The Ofttimes Overlooked Food-Drug Interactions in Psychopharmacotherapy

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Food-drug interactions, akin to herbal-drug interactions, are often overlooked on clinical grounds and are replete with outcomes ranging from "pharmacologic" drug failure[1] and "pseudoresistance" to potentially serious reactions and toxicity. Here, we provide some clinical tips and hacks of common food-drug interactions[2,3] relevant to the practice of psychopharmacology to bear in mind.

Generally speaking, food delays absorption of drugs by delaying gastric emptying and increasing transit time. Psychotropic drugs that are best taken on an empty stomach include quetiapine XR (as high-fat meals cause the XR capsule to rapidly "dump" its dose, risking oversedation and orthostasis), asenapine (absorbed in mouth, and absorption drops 30% with food), and the Z-hypnotics (eg, zolpidem) and the dual orexin receptor antagonist inhibitors (eg, suvorexant) (where food delays release by 1 to 2 hours, which sounds impractical for insomniac patients).

Interestingly, some drugs are exceptionally better absorbed faster with food. This may be because some medications require an acidic medium for solubility and absorption, hence the need for food-stimulated release of gastric acidity. This is notable for lurasidone (to be taken with a 350-calorie meal or absorption drops 30%–70%), ziprasidone (to be taken with a 500-calorie meal or absorption drops by 50%), paliperidone (food increases serum levels by 50% to 60%), the antidepressant vilazodone (absorption drops 50% and to alleviate nausea as well), and gabapentin XR (absorption drops 50% on an empty stomach). Moreover, a high-fiber diet has been reported to decrease absorption of tricyclic antidepressants (eg, amitriptyline).

Some food induces cytochrome P450 (CYP) 1A2, which lowers levels of psychotropic agents that are substrate to CYP1A2[4] (eg, clozapine, olanzapine, asenapine, agomelatine, mirtazapine). These foods include broccoli, Brussels sprouts, cabbage, cauliflower, chargrilled meats, radishes, and arugula. Of note, carrots, celery, coriander, cumin, and parsley can inhibit CYP1A2, increasing drug levels.

Grapefruit is worthy of mention on its own merits.[5] Furanocoumarins in grapefruit can strongly inhibit CYP3A4, increasing levels of psychotropic drugs substrate to CYP3A4 (eg, lumateperone, lurasidone, quetiapine, carbamazepine). One grapefruit or two-thirds of a cup of juice can double or triple the levels. This effect is more pronounced within the first 6 hours and can last up to 72 hours. The levels tend to decline by 75% at 24 hours after grapefruit intake. Concentrated grapefruit juice is notoriously listed among the causes of prolonged QTc interval.[6] For these reasons, many hospitals have taken grapefruit off the menu altogether.

Also, patients on low sodium diets will reabsorb more lithium, along with sodium, raising lithium's levels. Caffeine has both kinetic and dynamic actions. It tends to inhibit CYP1A2, increasing levels of psychiatric drugs metabolized via CYP1A2, as described previously. It also has synergistic actions with stimulants (eg, causing tremors and insomnia) and can antagonize the actions of anxiolytics.

A classic example of a food-drug interaction is that of tyramine-rich foods (eg, aged cheese) for those on monoamine oxidase inhibitors (eg, phenelzine), which was once favored for atypical and treatment-resistant depression but can precipitate a serious hypertensive crisis ("cheese reaction").[7] Last but not least, alcohol potentiates central nervous system depressant actions and disulfiram reactions (eg, headache, flushing).

This list of food-drug interactions is by no means all inclusive, and prescribers are urged to consult national formularies when in doubt.

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