REV COLOMB ANESTESIOL. 2017;xxx(xx):xxx–xxx

Revista Colombiana de Anestesiología
Colombian Journal of Anesthesiology
www.revcolanest.com.co

Case report

Pregabalin-induced liver injury – Case report☆

Manuel Quintero-Castellanos[a,b,*]

[a] *Universidad Pedagógica y Tecnológica de Colombia, Tunja, Colombia*
[b] *Unidad Manejo del Dolor Hospital San Rafael, Tunja, Colombia*

ARTICLE INFO

Article history:
Received 3 February 2017
Accepted 25 July 2017
Available online xxx

Keywords:
Low back pain
Pregabalin
Jaundice
Liver failure
Toxicity

ABSTRACT

The first case of idiopathic pregabalin-induced toxicity in Latin America is reported in a patient with radicular pain secondary to lumbar spinal stenosis, who presented with jaundice and elevation of liver enzymes, associated with the use of pregabalin. A diagnosis of drug-induced liver injury was made. Liver function was normalized once the drug was discontinued without any sequelae. It is important to be aware of the potential hepatic toxic effects of pregabalin, despite the fact that the drug shows no evidence of liver metabolism and liver toxicity is very unusual. The liver injury mostly resolves upon pregabalin removal.

Lesión hepática inducida por el uso de pregabalina. Reporte de Caso

Palabras clave:
Dolor de la región lumbar
Pregabalina
Ictericia
Fallo hepático
Toxicidad

RESUMEN

Se reporta el primer caso de toxicidad idiosincrática inducida por pregabalina en Latinoamérica, en un paciente con dolor radicular secundario a canal lumbar estrecho, el cual se presentó con ictericia y elevación de enzimas hepáticas, asociada al uso de pregabalina. Se hace diagnóstico de lesión hepática inducida por drogas. La función hepática se normalizo una vez se suspendió el medicamento sin dejar ninguna secuela. Es importante tener en cuenta que la pregabalina puede tener efectos tóxicos severos a nivel hepático, a pesar de no tener metabolismo evidente a este nivel y ser muy poco frecuente, en la mayoría de casos la lesión hepática resuelve al suspender la pregabalina.

☆ Please cite this article as: Quintero-Castellanos M. Lesión hepática inducida por el uso de pregabalina. Reporte de Caso. Rev Colomb Anestesiol. 2017. http://dx.doi.org/10.1016/j.rca.2017.07.007

* Correspondence to: Avenida Norte 47-18, Tunja, Colombia.
E-mail address: manuelquinteromd@yahoo.com

Introduction

At least 6 cases of acute liver disease secondary to the use of pregabalin have been reported worldwide.[1–6] No cases of liver toxicity associated to the drug had been so far reported in Latin America so this is the first report. In this case, the evolution was similar to the cases previously reported. After 8 days of continued use of pregabalin 75 mg every 12 h, the patient presented jaundice associated with a significant elevation of liver transaminases that were normalized a few days after interrupting the use of the medication, with no evidence of sequelae.

Patient information

A 53-year old male patient, farmer living in a rural area, who presented at the emergency department due to severe lumbar pain for 3 days (VAS 10/10). The pain irradiated to the lower right limb, and was associated with a loss of strength of the extremity after manipulation of a heavy object. The patient self-medicated with diclofenac and acetaminophen with no pain relief, resulting in his visit to the ER. The patient's history included hypertension treated and controlled with losartan 50 mg every 12 h, type II diabetes mellitus treated and controlled with vildagliptin 50 mg-metformin hydrochloride 850 mg. The patient is an occasional user of alcoholic drinks, with no relevant infections, surgical or family history.

