Peer reviewed article

Hepatotoxicity induced by celecoxib and amlodipine

Philipp Zinsser[a], *Beat Meyer-Wyss*[a], *Prisca Rich*[b]

[a] St. Claraspital, Division of Internal Medicine, Basel, Switzerland
[b] Medical office, Baden, Switzerland

Introduction

We report two cases with severe hepatotoxicity induced by celecoxib and amlodipine respectively. In both patients the observed liver damage was of the mixed cytolytic/cholestatic type and was entirely reversible.

Case reports

Case 1

A 58-year old woman received celecoxib (Celebrex®) for 2 years to treat fibromyalgia. Pathological liver enzyme levels were discovered incidentally. Abdominal sonography showed no cholelithiasis, the bile ducts were normal, and there were no signs of chronic liver disease. At admission the patient was icteric and physical examination revealed no signs of chronic liver disease. Her history confirmed that she was taking celecoxib more or less regularly but no other medication within the last three months. She tested negative for anti-HAV, anti-HCV, HBs-antigen, antimitochondrial antibody and antinuclear antibodies. Laboratory tests showed (upper limit of normal): bilirubin 151 (20) umol/L, ASAT 1032 (37) U/L, ALAT 1058 (40) U/L, alkaline phospatase 1101 (270) U/L, gamma-GT 467 (61) U/L, thromboplastin time 81 (>70) %, albumin 35 (>38) g/L.

A percutaneous liver biopsy revealed severe, acute hepatitis with marked, mixed inflammatory infiltrates of the portal fields, and confluent, focal necrosis. After discontinuation of celecoxib, the cholestatic parameters normalised during the following 3 months. The transaminases however returned to normal only after 1 year (Fig. 1).

Case 2

A 87-year-old woman was treated with amlodipine (Norvasc®) for several years for hypertension. One month before she was admitted to the hospital, she developed pruritus and 2 weeks later painless jaundice. Abdominal CT revealed a normal, homogeneously structured liver without focal injury and abdominal sonography excluded cholelithiasis. Laboratory tests excluded viral or autoimmune hepatitis and showed (upper limit of normal): bilirubin 356 (20) umol/L, ASAT 291 (37) U/L, ALAT 300 (40) U/L, alkaline phospatase 1019 (270) U/L, gamma-GT 323 (61) U/L, thromboplastin time 76 (>70) %, albumin 30 (>38) g/L. A liver biopsy showed severe intra-hepatocellular and canalicular cholestasis with moderate inflammatory infiltrates without necrosis, compatible with drug-induced liver damage.

After discontinuation of amlodipine, the transaminases and parameters of cholestasis decreased markedly within 2 weeks (Fig. 2). However, after developing urosepsis, this multi-morbid patient died as a consequence of pulmonary embolism.

Comment

The two patients discussed in this letter were admitted to the hospital for severe, drug induced hepatitis. We were able to incriminate celexoxib and amlodipine respectively as the responsible drugs. Besides celecoxib [2–4] other COX-2 inhibitors have been reported to be associated with hepatotoxicity, culminating in fulminant liver necrosis and death as well as in severe, acute pancreatitis. According to "Swissmedic", three other cases of hepatotoxicity possibly associated with amlodipine had been reported until August 2002. Hepatotoxicity induced by amlodipine is highly unusual [5].

In summary drug induced liver disease should not be underestimated in everyday clinical practice, even if this side effect may not be listed in current reference books as it is in the case of amlodipine [1].

