

# A Case Report of Pain Management in Calciphylaxis Associated with End Stage Renal Disease

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## Introduction

- Prevalence of calciphylaxis is 3.5 new cases/1000 patient-years in patients with ESRD<sup>1</sup>.
- Risk factors include obesity, female sex, diabetes<sup>2</sup>.
- Development of calciphylaxis is thought to be due to decreased expression of calcification inhibitors which in term increases precipitation of calcium phosphate in microvessels, leading to infarctions in the subcutaneous adipose tissue and dermis<sup>3,4</sup>.
- The resulting presentation is an overlying necrotic skin tissue with frequent development of painful lesions<sup>4</sup>.

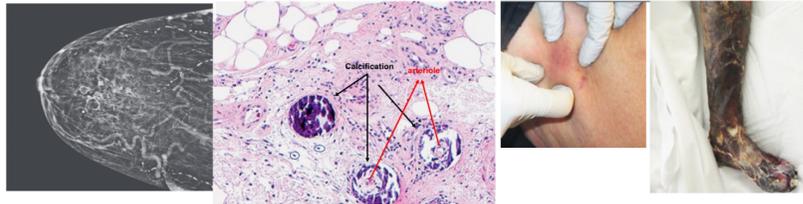


Photo taken from Nigwekar et al. N Engl J Med. 2018

-Pain management can be challenging due to pain severity, especially during removal of necrotic tissues.

-Combination of acetaminophen, topical anesthetics, opioids, gabapentin, ketamine, and/or spinal anesthetic agents are needed<sup>4,7</sup>.

-Opioid choice can partly depend on renal function of patients who often have impaired GFR.

- Codeine and its main active metabolite morphine are renally excreted and accumulate over time in patients undergoing hemodialysis<sup>8</sup>.
- Morphine metabolites can accumulate in renally impaired patients and can cause respiratory depression and seizures<sup>8,9</sup>.
- Hydrocodone and its metabolites can accumulate in renal failure<sup>9</sup>.
- Meperidine metabolites can accumulate during renal failure and cause seizures. Because of these characteristics, they are not recommended for use if a patient develops ESRD.

## The Case

The patient is a 61-year-old male with history of diabetes, ESRD with kidney transplant on chronic steroids, coronary artery disease status-post myocardial infarction and percutaneous coronary intervention, and peripheral arterial disease (PAD).

### Treatment

- Withholding calcium and vitamin D supplement.
- IV sodium thiosulfate and cinacalcet 30mg daily.

Eight admissions spanning 2 years related to complications of calciphylaxis due to ischemic events

- Multiple partial amputations including right index and middle finger, left middle finger.
- Transphalangeal amputation of left hallux and open transmetatarsal amputation toes 2 through 5 in left foot.

### Inpatient treatment

- Oxycodone 7.5mg five times daily plus oxycodone 5mg four times daily as needed which was effective for five admissions
- Rotation to tramadol 50mg every 12 hours and later onto hydromorphone up to 2mg every four hours as needed.
- Gabapentin 300mg three times daily or pregabalin 50mg three times daily, diclofenac gel 1% gel four times a day, and/or topical lidocaine patches daily as needed.
- Diazepam 2 mg daily as needed and trazodone 50mg nightly for anxiety and insomnia.

### Outpatient treatment

- Hydromorphone 6mg every six hours as needed
- Mirtazapine 15mg nightly for insomnia
- Good pain relief on a follow up appointment four months after his last admission. He continued to live alone and was able to perform all ADLs independently.

## Discussion

The three opioids our patient has used are tramadol, oxycodone and hydromorphone.

- Tramadol is used frequently in CKD patients as its not nephrotoxic.
- Oxycodone is dialyzable based on the fact it's hydrophilic;
- Hydromorphone is also hydrophilic but its metabolite 3-glucuronide metabolite can accumulate in dialysis<sup>8,9</sup>.
- It is recommended that dosage be adjusted/reduced when using tramadol, oxycodone and hydromorphone in ESRD<sup>9-11</sup>.

Other opioids to consider using in renally impaired patients are methadone, fentanyl and buprenorphine.

- Methadone and its metabolites are excreted through the GI system<sup>8,9</sup>.
- Fentanyl is adsorbed onto the dialysis filter itself<sup>8</sup>.
- Buprenorphine is excreted through the liver<sup>13</sup>. It also appears buprenorphine does not accumulate in ESRD<sup>14</sup>.
  - It's not removed by dialysis so redosing is not necessary post dialysis
  - Buprenorphine appear to not need dose adjustment with studies demonstrating safety in high doses up to 70mcg/hr

## Discussion continued

It is thought that the pain in calciphylaxis is of neurogenic origin with nerve inflammation<sup>16,17</sup>.

- Our patient found some temporary relief with gabapentin and pregabalin.
- Topical NSAID can be used due to limited systemic absorption.

-Our patient's pain was well-controlled during his eight inpatient hospitalizations spanning 2 years using various combinations of non-opioids and oxycodone.

-Our patient's pain was eventually controlled with hydromorphone alone.

-Additional options include rotating opioids, especially methadone and buprenorphine.

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