Letter

Alterations in Thyroid and Hepatic Function Tests Associated With Preparations of Sustained-Release Niacin

In the May 1992 issue of the *Mayo Clinic Proceedings* (pages 465 to 468), O'Brien and colleagues described the first cases of decreased levels of thyroxine-binding globulin attributed to sustained-release nicotinic acid. After I read that report, I reviewed the laboratory files of the seven residents at the Wisconsin Veterans Home who were taking preparations of sustained-release niacin. All the residents undergo an annual physical examination. Most of the attending physicians have preprinted order forms that allow them to elect thyroid function tests or a screening chemistry panel (or both). Thyroid function tests before and after the initiation of therapy were analyzed. The dates when these patients began taking niacin were noted, and the results of all liver function tests, including protein, albumin, aspartate aminotransferase, alkaline phosphatase, bilirubin, and prothrombin time, were reviewed. If abnormalities were noted, determinations before administration of niacin therapy were reviewed. In many instances, the data base was incomplete.

I identified three patients who had determinations of total thyroxine, triiodothyronine uptake, and free thyroxine index before the initiation of sustained-release niacin therapy and later during treatment. In two of these patients, the triiodothyronine uptake was normal before therapy, but increases during therapy were consistent with decreases in thyroid hormone binding capacity (Table 1). One patient was an otherwise healthy 45-year-old man with left hemiparesis attributed to an automobile accident. Values of aspartate aminotransferase, alkaline phosphatase, and bilirubin were normal on Jan. 31, 1991. Liver function tests were not done on Feb. 28, 1991, when the triiodothyronine uptake was increased. The other patient was a 64-year-old man with organic heart disease, mitral insufficiency, tricuspid insufficiency, chronic obstructive pulmonary disease, right-axis deviation, and peripheral vascular disease with carotid stenosis. He smoked 2 packs of cigarettes per day. His other medications included aspirin, gemfibrozil, dipyridamole, and diltiazem hydrochloride. In addition to the abnormal results of the thyroid function test, this resident also had other evidence of hepatic damage that was recognized during the 14th month of treatment with sustained-release niacin (1.5 g/day). At that time, the level of the aspartate aminotransferase was 1½ times the normal value, alkaline phosphatase was 2 times the normal limit, prothrombin time was 16.6 seconds (upper limit of normal, 12.2), and serum albumin was 2.6 g/dl. Four to 9 weeks after the discontinuation of niacin therapy, the enzyme levels and prothrombin time were normal, and the albumin had increased to 3.7 g/dl.

Experience with sustained-release niacin at the Wisconsin Veterans Home suggests that it should be used cautiously and that aspartate aminotransferase, alkaline phosphatase, and serum albumin values should be monitored. The 45-year-old resident who had a low concentration of thyroid-binding globulin (Table 1) is apparently tolerating the medication well at this time; levels of aspartate aminotransferase, alkaline phosphatase, and albumin are within the normal range. These findings suggest that changes in thyroid-binding globulin may not necessarily be related to toxicity but rather to the mechanisms that mediate the desired therapeutic effect of the drug.

Table 1.—**Laboratory Findings in Two Men Receiving Sustained-Release Niacin Therapy, Stratified by Dates and Dosages***

Niacin therapy	Date of test	T_4† µg/dl	T_3† uptake	FTI†	TSH† (mU/L)
45-yr-old man					
4/26/89: started	4/24/89	9.0	40.3	3.60	1.10
1/16/91: increased to 500 mg q.i.d.†	2/28/91	4.5‡	50.0§	2.25	1.18
9/11/91: changed to 1,000 mg (a.m.) and 250 mg (p.m.)	6/18/92//	6.1	42.0	2.56	0.73
64-yr-old man					
6/20/88: started	4/13/87	10.0	27.5	2.70	1.90
1/21/91: increased to 500 mg t.i.d.†	3/15/91	6.0	49.0§	2.94	1.61
4/7/92: discontinued	6/19/92	9.3	40.0	3.72	...

*All except three measurements (see other footnotes) were within the established normal ranges.
†FTI = free thyroxine index; q.i.d. = four times a day; T_3 = triiodothyronine; T_4 = thyroxine; t.i.d. = three times a day; TSH = thyroid-stimulating hormone.
‡Below the normal range.
§Above the normal range.
//Thyroxine-binding globulin, functional: 14.6 µg/dl (normal, 16.0-24.0). (Performed by Mayo Medical Laboratory, Rochester, Minnesota.)

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The authors reply

Dr. Drinka reports two cases of decreased thyroid hormone binding capacity in persons taking slow-release niacin. In one patient, liver function abnormalities were also confirmed, a finding consistent with our case report. In the other patient, liver function tests were unavailable when the thyroid function abnormalities were first noted. The dose of niacin had been decreased before the repeated blood tests that showed normal results of liver function tests and a mildly decreased thyroxine-binding globulin level. This adjustment may have resolved liver function abnormalities and caused partial improvement in the thyroxine binding capacity. For this reason, we believe that hepatotoxicity cannot be excluded in this patient. Nonetheless, this report again emphasizes the need to interpret results of thyroid function tests cautiously in persons receiving niacin.

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