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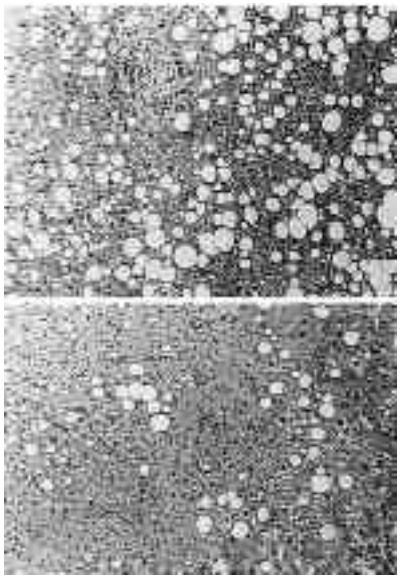
Bezafibrate for tamoxifen-induced non-alcoholic steatohepatitis

Sir—Karin Oien and colleagues (Jan 2, p 36)[1] report tamoxifen-induced liver cirrhosis. It is easy to withdraw tamoxifen from breast-cancer patients with non-alcoholic steatohepatitis (NASH), but the benefits of 5-year adjuvant tamoxifen undoubtedly outweigh the risk of cirrhosis if we can prevent the progression of NASH. Coadministration of bezafibrate to patients with tamoxifen-induced NASH, might help them to tolerate adjuvant tamoxifen.

400 mg bezafibrate, a peroxisome proliferator-activated receptor α (PPARα) activator, was given with tamoxifen to two patients with tamoxifen-induced NASH (liver/spleen ratio of computed tomography values –0·255 and –0·317 Housfield units) or with toremifene in a patient with toremifene-induced NASH (liver/ spleen ratio 0·071). The liver/spleen ratio reached normal values (>0·90) in two patients and recovered by more than 0·7 in the other patient within 10 months without any obvious changes in bodyweight. Liver biopsy revealed a substantial reduction in the numbers of fat droplets in the liver (figure).



Liver biopsy showing fat droplets before (upper) and after (lower) bezafibrate administration

These in-vivo findings are in accordance with the report that NASH-inducing drugs inhibit mitochondrial β-oxidation of fatty acids and respiration to include lipid deposition in human hepatocytes[2] and that the activation of peroxisomal β-oxidation of fatty acids through PPARα stimulation can compensate for insufficient mitochondrial β-oxidation.[3] Regular computed tomographic examination or ultrasonography in addition to laboratory tests are recommended to rule out liver metastasis and to monitor steatosis of the liver during tamoxifen treatment to prevent the progression of fatty liver to NASH and cirrhosis.

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Sexual dysfunction with protease inhibitors

Sir—Eduardo Martínez and colleagues (March 6, p 810)[1] describe 14 HIV-1 infected men who developed sexual dysfunction during protease inhibitor treatment. In the same issue, Rak Nandwani and Ysobel Gourlay report ten HIV-1-positive men receiving highly active antiretroviral treatment (HAART) who were treated wtih sildenafil citrate to improve erectile function.[2]

Despite the fact that their general condition has improved, many patients on HAART complain of sexual dysfunction. So far, little scientific attention has been given to this occurrence because this side-effect is reported only occasionally on patients' case report forms during clinical trials. However, if patients are questioned systematically, many report sexual dysfunction. This discrepancy is shown in two studies by the Institute of Tropical Medicine, Antwerp, Belgium.

In a randomised clinical trial that compared ritonavir plus saquinavir plus one nucleoside analogue with indinavir plus two nucleoside analogues[3] in 104 patients with longer than 36 weeks of follow-up, sexual dysfunction was reported on only four (4%) patients (one man in the ritonavir plus saquinavir group and three men in the other group). In an anonymous questionnaire survey of 97 patients treated with HAART, including a protease inhibitor, 32 (42%) of 77 men and eight (40%) of 20 women reported a decrease in their sexual appetite since the start of their treatment, whereas 27 (35%) of 77 men reported erectile dysfunction. Sexual dysfunction developed with all protease-inhibitor containing regimens, and no significant differences between the different protease inhibitors were seen.

These results underscore the importance of systematically questioning patients on HAART therapy about possible sexual dysfunction. In addition, further studies will have to be undertaken to unravel the underlying mechanisms by which protease inhibitors could cause this problem. If this issue is not adequately addressed, patients may not comply with their protease inhibitor treatment, wish to switch to less effective treatment regimens, or use sildenafil citrate with potential harmful side-effects due to pharmacokinetic interactions of this drug with protease inhibitors.

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