Clinical findings

The physical examination showed nerve root signs, positive right Lasegue's sign, positive right Bragard's, and loss of strength in the same extremity. The diagnosis was mixed severe acute lumbar pain requiring further study, controlled high-blood pressure and controlled type II diabetes mellitus. On day 12 of hospitalization the patient presented clinical signs of jaundice and paraclinical tests were done (see Table 1). Pregabalin-induced liver injury was suggested, in the absence of any other associated causes. 3 days after stopping the use of the medication, the jaundice resolved with no apparent sequelae at the time of hospital discharge, or during the following visits over the next 6 months.

Diagnostic evaluation

Imaging studies: lumbosacral spine X-rays: L4–L5 space narrowing, antalgic scoliosis, and lumbar MRI evidencing L2–L3 compressive disc hernia with stenosis of the right foramen, changes in facet joints arthrosis, and spondylolisthesis L4–L5.

Pre-surgical testing was done: TGO/ASAT 10.4 U/l (reference value 0–32 U/l), TGP/ALAT 23.1 U/l (reference value 0–41 U/l), total bilirubin 1.01 mg/dl (direct 0.36 mg/dl, indirect 0.65 mg/dl), alkaline phosphatase 58 U/l, glycaemia 129 mg/dl, BUN 20.2 mg/dl, creatinine 0.77 mg/dl, sodium 136.1 meq/dl, potassium 4.18 meq/dl, chlorine 101.1 meq/dl, prothrombin time (PT) of 11.8 s, INR 0.84, partial thromboplastine time (PTT) of 36.2 s and blood count within the normal limits. All tests were within the normal range, with no evidence of liver dysfunction. On day 12 of hospitalization the patient presents jaundice and new liver tests were ordered: TGO/ASAT 480 U/l TGP/ALAT 1012.5 U/l, total bilirubin 0.58 mg/dl (direct 0.22 mg/dl, indirect 0.36 mg/dl), lactic dehydrogenase 415 U/l (reference value 280–480 U/l), blood test within the normal limits. There were no economic, language, or cultural barriers for the diagnosis. Based on these results, a diagnosis of drug-associated hepatitis was made, ruling out infectious hepatitis since no evidence of fever, hepatomegaly, or relevant blood test changes was found. Possibly the hepatitis was secondary to the use of pregabalin and the drug was immediately removed. There is progressive jaundice improvement and 3 days later the patient undergoes hepatic enzymes control with the following results: TGO/ASAT 49 U/l TGP/ALAT 348 U/l, thus confirming drug related hepatitis, secondary to the use of pregabalin. Afterwards the patient evolves with no evidence of liver or other sequelae until the time of discharge, with a significant reduction in liver enzymes and resolution of jaundice.

Therapeutic intervention

Medical management was introduced with intravenous diclofenac every 12 h and IV tramadol 50 mg every 8 h, with rescue doses of 25 mg between doses. In view of the pain severity and poor analgesic regime response, an interconsultation with the pain management service resulted in the additional prescription of pregabalin 75 mg every 12 h on day 4 of hospitalization, while waiting for the decision of the surgical team to define the approach. The persistence of severe pain lead to exploration and decompression of the L2–L3 canal with posterior arthrodesis of the lumbar spine on day 9 of hospitalization with no major complications. After 8 days of continued use of pregabalin, the decision was made to remove the drug as the potential etiological agent of the drug-associated hepatitis. Clinical and paraclinical improvement was observed.

Follow-up and results

The pre-surgical tests indicate that the patient's liver function was normal at admission and his baseline pathologies were controlled. The lumbar MRI clearly established the etiology of the patient's pain, which based on its severity and refractory management required a surgical approach. The quite significant elevation of the hepatic transaminases, particularly TGP/ALAT (that increased over 40 times its initial value) showed the presence of a liver inflammatory injury. Such injury was associated with the use of pregabalin, since upon removal of the drug, the transaminase levels experienced a positive response.

Discussion

Pregabalin is an FDA approved medication for managing pain associated with diabetic neuropathy, post-herpetic neuralgia, as adjuvant therapy in the management of partial convulsive crisis in adults, management of fibromyalgia, and neuropathic