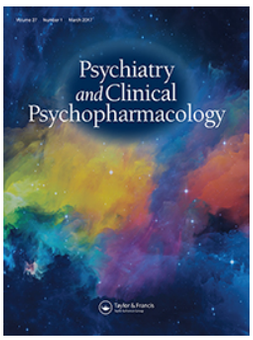

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LETTER TO THE EDITORS

Symptomatic cholelithiasis associated with combined use of methylphenidate and fluoxetine in an otherwise healthy adolescent girl

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To the Editor:

Cholelithiasis is defined as the presence of one or more calculi (gallstones) in the gallbladder [1]. Both methylphenidate (MPH) and fluoxetine have rarely been reported to cause cholelithiasis [2,3]. Here, we present an otherwise healthy adolescent girl who developed symptomatic cholelithiasis while under combined treatment with MPH and fluoxetine.

Case

A 17-year-old girl with normal developmental history has been followed up with diagnosis of social anxiety disorder, generalized anxiety disorder and attention deficit hyperactivity disorder for more than two years. She has been taking fluoxetine 20–40 mg/day and MPH 36–54 mg/day for almost two years. Her anxiety and inattention symptoms showed much to very much improvement with the treatment. She tolerated medications generally well without any significant side effects. Her weight was 49 kg at first presentation and 53 kg when her medications were stopped after two years due to a possible side effect. She developed a sudden onset abdominal pain accompanied with nausea and vomiting after a dinner. She had no fever or other systemic signs of infection at that time. She was referred to emergency service and was diagnosed with biliary colic with multiple gallstones. Her abdominal and biliary ultrasound examination revealed no significant problems except multiple gallstones, with largest one being 7 mm. She was extensively examined in a faculty hospital for possible causes of cholelithiasis but no obvious reasons were found. Her weight was 53 kg and body mass index was 18.7. She did not have any medical disease or known risk factors, including family history, to develop cholelithiasis. Cholelithiasis was considered to be MPH- and fluoxetine-related and she was recommended to stop her medications and planned for a clinical follow-up before no further interventions were done. During the 10 months of medication-free period, she had no biliary symptoms. A second detailed examination for gallstones revealed some reduction in the size of the gallstones. Previous medication history (MPH and fluoxetine) was reconsidered as the most probable cause by her physicians.

Discussion

Our search in PubMed and Google Scholar revealed no reports of MPH-related cholelithiasis in scientific literature. However, an internet-based resource reported 32 patients (0.28%), in a large sample of patients who were using MPH (Concerta), who developed cholelithiasis when taking MPH [2]. More than half of the patients who developed cholelithiasis were between 10 and 30 years of age and 80% of them were female. Similarly, we could not see any reports of fluoxetine-related cholelithiasis in scientific literature; however, the same internet-based resource reported 293 people (0.72%), in a large sample of patients who used fluoxetine, developed cholelithiasis when taking fluoxetine. Eighty-three per cent of those who developed cholelithiasis were female [3]. Cholelithiasis and biliary pain were also reported among the side effects in the FDA-provided product information sheets for fluoxetine [4], but not for MPH [5]. Given the absence of other possible causes and reduction in the size of the gallstones after discontinuation of MPH and fluoxetine, we considered cholelithiasis in this case as medication-related. Although there are no clear pathopysiological mechanisms for either medications to induce cholelithiasis, being female and using multiple medications may be risk factors in this case. Assessment with the Naranjo causality scale revealed a score of 6, showing probable adverse drug reaction [6]. Mental health clinicians using psychopharmacological interventions should keep in mind this rare

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side effect, particularly in female subjects and in the use of multiple psychopharmacological agents.

Disclosure statement

No potential conflict of interest was reported by the authors.

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