Use of Mifepristone in a Hypercortisolemic Patient With End-Stage Renal Disease on Hemodialysis

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INTRODUCTION

• Establishing a diagnosis of hypercortisolism in a patient with chronic kidney disease (CKD) and end-stage renal disease (ESRD) can be challenging. Increased hypothalamic-pituitary-adrenal (HPA) axis activity may occur in these patients due to the inflammatory state of their CKD and stress from chronic dialysis.5

• Traditional laboratory tests (overnight 1 mg dexamethasone suppression test [ODST], late-night salivary cortisol [LNSC], serum cortisol, urinary free cortisol [UFC], and adrenocorticotropic hormone [ACTH]) used in assessing patients for hypercortisolism can render abnormal results in patients with renal failure, making diagnosis challenging.

• UFC is not helpful in patients with a glomerular filtration rate (GFR) <60 mL/min because renal failure may produce falsely low results6

• Furthermore, many patients with ESRD produce very little urine or are anuric, reducing the utility of the UFC test

• There are limited data available on treating patients with hypercortisolism on hemodialysis following the diagnosis of hypercortisolism

• To date, there are no published studies reporting the use of mifepristone (Korlym®, Corcept Therapeutics), a competitive glucocorticoid receptor antagonist, in patients with ESRD on hemodialysis and diagnosed with hypercortisolism

• Here we present a case of a patient with ESRD demonstrating the safe and efficacious long-term use (>4 years) of mifepristone

CASE HISTORY AND PRESENTATION

• A 67-year-old woman presented with a history of ESRD on hemodialysis since 2008 due to HIV-associated nephropathy and multiple comorbidities (type 2 diabetes mellitus [T2DM], hyperlipidemia, obesity, hypertension, hyperparathyroidism, herpetic simplex virus, anemia, and depression) (Table 1)

Table 1. Baseline Characteristics (2015)

| Parameter                  | Value
|---------------------------|------
| Age (yr)                  | 67   |
| Sex                       | Female |
| Weight (kg)               | 108  |
| BMI (kg/m²)               | 36.2 |
| Blood pressure (mmHg)     | 144/44 (on multiple medications) |
| HbA1c (%)                 | 7.2  |
| Daily insulin requirements | 36 units Novolin 70/30 |

• Renal parameters
  - GFR (10 mL/min/1.73 m²): 6.4
  - Creatinine (0.8-1.3 mg/dL): 7.6
  - Potassium (3.5-5.5 mEq/L): 4.8

• Diabetes medications at Month 7: glimepiride 6 mg daily, metformin 1000 mg daily, and lanthanum carbonate 2 grams daily.

• Due to the patient’s poor surgical candidacy and the lack of FDA-approved medical therapy to treat hypercortisolism in 2010, she was managed conservatively for 5 years with treatment of her underlying comorbidities

• In 2015, she was reevaluated (Table 1) and started on mifepristone 300 mg OD and titrated to the maximum dose for patients with renal impairment7,8 600 mg OD, at Month 2

• Mifepristone dose and frequency were not adjusted to account for hemodialysis (scheduled 3 days/week) and medication was taken every day in the evening

• Due to mifepristone being highly protein-bound, hemodialysis did not alter its efficacy9

RESULTS WITH MIFEPRISTONE

• Over 55 months of treatment with mifepristone, glycemic control improved, with all insulin discontinued at Month 15 (Figure 2)

• The patient was hospitalized in 2008 for the placement of a percutaneous dialysis catheter. Her abdominal CT showed incidentally found bilateral adrenal gland enlargement

• Left:
  - Adrenal CT: bilateral adrenal gland enlargement
  - Right: 1.8 cm low-density nodule consistent with myelolipoma; 7.6 HU
  - Left: 2.0 cm Island-poor nodule: 25 HU

• Pituitary MRI with contrast: normal

• Right adrenal CT: bilateral adrenal adenomas

• Patient was hospitalized in 2008 for the placement of a percutaneous dialysis catheter. Her abdominal CT showed incidentally found bilateral adrenal gland enlargement

• Pituitary MRI with contrast was performed to rule out ACTH-dependent hypercortisolism.

• Due to anuria, 24-hour UFC was not conducted (Table 2)

• With Endo-Tec Suppression Test (ODST), late-night salivary cortisol (LNSC), and adrenocorticotropic hormone (ACTH) imaging (CT images are presented in Figure 1), Because her ACTH levels were >20 pg/mL, a pituitary MRI with contrast was performed to rule out ACTH-dependent hypercortisolism.

CONCLUSIONS

• Patients with ESRD present many diagnostic and treatment challenges:
  - Increased HPA axis activity from the inflammatory state of CKD and stress from chronic dialysis can produce false-positive results during the work-up for hypercortisolism
  - Anuria can prevent the utilization of traditional 24-hr UFC collections
  - Data are limited on treatment approaches for patients with hypercortisolism with ESRD on hemodialysis

• This is the first presented case of a patient with ESRD on hemodialysis using mifepristone to control hypercortisolism

• Efficacy was demonstrated through the resolution of hyperglycemia and hypertension, along with significant weight loss

• Long-term safety of mifepristone was demonstrated by the lack of any serious adverse events over the 4+ years of treatment

REFERENCES


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DISCLOSURES

AWC: Consultant, Corcept Therapeutics. RR: Employee, Corcept Therapeutics.