

LETTERS TO THE EDITOR EDİTÖRE MEKTUP

Severe liver enzyme elevation due to single-dose ranitidine in a pregnant woman

Bir gebede tek doz ranitidine bağlı şiddetli karaciğer enzim yüksekliği

To the Editor

Ranitidine is one of the widely used H₂ receptor blockers for gastric disorders as it rarely has severe hepatotoxicity (1, 2). To our knowledge, hepatotoxicity due to ranitidine has not been reported in a pregnant yet. We aimed to present a severe liver function test elevation after single-dose ranitidine in a nine-week pregnant woman.

A 36-year-old pregnant woman (nine gestational weeks) was admitted with severe epigastric pain, pyrosis and regurgitation after a lunch and was hospitalized. Esophagogastroduodenoscopy was performed and antral gastritis and mild hiatal hernia were detected. Biochemical parameters were in normal range. Ranitidine 150 mg bid and alginic acid were given to the patient for severe epigastric pain and pyrosis, and her pain was relieved with this treatment. On the second day of ranitidine treatment, ALT elevated to 1153 U/L, AST: 742 U/L, ALP: 88 mg/dl, GGT: 196 mg/dl, total bilirubin: 3.66 mg/dl, conjugated bilirubin: 2.72 mg/dl, PT: 11.9 sec, and INR: 1.09. Hepatitis and TORCH serologies were negative. Upper abdominal ultrasonography was normal except for two hemangiomas in the liver and mild enlargement of the spleen (13 cm). Ranitidine was discontinued. It was observed that liver function tests decreased gradually by day and at the end of the seventh day had decreased to nearly normal values. Two weeks later the liver function tests were completely in normal ranges. Ranitidine has been used widely

and safely in pregnancy, especially in the first trimester, due to its having no major teratogenic risk (3). There are limited papers about the use of proton pump inhibitors (PPIs) in pregnancy (4), but evidence about this issue remains insufficient. Follow-up of liver function tests is usually not needed in ranitidine use since only rare and mild hepatotoxicity of ranitidine has been reported (5). We followed the liver function tests of our patient since she was pregnant and were thus able to detect the severe elevation in enzymes on the second day. This condition could indicate the idiosyncratic hepatotoxic effect of ranitidine. A well-described idiosyncratic hepatic injury due to cimetidine has been reported, but there has been no report of such a reaction due to ranitidine. However, Luyendyk et al. (6) has described an idiosyncrasy-like hepatic injury due to ranitidine in rats (6). Black et al. (7) reported three cases of ranitidine hepatotoxicity - two without icterus and one with severe cholestatic condition; the liver function tests of those cases were not severely elevated. The other case, as reported by Lauritsen et al. (8), had severe cholestatic table and severe liver function test elevation. As a result, following liver function tests, especially in pregnant, may be useful during ranitidine treatment, which has been determined safe in general practice widely and also in pregnancy.

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REFERENCES

1. Lewis JH. Hepatic effects of drugs used in the treatment of peptic ulcer disease. *Am J Gastroenterol* 1987; 82: 987-1003.
2. Zeldis JB, Friedman LS, Isselbacher KJ. Ranitidine: a new H₂-receptor antagonist. *N Engl J Med* 1983; 309: 1368-73.
3. Ruigomez A, Garcia Rodriguez LA, Cattaruzzi C, et al. Use of cimetidine, omeprazole, and ranitidine in pregnant women and pregnancy outcomes. *Am J Epidemiol* 1999; 150: 476-81.
4. Nikfar S, Abdollahi M, Moretti ME, et al. Use of proton pump inhibitors during pregnancy and rates of major malformations: a meta-analysis. *Dig Dis Sci* 2002; 47: 1526-9.
5. Barr GD, Piper DW. Possible ranitidine hepatitis. *Med J Aust* 1981; 2: 421.
6. Luyendyk JP, Maddox JF, Cosma GN, et al. Ranitidine treatment during a modest inflammatory response precipitates idiosyncrasy-like liver injury in rats. *J Pharmacol Exp Ther* 2003; 307: 9-16.
7. Black M, Scott WE Jr, Kanter R. Possible ranitidine hepatotoxicity. *Ann Intern Med* 1984; 101: 208-10.
8. Lauritsen K, Havelund T, Rask-Madsen J. Ranitidine and hepatotoxicity. *Lancet* 1984; 2: 1471.

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