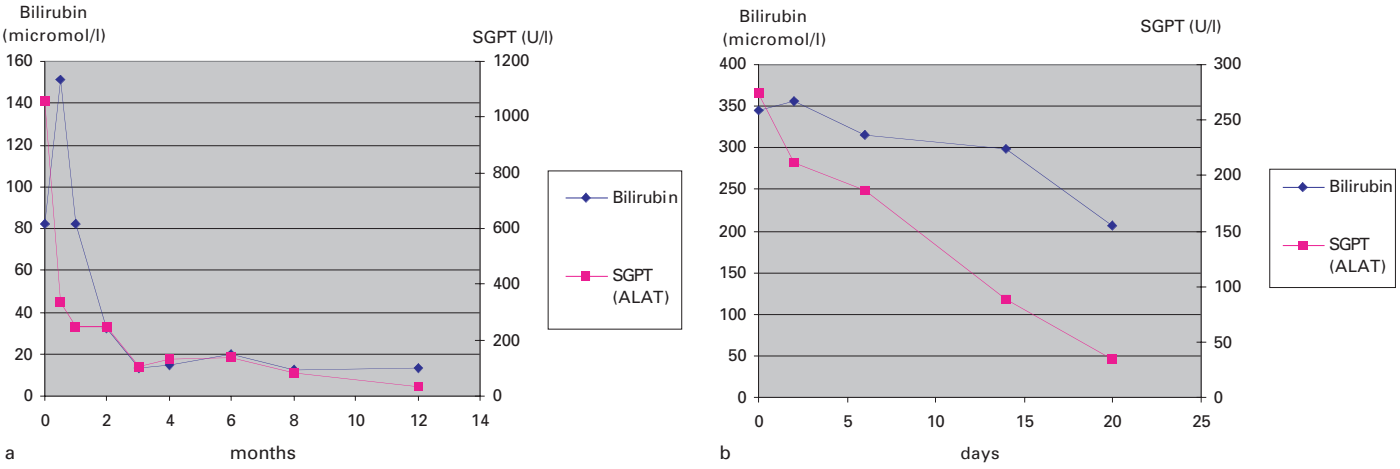
Correspondence:
Beat Meyer-Wyss
St. Claraspital
Kleinriehenstrasse 30
CH-4016 Basel, Switzerland
E-Mail: beat.meyer@claraspital.ch

References

1 Arzneimittelkompendium der Schweiz 2003. Documed 1883–1884.
2 O'Beirne JP, Cairns SR. Cholestatic hepatitis in association with celecoxib. BMJ 2001;323:23.
3 Galan MV, Gordon SC, Silverman AL. Celecoxib-induced cholestatic hepatitis. Ann Intern Med 2001;134:254.
4 Alegria P, Lebre L, Chagas C. Celecoxib-induced cholestatic hepatotoxicity in a patient with cirrhosis. Ann Intern Med 2002;137:75.
5 Lafuente NG. Calcium cannel blockers and hepatotoxicity. Am J Gastroenterol 2000;95:2145.

Figure 1

a: values of bilirubin and SGPT after withdrawal of celecoxib (case 1).
b: values of bilirubin and SGPT after withdrawal of amlodipine (case 2).



No financial support declared.

Swiss
Medical Weekly

Official journal of
the Swiss Society of Infectious disease
the Swiss Society of Internal Medicine
the Swiss Respiratory Society

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website http://www.smw.ch (direct link from each SMW record in PubMed)

- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses

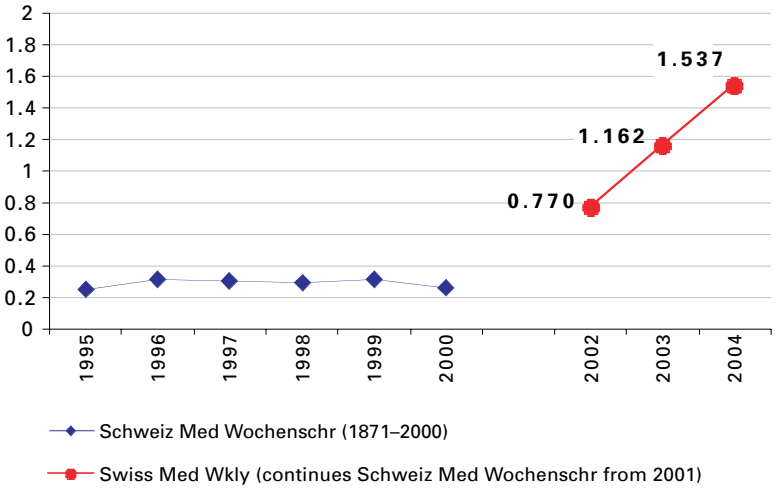
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:
http://www.smw.ch/set_authors.html

Impact factor Swiss Medical Weekly



EMH FMH Schwabe
Editores Medicorum Helveticorum

All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
SMW Editorial Secretariat
Farnsburgerstrasse 8
CH-4132 Muttenz

Manuscripts: submission@smw.ch
Letters to the editor: letters@smw.ch
Editorial Board: red@smw.ch
Internet: http://www.smw.ch