, Cardinali P, Valente G, Parisi L, Pierelli F et al. Gabapentin treatment for muscle cramps: an open-label trial. *Clin Neuropharmacol* 2000; 23:45.
 - In one small open-label trial (n=30), gabapentin was effective in reducing muscle cramps by 50% or more in 100% patients with eGFR > 60 mL/min and this effect lasted at 6 months. Mean gabapentin daily dosage was 892 ± 180 mg. 2 pts didn't tolerate the treatment.
6. Lynch KE, Feldman HI, Berlin JA, et al. Effects of L-carnitine on dialysis-related hypotension and muscle cramps: A meta-analysis. *Am J Kidney Dis* 2008; 52: 962-71.
 - Meta-analysis of 6 RCTs including 167 hemodialysis patients. When the analysis was limited to studies after 1990 with more modern dialyzers, the results of all the studies, except one outlier, didn't show any benefit of L-carnitine for muscle cramps compared to placebo.
7. Orguma S, Ando I, Hirose T, Totsune K, Sekino H, Sato H, et al. Biotin ameliorates muscle cramps of hemodialysis patients. *Tohoku J Exp Med* 2012; 227: 217-223.
 - Biotin 1 mg/d was given to a group of 14 hemodialysis patients with severe leg cramps. Biotin reduced cramps at night and during dialysis (p=0.0017). After 1 month on biotin, 5 patients stopped biotin and muscle cramps reoccurred within a few days, which were treated

successfully by restarting biotin.

General References

- a) Raymond CB, Wazny LD. Treatment of leg cramps in patients with chronic kidney disease receiving hemodialysis. *CANNT J* 2011; 21: 19-21.
- b) Allen RE, Kirby KA. Nocturnal leg cramps. *Am Fam Physician* 2012; 86: 350-5.