clinical cases DDIs

Date of report 02 Sep 2021

Reported case interaction between **Ritonavir** and **Fluticasone**

Drugs suspected to be involved in the DDI

Perpetrator
Ritonavir

Daily Dose
100 (mg)

Dose adjustment performed
No

Administration Route
Oral

Start date
Unknown

End date
Unknown

Victim
Fluticasone

Daily Dose
110 (mcg)

Dose adjustment performed
No

Administration Route
Inhaled

Start date
Unknown

End date
Unknown

Complete list of drugs taken by the patient

Antiretroviral treatment

Darunavir (with Ritonavir or Cobicistat)
Raltegravir

Complete list of all comedications taken by the patient, included that involved in the DDI

fluticasone aerosol 110 mcg 2x/d fluticasone nasal spray 50 mcg 2 spray in each nostril once daily

Clinical case description

Gender

Female

Age

45

eGFR (mL/min)

>60

Liver function impairment

No

Description

A 45-year-old HIV infected African-American woman was seen for evaluation of goiter. The patient presented with a cushingoid appearance. Her medical history included asthma, hypertension and obstructive sleep apnea. The patient's clinical picture was compatible with a Cushing Syndrome. A diagnosis of adrenal insufficiency was also established. The patient was initiated on hydrocortisone (10 mg twice daily) and fluticasone (nasal spray and aerosol) was stopped due to a suspicion of drug-drug interaction with darunavir/ritonavir. The symptoms of Cushing Syndrome improved over several months after stopping fluticasone. An ACTH stimulation test was normal indicating recovery of adrenal function. However, the patient developed non-PTH mediated hypercalcemia. A DEXA scan demonstrated osteopenia. While the etiology of

hypercalcemia remained unclear, new symptoms of hip pain developed. MRIs of both hips revealed bilateral avascular necrosis of the right hip necessitating hip replacement. Since the patient developed non-PTH mediated hypercalcemia after adrenal function returned to normal, hypercalcemia was deemed secondary to avascular necrosis. Serum calcium normalized over the next few months and both Cushing syndrome and adrenal insufficiency had resolved. The non-PTH mediated hypercalcemia and avascular necrosis of the hip were likely the complication of iatrogenic Cushing Syndrome caused by the interaction between darunavir/ritonavir and fluticasone. This case has been published by Kant R et al. in Cureus 2020; 12(8):e9644.

Clinical Outcome

Toxicity

Drug Interaction Probability Scale (DIPS)

Score

8 - Probable

Editorial Comment

Coadministration of darunavir/ritonavir and fluticasone is not recommended unless the potential benefit of treatment outweighs the risk of systemic corticosteroid effects. Systemic corticosteroid effects including Cushing's syndrome and adrenal suppression have been reported in patients receiving

ritonavir and inhaled or intranasally administered fluticasone; this could also occur with other corticosteroids metabolised via the P450 3A pathway e.g. budesonide. A dose reduction of the glucocorticoid should be considered with close monitoring of local and systemic effects or a switch to a glucocorticoid, which is not a substrate for CYP3A4 (e.g. beclometasone). Moreover, in case of withdrawal of glucocorticoids progressive dose reduction may have to be performed over a longer period.

University of Liverpool Recommendation

- These drugs should not be coadministered

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