

TITLE: Rapid Transition from High Dose Methadone to Long-Acting Injectable Buprenorphine

BACKGROUND: Long-acting injectable (LAI) buprenorphine is an appealing option for patients who prefer the ease of once-monthly dosing of their medication for opioid use disorder (mOUD). LAI buprenorphine releases a controlled amount of buprenorphine over one month while maintaining a steady amount of buprenorphine in the blood [1]. For patients on high-dose methadone, >100 mg daily, transitioning to LAI buprenorphine is a lengthy and demanding process. Standard protocols require a gradual reduction of methadone dose to ~30-40 mg daily, discontinuation of methadone, and development of moderate withdrawal before initiating sublingual (SL) buprenorphine [2]. Using these approaches, the SL buprenorphine dose would need to be titrated and optimized for at least seven days prior to administering the first dose of LAI buprenorphine. This process could take several weeks to complete, and the discomfort of being on sub-optimally dosed mOUD increases the risk of relapse. Very low dose (< 1 mg) buprenorphine initiation protocols have been described in the literature [3,4,5] and enables patients to transition from methadone to SL buprenorphine without having to reduce the methadone dose. However, to our knowledge, no published report has described a protocol to reduce the recommended SL buprenorphine stabilization period prior to administration of LAI buprenorphine.

CASE DESCRIPTION: This case series describes the protocol used to transition two patients from high-dose Methadone to LAI buprenorphine during an inpatient hospitalization.

Patient A is a 47-year-old woman with a history of asthma, hypertension, opioid use disorder, and cocaine use disorder. Her maintenance dose of Methadone was 150 mg daily. Her QTc was persistently prolonged, 532-580 ms, for 3 months prior to the crossover. Her clinic provider reduced her dose to 60 mg twice daily to improve her QTc; however, her QTc remained prolonged. The shared decision was made to switch her mOUD from Methadone to LAI buprenorphine due to persistent QTc prolongation and the patient's desire for greater flexibility with mOUD dosing.

Patient B is a 69-year-old woman with a history of opioid use disorder, cocaine use disorder, hypertension, and HIV. She was on a maintenance dose of 100 mg daily. However, she had inconsistent attendance at her methadone clinic due to unreliable transportation. This resulted in multiple dose reductions and concurrent use of extra medical opioids. The shared decision was made to switch her mOUD from methadone to LAI buprenorphine so that she would only need to present to the clinic once monthly.

The protocol uses a very low dose buprenorphine initiation to transition from methadone to SL buprenorphine. The patient's full Methadone dose, 120 mg for Patient A and 100 mg for Patient B, is continued as a split dose with twice daily dosing, while simultaneously giving increasing doses of IV buprenorphine every 6 hours for the first 48 hours of the protocol. Once the patient received at least one dose of 0.3 mg IV buprenorphine, the methadone was discontinued, and the patients were started on SL buprenorphine. The SL buprenorphine doses varied between the patients. Patient A started at 2 mg SL buprenorphine and had a slower up-titration because she

was extremely anxious about precipitated withdrawal. However, the slower titration increased her process by just 8 hours compared to Patient B. Patient B started at 4 mg SL buprenorphine every 6 hours for 5 doses. Both patients received 300 mg LAI buprenorphine with the final dose of SL buprenorphine. They were discharged from the hospital after receiving LAI buprenorphine. Patient A's length of stay was 4 days and Patient B's length of stay was 3 days.

CONCLUSIONS: Here we describe a novel approach to transition patients from high dose Methadone to LAI buprenorphine using a very low dose buprenorphine initiation. The protocol highlights that a rapid transition from high dose Methadone to LAI buprenorphine is possible without decreasing the Methadone dose or stabilizing the patient on SL buprenorphine for 1 week prior to administration of LAI buprenorphine. Patients experienced mild withdrawal symptoms during the first 24-48 hours of the protocol and were treated with adjunct medications for their comfort. COWS score remained < 10 for both patients throughout the protocol. Patients reported a smooth experience with this protocol and reported an overall positive experience with LAI buprenorphine. They both continued treatment with a maintenance high dose (300 mg) of LAI buprenorphine monthly. They continue to follow up in the clinic regularly for their monthly injection.

This protocol is not generalizable to every inpatient setting because it requires nurses trained in administering LAI buprenorphine and prior authorization for LAI buprenorphine prior to hospitalization.

Further research efforts should seek to optimize the tolerability of the protocol and determine the patient population for which it is best suited to expand its clinical use.