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Potential Drug Interactions with Oral Hypoglycemics



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ABSTRACT

A 50 year old age woman with type 2 diabetes mellitus [T2DM], hypertension [HTN] and osteoarthritis [OA], and who takes aspirin 75mg [ECOSPRIN-75] daily, Losartan 50mg [LOSAR-50] daily, glipizide 5mg/metformin 50mg [GLUCORED FORTE] 2 tab twice daily and diclofenac modified release 75mg [VOVERAN] once daily, was diagnosed with recurrent vulvovaginal candidiasis [RVVC]. It should be noted that, even if isolated cases of hypoglycemia have been reported with some other NSAIDs or and sulphonylureas, with the exception of phenylbutazone like drugs, no adverse interaction usually occurs and a NSAID may be used as appropriate by a patient taking a sulphonylurea.



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CASE PRESENTATION

A 50 year old age woman with type 2 diabetes mellitus [T2DM] , hypertension [HTN] and osteoarthritis [OA], and who takes aspirin 75mg [ECOSPRIN-75] daily, Losartan 50mg [LOSAR-50] daily, glipizide 5mg/metformin 50mg [GLUCORED FORTE] 2 tab twice daily and diclofenac modified release 75mg [VOVERAN] once daily, was diagnosed with recurrent vulvovaginal candidiasis [RVVC].

INTRODUCTION AND DISCUSSION

A 50 year old aged woman with type 2 diabetes mellitus [T2DM] , hypertension [HTN] and osteoarthritis [OA], and who takes aspirin 75mg [ECOSPRIN-75] daily, Losartan 50mg [LOSAR-50] daily, glipizide 5mg/metformin 50mg [GLUCORED FORTE] 2 tab twice daily and diclofenac modified release 75mg [VOVERAN] once daily, was diagnosed with recurrent vulvovaginal candidiasis [RVVC].

- Patient was averse to use intravaginal clotrimazole [CANDID-V6] because she had used this in the past and didn't think it was effective, so was prescribed fluconazole 150mg [FLUCAN-150] weekly for three months.
- During the first month of treatment, she experienced giddy spells and trivial incidences of probable hypoglycemia, which were confirmed by testing of blood glucose levels.
- She was advised to reduce the GLUCORED FORTE 1 tab twice daily for the rest of the FLUCAN treatment, upon which the episodes of dizziness and hypoglycemia resolved and blood glucose levels under control.
- Sulphonylureas are metabolized by the cytochrome P450 isoenzyme CYP2C9. Because fluconazole inhibits this isoenzyme, an escalation in sulphonylurea levels and effects might occur and increases the risk of hypoglycemia.
- Numerous studies have found that daily use of fluconazole unassumingly increases levels of some of the sulphonylureas; although there are only a couple of case reports of hypoglycemia with the combination.

- There are no reports on single-dose interaction study on fluconazole, and it is likely to be used without problems since weekly use has not been studied. Another triazole antifungal agent, Itraconazole (a CYP3A4 inhibitor) would not be predictable to cause this interaction and might have been a better choice for this patient.
- Six months later, the patient's blood glucose and HbA1c were found to be steadily raised and her body weight had increased significantly, so the glucored forte was stopped and metformin alone [GLYCIPHAGE] was started. Because of continuing poor diabetes control, pioglitazone 15 mg [PIOZ] was added. At the same time, the dose of voveran was increased from 75mg once daily to 50mg twice daily.
- One month later, during a routine health check-up, the patient's blood pressure [BP] was noted to have increased to 155/95mmHg. As her BP had been well controlled for some time and pioz can cause fluid retention, it was considered that the addition of pioz was the cause of hypertension.
- It should be noted that non-steroidal anti-inflammatory drugs [NSAIDs] can also cause fluid retention and, in this case, the increase in the diclofenac regularity from once to twice daily might have added to the effects caused by pioglitazone. The patient was, however, indisposed to stop diclofenac because fixed drug combinations with paracetamol like analgesics had not previously helped with her pain. It was, therefore, decided that pioglitazone would be stopped and repaglinide 1mg [EUREPA-1] before meals started.
- Atorvastatin 40mg [ATORVAS 40] daily at bedtime was also recommended because the patient had elevated blood lipid levels. However, she did not tolerate any statins because she got experienced muscle pains and gastrointestinal adverse effects and Gemfibrozil 300 mg [LOPID 300] was advised instead. Within three days, she had a severe hypoglycemic episode and was admitted to hospital for evaluation and management.
- Lopid was stopped and she was discharged after one week with stable blood glucose levels. Lopid markedly inhibits the CYP2C8-mediated metabolism of repaglinide, and this is likely to have caused the hypoglycemia. Fenofibrate 160mg [FIBRATE] has no significant effects on CYP2C8 and would be a better choice than lopid.

- Eureka could also be substituted with either sitagliptin 50mg [JANUVIA] or vildagliptin 50mg [GALVUS] because they are primarily excreted unchanged in the urine and would not be anticipated to be affected by fenofibrate or gemfibrozil.

CONCLUSION

It should be noted that, even if isolated cases of hypoglycemia have been reported with some other NSAIDs or and sulphonylureas, with the exception of phenylbutazone like drugs, no adverse interaction usually occurs and a NSAID may be used as appropriate by a patient taking a sulphonylurea.

COMPETING INTERESTS

The author declares that he has no competing interests.

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