

## **‘Start Low & Delay Until in Withdrawal’ –Lessons Learned from Precipitated Withdrawal after Early Buprenorphine Initiation after Methadone**

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### **Background:**

Buprenorphine is a potent partial agonist at the mu-opioid receptor. It is generally considered a safe drug, and has become increasingly available for pain, typically in lower-dose formulations, or off-label prescribing using standard formulations for opioid dependence. Despite its safety profile, toxicity can occur in patients taking long-acting or sustained-release opioids. We describe a case of severe precipitated withdrawal induced by high doses of buprenorphine without adequate wash-out from methadone and SR oxycodone. We also discuss treatment for patients experiencing precipitated opioid withdrawal.

### **Case report**

A 55 year-old male with PMH of prostate cancer with debilitating chronic post-surgical pain and radiation-induced neuropathy received gradually escalating doses of methadone and oxycodone without significant relief. He was taking 100 mg of methadone daily. His Xwaivered pain provider proposed transition to buprenorphine. The patient brought prescribed buprenorphine/naloxone doses to the pain clinic for induction after instructions to stop his methadone 18 hours prior (30 mg noon dose and 20 mg in the AM) and to take the last SR oxycodone 40 mg dose the morning prior to induction. The patient was told to take 8 mg buprenorphine and, “15 minutes later ‘my’ ears started to get warm and he told me to take another 4 mg.” Shortly after he developed severe diffuse pain, cramping, muscle spasms and myoclonic jerks. His wife reported, “he was flailing his arms out and screaming for help!” The clinic physician administered midazolam and another buprenorphine 4mg but his symptoms worsened and EMS was called. On arrival to the ED he was intermittently confused, severely diaphoretic, and reporting dyspnea, palpitations, dizziness, tremors, diarrhea, nausea and abdominal pain. Clonidine and lorazepam were administered in 0.2 mg and 2 mg doses incrementally along with parenteral ketorolac and dextrose-containing fluids. He was admitted to the ICU where symptoms stabilized throughout the following day with repeated doses of clonidine, lorazepam, and other adjunctive agents. On hospital day 4 buprenorphine was reinitiated with slow titration to 8/2 mg TID by hospital discharge.

### **Discussion**

At therapeutic doses (16-24 mg), buprenorphine has almost total occupancy of the mu opioid receptor. Its high affinity prevents other opioids from binding or displaces them when given too closely. This case illustrates to delay long-enough before initiating buprenorphine. Lower doses of buprenorphine (‘micro-induction’) will decrease the risk of withdrawal. When precipitated withdrawal does occur we recommend treatment using sympatholytics, appropriate sedatives, and other adjunctive agents with reinitiation of buprenorphine (depending on initial dose and timing).

### **Conclusions**

The risk of precipitated withdrawal increases when large doses of buprenorphine are started shortly after cessation of full opioid agonists. Patients with higher degrees of medical comorbidity risk more serious outcome. Transitioning high doses of full agonists to buprenorphine should involve guidance from experienced providers.