Adrenal Suppression and Cushing’s Syndrome Secondary to Ritonavir and Inhaled Budesonide

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Received Date: 04 Jan 2016
Accepted Date: 01 Feb 2016
Published Date: 03 Feb 2016

ABSTRACT

A 65 year old male with HIV and COPD developed Cushing’s syndrome and adrenal suppression after receiving low-dose inhaled budesonide and ritonavir. Discontinuation of ritonavir led to improvement in Cushingoid complications, however evidence of adrenal suppression still persisted 6 months later. Low-dose budesonide is often viewed as a safer alternative to fluticasone when inhaled corticosteroid therapy is required in a patients on ritonavir. Our case illustrates that patients receiving low-dose budesonide and ritonavir should also be considered at high risk of Cushingoid complications.

KEY WORDS: Ritonavir; Budesonide; Cushing’s syndrome; Adrenal suppression.

INTRODUCTION

Ritonavir-based inhibition of the hepatic cytochrome P450 CYP3A4 isoenzyme can be used to pharmacologically boost the levels of other protease inhibitors in antiviral regimens for human immunodeficiency virus (HIV) and more recently, Hepatitis C. However, a consequence of CYP3A4 inhibition is the accumulation of other substrates that are metabolized by the CYP3A4 system, including many of the inhaled corticosteroids (ICS) used in the treatment of asthma and chronic obstructive pulmonary disease (COPD) [1,2]. This can lead to iatrogenic Cushing’s syndrome and has been frequently reported in patients with combined use of inhaled/intranasal fluticasone and ritonavir [3]. As a result, budesonide is a preferred ICS in patient’s taking ritonavir because of its reported shorter half-life, lower lipophilicity and reduced systemic absorption [4].

Although iatrogenic Cushing’s syndrome with the use of ritonavir and budesonide has been documented, these patients typically received doses of inhaled budesonide as high as 1600 micrograms or 800 micrograms twice a day [5,6]. We describe a case that illustrates the risk of iatrogenic Cushing’s syndrome even when budesonide is administered at low doses (160 micrograms twice a day), highlighting the need for careful monitoring of these patients.

CASE REPORT

A 65 year-old African American male with HIV, GOLD Stage IV chronic obstructive pulmonary disease (COPD), chronic Hepatitis B and hypertension, presented with a six-month history of fatigue, weakness and mild persistent leukocytosis. The patient’s anti-retroviral regimen consisted of emtricitabine 200 mg, tenofovir 300 mg, darunavir 800 mg and ritonavir 100 mg once daily. In addition, the patient was taking inhaled albuterol as required and daily inhaled tiotropium bromide for control of his COPD. Budesonide-formoterol (80/4.5 micrograms) two puffs, twice a day was added one year prior to his presentation to improve control of COPD related symptoms. Physical examination was notable for uncontrolled hypertension (155/94 mmHg), and new-onset proximal myopathy of the upper and lower extremities with power grading of 4 out of 5. No hepatosplenomegaly or systemic lymphadenopathy was present.

Laboratory tests revealed a white blood count of 15,000 cells/ml (71% neutrophils), hemoglobin of 14.6 g/dL, platelets of 263/µL, creatinine of 1.2 mg/dL. His hemoglobin A1C was found to be 8.2%, increased from 6.5% five months prior. His CD4 count was 942 cells/µL with an HIV viral load of < 20 copies/mL.

The patient underwent evaluation for steroid accumulation and secondary adrenal suppression. A morning cortisol level was < 0.2 µg/dL (reference range 7-28 µg/dL). Subsequent ACTH (cosyntropin) stimulation testing (250 µg intravenously) revealed a baseline ACTH of 7.7 pg/ml (reference range 7-60 pg/ml) and cortisol levels of < 0.2 µg/dL (baseline), 1.2 µg/dL (30 minutes post ACTH) and 1.3 µg/
Written informed consent was obtained from the patient prior to publication of this manuscript.

Patient Consent: Written informed consent was obtained from the patient prior to publication of this manuscript.

REFERENCES

Citation: Reuben JA and Patel SM. (2016). Adrenal Suppression and Cushing’s Syndrome Secondary to Ritonavir and Inhaled Budesonide. MJ HIV. 1(1): 003.