Meloxicam-induced liver toxicity

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Abstract

We report the case of a female patient with rheumatoid arthritis who developed acute cytolytic hepatitis due to meloxicam. Recently introduced in Belgium, meloxicam is the first nonsteroidal antiinflammatory drug with selective action on the inducible form of cyclooxygenase 2. The acute cytolytic hepatitis occurred rapidly after meloxicam administration and was associated with the development of antinuclear antibodies suggesting a hypersensitivity mechanism. This first case of meloxicam related liver toxicity demonstrates the potential of this drug to induce hepatic damage. (Acta gastroenterol. belg., **1999**, 62, **255-256**).

Key words : meloxicam, hepatitis, nonsteroidal antiinflammatory drug.

Introduction

Meloxicam is a nonsteroidal antiinflammatory drug (NSAID) belonging to the oxicam family. It has been recently introduced on the Belgian market to treat rheumatoid arthritis and osteoarthritis. Its main advantage has been claimed to be related to its selective action on the inducible form of cyclooxygenase 2 (COX-2 isoform) (1).

With regard to its potential toxicity, even if meloxicam seems to induce less gastrointestinal side effects, a similar incidence in perturbations of liver function tests between meloxicam and other NSAID's has been demonstrated during clinical trials (1-3). Until now and to the best of our knowledge, no case of meloxicam-induced hepatitis has been reported. We describe the first case of a woman who developed a hepatitis following meloxicam administration.

Case report

A Belgian 46-year old woman was seen for acute hepatitis on March 4th, 1998.

Her medical history was only marked by rheumatoid arthritis since 1990 and venous insufficiency since 1997. She had no previous history of liver disease, blood transfusion, drug addiction, or alcohol abuse.

Her medication included : prednisolone 5 to 7.5 mg daily since February 1997 and coumarin 400 mg daily for lower extremities' discomfort related to venous insufficiency since September 1997. From 1990 to September 1997, she also received piroxicam during numerous periods of severe arthralgias and salazopyrine between 1994 and 1996.

Numerous biochemical work-up including liver biochemistry and antinuclear antibodies performed from 1990 until February 3th 1998 were unremarkable.

On February 9th, she was started on meloxicam treatment, 15 mg daily, for acute exacerbation of arthralgias.

On February 12th, meloxicam administration was stopped due to the occurrence of inappetency.

On February 20th, jaundice and asthenia were observed. Laboratory data performed on February 24th revealed increased serum aminotransferase activities (ALT = 2340 I.U./L (N < 42) ; AST = 710 I.U./L (N < 35)) and serum total bilirubin 10.4 mg/dl (N < 1). Serum gamma-glutamyltransferase and phosphatase alkaline levels were 190 I.U./L (N < 45) and 520 I.U./L (N < 330), respectively. The hemogram was normal. At that time, all medications were withdrawn.

On March 4th, the patient was feeling better. Her clinical examination was normal at the exception of jaundice. A blood analysis showed decreasing serum transaminase levels : ALT = 56 I.U./L, N < 32 ; AST = 198 I.U./L, (N < 25), and bilirubin level : 5.1 mg/dl (N < 1). Serum gamma-glutamyltransferase and phosphatase alkaline levels were 141 I.U./L (N < 45) and 98 I.U./L (N < 60), respectively. A complete serological examination for IgM HAV, HBsAg and HBcAb, anti-HCV antibodies as well as recent infection by Epstein-Barr virus, Herpes simplex virus, and cytomegalovirus was negative. Test for antinuclear antibodies were positive at 1/320. Smooth muscle and antimitochondrial antibodies remained negative. The serum levels of iron, ceruloplasmin and α1-antitrypsin were normal. Ultrasonography of the upper abdomen was normal. At that time, prednisolone was restarted because of increasing arthralgias.

On April 8th and May 5th new blood analyses showed normal liver function tests despite the fact that prednisolone and coumarin have been reintroduced on April 2th. A second serological test for hepatitis C was again negative. Test for antinuclear antibodies were still positive at 1/320 whereas smooth muscle and antimitochondrial antibodies remained negative.

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Discussion

We describe the case of a woman presenting acute cytolytic hepatitis immediately after meloxicam administration.

The hepatitis can be reasonably ascribed to meloxicam for the following reasons : (a) recent viral infection has been excluded by appropriate serological tests ; (b) other drugs taken by the patient have been reintroduced without inducing perturbations of liver function tests ; (c) no other toxic or alcohol have been taken by the patient ; (d) another cause of acute cytolytic hepatitis such autoimmune hepatitis or metabolic disease has also been excluded ; (e) finally, there was a clear relationship between meloxicam administration and the occurrence of hepatitis as well as between drug discontinuation and the normalisation of liver function tests.

The mechanism of meloxicam-induced hepatitis remains unknown. There was no clinical sign suggesting a hypersensitivity mechanism. However, the rapid occurrence of hepatitis after meloxicam administration as well as the development of antinuclear antibodies are indirect arguments in favour of a hypersensitivity mechanism. A toxic mechanism seems very unlikely since meloxicam was given at usual dose and during only three days.

Interestingly, it must be outlined that piroxicam was given during several years without inducing any perturbation of liver function tests. This could suggest an absence of cross-reactivity between piroxicam and meloxicam liver toxicity. Conversely, it is difficult to exclude the possibility that previous administration of piroxicam might have been responsible for a sensibilization phenomenon to meloxicam. This last hypothesis seems however to be unlikely since piroxicam has been taken intermittently during a very prolong period.

With regard to piroxicam, several case reports have described the occurrence of acute hepatitis after its administration, varying from cholestatic or a mixed cholestatic-hepatocellular type of injury to a predominantly hepatocellular pattern of injury (4). No case of acute hepatitis has been reported with other oxicam agents such as pivoxicam, tenoxicam, lornoxicam or cinnoxicam but the majority of these agents are always under study.

In conclusion, this first case of meloxicam related liver toxicity demonstrates the potential of this drug to induce hepatic damage.

References

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