Interstitial lung disease induced by fluoxetine

A. Deidda[1,2], S. Lampus,[2] A. Bocchetta[1,3], C. Pisanu[1], L. Micheletto[2], M.V. Sanna[2], M.E. Stochino[2]

[1]Dept. of Biomedical Sciences, Section of Neuroscience and Clinical Pharmacology, University of Cagliari, Italy
[2]Sardinian Regional Center of Pharmacovigilance, Cagliari, Italy
[3]Unit of Clinical Pharmacology, Azienda Ospedaliero-Universitaria, Cagliari, Italy

Fluoxetine is one of the most commonly prescribed selective serotonin reuptake inhibitors and has a better side effect profile compared to classical tricyclic antidepressants. Among other safety concerns, there are a few isolated case reports linking fluoxetine to lung disease. We describe a case of interstitial lung disease following prolonged fluoxetine treatment and discuss it in view of the existing literature.

A 67 years old woman had suffered from recurrent major depression since the age of 38. She had also attempted suicide twice. In 1989 she was prescribed fluoxetine and lithium. She responded well to acute treatment but, given the severity and recurrent nature of her episodes, she was continued with the same combination. She was referred to our unit for monitoring of her lithium therapy. Over the following 23 years, fluoxetine doses ranged between 20 and 40 mg/daily, whereas lithium was maintained within the therapeutic range (0.60-0.80 mmol/l). Since 1997, the patient started to complain recurrent respiratory symptoms which were first attributed to inflammation (recurrent bronchitis). However, respiratory symptoms worsened over the years and the patient was eventually hospitalized in a pneumology unit (October 2012). The hospital diagnosis was 'interstitial lung disease'.

A suspected adverse drug reaction was reported to the Italian regulatory authority. The adverse reaction was considered 'severe' as it had resulted in hospitalization. The role of concomitant medications and comorbidities was excluded and the causality assessment, evaluated by the Naranjo algorithm, was 'probable' also based on previous reports of lung disease associated with fluoxetine. Fluoxetine was withdrawn, but clinical conditions did not improve and respiratory function tests remained unchanged.

As lung disease diagnoses varied across reports, we conducted a systematic review of the literature using the keywords "drug-induced lung disease", "interstitial pneumonia", "acute interstitial pneumonitis", "fluoxetine hydrochloride" and MeSH terms "Humans", "Lung Diseases, Interstitial/chemically induced" "Fluoxetine/adverse effects" and "Alveolitis, Extrinsic Allergic/chemically induced". We found seven case reports (Bass et al., 1992; Gonzalez-Rothi et al., 1995; de Kerviler et al., 1996; Vandezande et al., 1997; Braun et al., 1999; Estarriol et al., 2002; Bernard et al., 2009).

Interestingly, we also found an experimental animal model showing that fluoxetine can reproduce chronic interstitial pneumonia similar to that observed in humans (Capelozzi et al., 2007).

In conclusion, fluoxetine-induced pneumopathy should be considered in patients presenting with dry cough, associated or not with dyspnoea. According to the literature and to our case report, special attention should be devoted to increases in fluoxetine doses and to long-term therapy.

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