Mifepristone Provides Beneficial Clinical Improvement in Two Cushing Disease Cases in a Community Endocrinology Practice

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INTRODUCTION

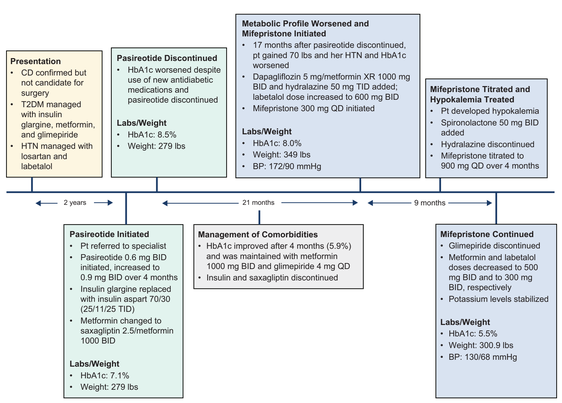
- Cushing disease (CD) is associated with cardiovascular risk factors and psychiatric illness[1-3]
- In CD, excess circulating cortisol leads to[4]:
  - Body composition changes (eg, central obesity)
  - Adverse metabolic profile (eg, dyslipidemia, insulin resistance, diabetes mellitus)
  - Arterial hypertension
- Resulting hypercortisolism can also lead to depression, anxiety, and psychosis[3]
- Mifepristone (Korlym®, Corcept Therapeutics) is a competitive glucocorticoid receptor antagonist approved to treat patients with endogenous hypercortisolism of all etiologies
- In patients with CD, mifepristone has been shown to improve:
  - Hyperglycemia, insulin resistance, and insulin requirements[5-7]
  - Depression, mental health, and social functioning[5,8]
  - Quality of life[5,8]
- Here we describe 2 patients with previously diagnosed CD who were treated with mifepristone following pasireotide use in a community endocrinology practice

CASE 1

INITIAL PRESENTATION AND TREATMENT

- 50-year-old woman presented to community endocrinologist with previously confirmed CD and comorbidities, including diabetes and hypertension, managed by other providers (**Figure 1**)
  - Surgeon declined to operate (tumor not visible)
- Patient was treated with pasireotide initiated at 0.6 mg twice daily and increased to 0.9 mg twice daily
  - Glycemic control subsequently worsened, leading to discontinuation of pasireotide (**Figure 1**)
- Patient returned 17 months later with worsening metabolic profile

Figure 1. Case 1: History of CD Management

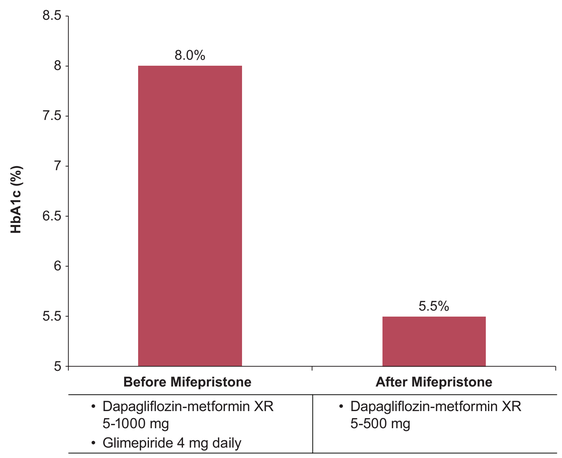


BID, twice daily, BP, blood pressure; CD, Cushing disease; HbA1c, glycated hemoglobin; HTN, hypertension; Pt, patient; QD, once daily; T2DM, type 2 diabetes mellitus; TID, three times daily, UFC, urinary free cortisol.

INITIATION OF MIFEPRISTONE

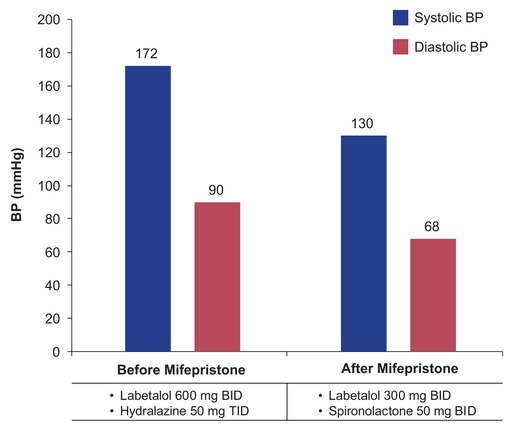
- Due to persistent hypercortisolism and worsening glycemic control and hypertension (HTN):
  - Antihypertensive and antidiabetic therapies were adjusted (hydralazine and dapagliflozin/metformin XR were added; labetalol was increased) (**Figures 2** and **3**)
  - Mifepristone 300 mg was initiated
- Hypokalemia developed after initiation of mifepristone
  - Hydralazine discontinued; spironolactone 50 mg twice daily added
- Over next 4 months, mifepristone titrated to 900 mg and medications modified
  - Glimepiride discontinued
  - Dapagliflozin/metformin and labetalol decreased
- Potassium levels stabilized, patient took a drug holiday and restarted mifepristone 300 mg once daily
- The patient achieved glycemic and HTN control after 9 months on mifepristone (**Figures 2** and **3**)
- After 12 months, the patient lost 49 lbs (**Figure 4**)

