Rapid Conversion of High Dose Methadone to Buprenorphine Due to Persistent Hypoglycemia

[1]Menke N, MD PhD FASAM; [1]Preston Y, RN CARN; [1]Smith E, LMSW CAADC; [1]Szczotka D, LLMSW; and [1]DiClemente J, PharmD
[1]Michigan Medicine; University of Michigan

Background & Introduction

- Methadone is a synthetic opioid receptor agonist that is used in the treatment of pain and opioid use disorder. Hypoglycemia has rarely been reported as an adverse effect associated with methadone.
- The mechanism of hypoglycemia from methadone exposure is unknown. The current evidence suggests direct action of methadone on pancreatic islets and resulting hypoglycemia may be prevented with naloxone.
- Signs and symptoms of hypoglycemia include tachycardia, diaphoresis, tremor, anxiety, altered mental status, and seizure. If hypoglycemia is not rapidly corrected, permanent brain damage or death is possible. Thus, it is imperative that the risk of hypoglycemia must be recognized and mitigated.
- Buprenorphine is a partial opioid agonist also use for pain and opioid use disorder that has not been found to cause hypoglycemia.
- Herein, we describe a case of persistent hypoglycemia in a patient with end stage renal disease on high dose methadone that was successfully treated with a rapid conversion to buprenorphine with minimal withdrawal symptoms.

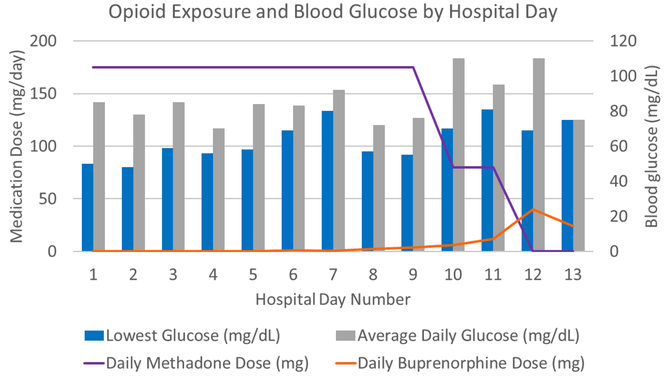
Case Description

42-year-old male with PMH of SLE, ESRD on hemodialysis, and chronic pain on 175mg of methadone from an opioid treatment program was admitted for persistent hypoglycemia. The patient had been on methadone for over ten years and had begun having episodes of hypoglycemia after developing renal failure three months prior to admission.

Case Description Continued

The patient was evaluated by the endocrine service and was diagnosed with methadone induced hypoglycemia. During episodes of hypoglycemia, he had normal insulin levels and elevated c-peptide. Diagnostic evaluation demonstrated no evidence of insulinoma, insulin autoantibody, nor pancreatogenous hypoglycemia. As a temporizing measure, the patient was placed on diazoxide, supplemental cornstarch, and dextrose boluses as needed. The addiction service was consulted to evaluate alternatives to methadone. Given the morbidity associated with hypoglycemia, the patient was offered rapid methadone taper or conversion to buprenorphine.

The patient did not believe that he would tolerate a taper to 40mg. With much trepidation due to concerns for precipitated withdrawal, the patient elected to be converted to buprenorphine. The conversion was done using a low dose initiation technique utilizing buccal buprenorphine (see Table I). The patient only experienced mild withdrawal symptoms during the process described as leg and arm "stretching". Once the patient was on full dose buprenorphine, the patient's chronic pain was no longer present; he stated it was the best he has felt in years. Prior to discharge, the diazoxide and cornstarch were discontinued, and the patient suffered no further episodes of clinically significant hypoglycemia (Table I). During telephone follow up three months after discharge, the patient denied any further hypoglycemia episodes.



Day	# HGE	Lowest Glucose (mg/dL)	Average Glucose (mg/dL)	Methadone Dose(mg)	Buprenorphine Order
1	1	50	85	175	0
2	3	48	78	175	0
3	3	59	85	175	0
4	3	56	70	175	0
5	3	58	84	175	0
6	1	69	83	175	Bup buccal film 150mcg q6H
7	0	80	92	175	Bup buccal film 300mcg Q6Hr
8	2	57	72	175	Bup buccal film 450mcg Q6Hr
9	2	55	76	175	Bup buccal film 600mcg Q6Hr
10	0	70	110	80	Bup/naloxone film 2-0.5mg SL TID
11	0	81	95	80	Bup/naloxone film 4-1mg SL TID
12	1	69	110	0	Bup/naloxone film 16-4mg SL followed by 8-2mg TID
13	0	75	75	0	Bup/naloxone film 8-2mg SL TID

Table I:Hypoglycemia episodes (HGE) by hospital day with corresponding methadone and buprenorphine (bup) dosing

Conclusion & Discussion

- Animal studies with methadone have demonstrated a dose dependent association with hypoglycemia.
- Risk factors for methadone induced hypoglycemia in humans include overdose, rapid dose escalation, doses >40mg, and renal failure. Identifying methadone as a potential cause of persistent hypoglycemia is imperative given the consequences of prolonged hypoglycemia.
- Buprenorphine offers a safe alternative for the treatment of both opioid use disorder and pain. Low dose buprenorphine initiation strategies may be utilized to rapidly convert patients from high dose methadone with minimal opioid withdrawal symptoms.
- Rapid initiation strategies such as this may significantly decrease the morbidity and mortality from unrecognized hypoglycemia by rapidly resolving persistent hypoglycemia associated with methadone while avoiding the suffering associated with untreated opioid withdrawal.
- Utilizing buccal formulations of buprenorphine allows a safe and easy way to implement a low dose buprenorphine initiation strategy.

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