A Case of Caffeine Intolerance With Long-Term Use of Fluoxetine

To the Editor: Caffeine is the most widely consumed central nervous system (CNS) stimulant. At least 1 caffeinated beverage is consumed daily by 75%–98% of youth.[1]

The cytochrome P450 (CYP1) family of enzymes, also known as CYP450 enzymes, has been linked to drug metabolism. Previous literature has shown that CYP450 enzymes effect numerous drug-drug interactions. Here, we describe the case of a young woman who developed caffeine intolerance following long-term use of fluoxetine.

Case report. Ms A, an 18-year-old Southeast Asian woman, had been treated for depression (*DSM-5* criteria) for over a year with fluoxetine. Her symptoms of depression included low mood with anxiety and crying spells, inability to relax, and worrying about minor things. She also reported a decline in her grades. She had no medical conditions or history of substance use. Her mother had a history of major depression and anxiety. Ms A's symptoms had initially responded to fluoxetine, but she reported a worsening of symptoms a year after starting treatment. The dose of fluoxetine was increased to 40 mg/d, to which she responded.

Incidentally, she reported that about 8 months after starting fluoxetine, she could not drink coffee anymore. She would become extremely nervous, jittery, agitated with racing thoughts, and unable to sleep with very small amounts of coffee. This was unusual for her, as she loved coffee and was used to drinking a lot of coffee previously. It was concluded that she had symptoms of caffeine intoxication on drinking even small amounts of coffee and hence could not tolerate any amount of caffeine. This inability to tolerate coffee was seen when Ms A was rechallenged with coffee. It is also possible that some of the symptoms of anxiety the patient experienced and was treated for could have arisen from caffeine intolerance.

Caffeine is metabolized by CYP1A2.[2] It is one of the most abundant CYP liver enzymes and is responsible for metabolism of several critically important medications. Certain medications, including antidepressants such as fluvoxamine and fluoxetine, antiarrhythmics (mexiletine), and bronchodilators such as theophylline, have been reported to be potent inhibitors of this isoenzyme.[3] This activity might have important clinical implications, since medications that are metabolized by, or bind to, the same CYP enzyme have high potential for pharmacokinetic interactions due to inhibition of drug metabolism. Nicotine is also a CYP1A2 inducer, and use of medications like clozapine might necessitate dose adjustments in smokers. Pharmacokinetic interactions at the CYP1A2 enzyme level may cause toxic effects during concomitant administration of caffeine and certain drugs used for cardiovascular, CNS, gastrointestinal, infectious, respiratory, and skin disorders. Thus, patients who present with symptoms of increased caffeine intake and are taking medications that inhibit CYP1A2 enzymes should be advised to decrease their caffeine intake.

We recommend that whenever a patient presents with any side effects of medications, an accurate and thorough history be taken, with an emphasis on the temporal onset of symptoms in relation to medication changes or adjustments. The possibility of drug-drug interaction should always be considered.

References

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