Dig Dis Sci (2010) 55:1806–1807
DOI 10.1007/s10620-010-1192-7

CORRESPONDENCE

Sertraline Hepatotoxicity: Report of a Case and Review of the Literature

Virginia Collados · Hacibe Hallal · Raúl J. Andrade

Published online: 22 April 2010

To the Editor,

We read with interest the recent case reported by Tabak et al. [1] on sertraline-induced liver injury. We completely agree with the conclusions drawn by the authors and we would add some comments.

In some databases of drug-induced liver diseases [2], antidepressants represent 5% of the reported cases with different levels of injury.

For all the types of antidepressants, the newer selective serotonin reuptake inhibitors (SSRIs) have a low incidence of hepatotoxicity, from 1.28 to 3.62 cases per patient-year and among them, the incidence of sertraline is the lowest of its group, 1.28 (0.42–3) cases per patient-year.

However, several cases of hepatotoxicity associated with this drug have been published in the scientific literature.

In addition to those articles cited by Tabak et al. [3], we could add another four cases (Table 1): a fatal hepatitis due to hypersensitivity reaction cholestasis that appeared 2 months after taking sertraline with a recovery time of 6 months [4]; another case of cholestasis that appeared 2 weeks after starting treatment with sertraline and bromazepam with normalization of analytic parameters at the fourth month [5]; and acute hepatocellular injury after 1 month of taking sertraline with a normalization period of 3 months [6]. Therefore, these cases make the range of sertraline hepatotoxicity broader, which ranges from asymptomatic hypertransaminasemia to fulminant hepatitis presentation.

In all published cases, the onset of symptoms occurs between the first and ninth week [7], except in the case reported by Verrico [8] in whom the symptoms developed immediately after the association of donepezil, a drug that, like sertraline, is metabolized through cytochrome P-450 2D6.

In the cases reported by Tabak et al., the hepatic injury developed with a 6-month delay, while the patient was taking a low dosage of sertraline (25 mg/day). This suggests metabolic idiosyncrasy. Indeed, although the mechanism of sertraline-induced hepatotoxicity is not yet clear, we agree with some authors that it might be related to the accumulation of sertraline in the body because sertraline acts as an inhibitor of its own metabolism.

For example, Lucena et al. [9] state that the incidence of elevated liver enzymes increases from 0.5 to 1.3% when the dose of sertraline is greater than 100 mg/day, and Lammert et al. [10] recently demonstrated a higher frequency of hepatotoxicity in drugs whose daily dose is equal to or higher than 50 mg/day.

Reporting of adverse drug reactions, which allows physicians to carefully determine the benefit/risk ratio of a given therapy, remains crucial. In addition, due to the current absence of a screening method to identify individuals susceptible to drug-induced liver injury, prompt drug withdrawal at symptom onset may help to prevent progression to irreversible liver damage.

V. Collados (✉)
Hospital Pharmacy Service, Hospital Sur, Madrid, Spain
e-mail: vircoll@wanadoo.es

H. Hallal
Gastroenterology Service, Hospital Morales Meseguer, Murcia, Spain

R. J. Andrade
Liver Unit, University Hospital Virgen de la Victoria, Málaga, Spain

Table 1 Other sertraline-induced hepatotoxicity cases

Case	Author (year)	Symptoms	Biochemical test	Time to resolution
1	Fartoux-Hyemann et al. (2001) [3]	Fatigue, jaundice, and somnolence	Bt 10,5 mg/dl AST 980 UI/l ALT 906 UI/l ALKP 121 UI/l	Exitus
2	Galan Navarro (2001) [4]	Jaundice, dark urine, pruritus	ALT 144 UI/l AST 70 UI/l ALKP 1034 UI/l GGT 250 UI/l Bt 4.54 mg/dl Bd 2.57 mg/dl	6 months
3	Martinez Martos (2002) [5]	Pruritus	ALT 215 UI/l AST 89 UI/l ALKP 1034 UI/l GGT 586 UI/l Bt 3.7 mg/dl Bd 1.9 mg/dl	4 months
4	Collados et al. (2008) [6]	Asthenia, abdominal pain, jaundice	ALT 500 UI/l AST 191 UI/l ALKP 377 UI/l GGT 508 UI/l Bt 2.66 mg/dl Bd 1.39 mg/dl	3 months

Bt Bilirubin, total, *Bd* Bilirubin, direct, *ALT* Alanine aminotransferase, *AST* Aspartate aminotransferase, *ALKP* Alkaline phosphatase, *GGT* gamma glutamyl transferase

References

1. Tabak T, Gunduz F, Tahan V, Tabak O, Ozaras R. Sertraline Hepatotoxicity: Report of a Case and Review of the Literature.
2. Carvajal GPA, del Garcia PJ, Sanchez AS, Velasco MA, de Rueda CAM, Lucena MI. Hepatotoxicity associated with the new antidepressants. *J Clin Psychiatry*. 2002;63:135–137.
3. Fartoux-Heymann L, Hezode C, Zafrani ES, Dhumeaux D, Mallat A. Acute fatal hepatitis related to sertraline. *J Hepatol*. 2001;35:683–684.
4. Galán Navarro JL. Hepatitis aguda colestásica probablemente causada por sertralina. *Rev Esp Enferm Dig*. 2001;93(12):822.
5. Martínez YM. Mujer de mediana edad con prurito y patrón analítico de colestasis aguda. *SEMERGEN*. 2002;28(2):105–107.
6. Collados Arroyo V, Plaza Aniorte J, Hallal H, Perez-Cuadrado E. Hepatotoxicidad asociada a Sertralina. *Farm Hosp*. 2008;32:60–61.
7. Drugs and Healthcare product Spanish Agency. https://sinaem4.agemed.es/consaem/especialidad.do?metodo=verFichaWordPdf&codigo=59718&formato=pdf&formulario=FICHAS
8. Verrico MM, Nace DA, Towers AL. Fulminant chemical hepatitis possibly associated with donepezil and sertraline therapy. *J Am Geriatr Soc*. 2000;48(12):1659–1663.
9. Lucena MI, Carvajal A, Andrade RJ, Velasco A. Antidepressant-induced hepatotoxicity. *Expert Opin Drug Saf*. 2003;2:249–262.
10. Lammert C, Einarsson S, Saha C, Niklasson A, Bjornsson E, Chalasani N. Relationship between daily dose of oral medications and idiosyncratic drug-induced liver injury: search for signals. *Hepatology*. 2008;47:2003