
When the Fire Won't Go Out

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Pomegranate juice, sildenafil, CYP3A4

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Abstract

This case discusses the pharmacokinetic interaction between pomegranate juice and sildenafil, resulting in priapism. Sildenafil is a cytochrome P450 3A4 substrate and pomegranate juice is a 3A4 inhibitor.

Case

The Urology chief resident called the operating room desk to schedule surgical intervention for a case of priapism and asked if anyone from the Anesthesiology on-call team was available to pre-op the patient and consult for pain control. The junior Anesthesiology on-call resident was dispatched to the ED (no pun intended) and found a 56-year-old man in significant distress having experienced an erection that began 7 hours ago. A thorough history and physical was done and was significant for hypertension, hypercholesterolemia, and erectile dysfunction. The patient was an occasional cigar smoker. His medications included lisinipril, atorvastatin, and sildenafil, the later taken “as needed.” He stated that he had no known drug allergies. Further questions about NPO status led to the patient revealing that he drank approximately a liter of pomegranate juice every day because he was told in his “men’s group” that that particular juice can help with erectile dysfunction.

The Anesthesiology resident had majored in food science in college and was married to a lady who was just finishing her PharmD program and so was keenly aware

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of the association between nutritional supplements and commonly prescribed medications. He alerted the patient and the Urology resident to the biologically activate compounds in pomegranate juice and grapefruit juice.

Discussion

This is an example of a substrate added to an inhibitor.

Sildenafil is phosphodiesterase type-5 inhibitor that is used for treatment of erectile dysfunction and pulmonary hypertension. There are numerous drug–drug interactions (DDIs) with sildenafil, notably nitrates, α -blockers, and β -blockers, which may all cause severe hypotension. Sildenafil is metabolized by cytochrome P450 (CYP) 3A4 (80%) and CYP2C9 (20%); in addition to known DDIs, patients are advised to avoid grapefruit juice when taking sildenafil.

Pomegranate juice has high concentrations of antioxidants and has been recommend as part of a heart-healthy diet and as a nutritional treatment of erectile dysfunction. However, like grapefruit juice, pomegranate juice has been reported to inhibit CYP enzymes based on laboratory studies. In our patient in this scenario, regular ingestion of pomegranate juice with concurrent administration of sildenafil likely resulted in inhibition of CYP3A4 which in turn resulted in elevated plasma levels of sildenafil. This then resulted in increased risk for side effects including priapism. Case reports of priapism associated with both grape fruit juice and pomegranate juice have been reported.¹

Take-Home Points

- A thorough preanesthesia history and physical must include questions regarding the patient's nutritional habits and consumption of vitamins, herbs, and other supplements that may possess biologically active compounds.
- Both pomegranate juice and grapefruit juice are inhibitors of CYP3A4 and possible other members of the CYP family.²
- Sildenafil is metabolized by two members of the CYP family, CYP3A4 and CYP2C9. The astute practitioner must develop an awareness for CYP-mediated DDIs and know where to expediently locate information regarding perioperative implications.³

Summary

Interaction: pharmacokinetic

Substrate: sildenafil

Enzyme: CYP3A4

Inhibitor: pomegranate juice

Clinical effects: priapism

References

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