Figure 2. Case 1: HbA1c Before and After Mifepristone Treatment



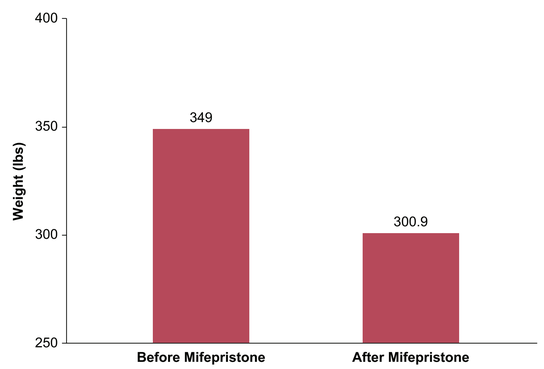
HbA1c, glycated hemoglobin.

Figure 3. Case 1: Blood Pressure Before and After Mifepristone Treatment



BID, twice daily; BP, blood pressure; TID, three times daily.

Figure 4. Case 1: Weight Before and After Mifepristone Treatment



CASE 2

PRESENTATION

- 26-year-old woman with history of confirmed CD, previously treated with pasireotide
  - Pasireotide discontinued by patient due to weight gain
- Presented to community endocrinologist with weight gain, depression, anxiety, and social withdrawal that interfered with her ability to work and live independently (required parental care)
  - The patient was uncommunicative; the mother spoke on patient's behalf during first visit
- Additional work-up revealed insulin resistance (**Table 1**)

TREATMENT AND RESULTS

- Mifepristone therapy was initiated at 300 mg and titrated up to a final dose of 900 mg
- After 12 months of mifepristone therapy, insulin resistance improved and the patient lost 23 lbs from baseline (**Table 1**)

Table 1. Case 2: Metabolic Characteristics Before and After Mifepristone Treatment

Parameters	Before Mifepristone	After 12 Months of Mifepristone
FPG, mg/dL	87	89
Fasting insulin, IU/mL	15	5
HOMA-IR	3.2	1.0
BP, mmHg	110/72	110/68
Weight, lbs	176	153.2

BP, blood pressure; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment of insulin resistance.

- Patient's mood and social behavior improved substantially
  - Lives independently, has a job, and is engaged to be married
  - No longer needs mother at appointments

SUMMARY/CONCLUSIONS

- This case series describes the effective medical management of 2 patients with CD who were previously treated with pasireotide
- In both patients, treatment of the signs and symptoms of hypercortisolism with mifepristone resulted in improved clinical outcomes and quality of life
  - In Case 1, mifepristone therapy allowed for fewer medications while controlling glucose levels
  - In Case 2, mifepristone therapy dramatically improved the patient's quality of life
  - Both patients lost weight while on mifepristone
- These cases also illustrate some of the common "real-life" challenges encountered by community endocrinologists, such as incomplete patient historical data and inconsistent follow-up

REFERENCES

1. Nieman LK, et al. *J Clin Endocrinol Metab.* 2008;93(5):1526-40.
2. Johnston PC, et al. *Pituitary.* 2017;20(4):430-40.
3. Geer EB, et al. *Endocr Pract.* 2017;23(8):962-70.
4. Hassan-Smith ZK, et al. *J Clin Endocrinol Metab.* 2012;97(4):1194-201.
5. Fleseriu M, et al. *J Clin Endocrinol Metab.* 2012;97(6):2039-49.
6. Wallia A, et al. *Diabetes Care.* 2013;36(9):e147-e8.
7. Fein HG, et al. *BMC Endocr Disord.* 2015;15:63.
8. Katznelson L, et al. *Clin Endocrinol.* 2014;80(4):562-9.

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DISCLOSURES

CI: Nothing to disclose
DC: Employee, Corcept Therapeutics

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