Dental and Gingival Pain as Side Effects of Niacin Therapy*

Richard F. Leighton, MD; Neil F. Gordon, MD, PhD, MPH; Gilbert S. Small, DDS; William J. Davis, DDS; and Earl S. Ward Jr., PharmD

Two 65-year-old white men with coronary heart disease, given niacin therapy for dyslipidemia for 5 months, developed intense dental and gingival pain that was associated with increases in dose and that was relieved with discontinuance of niacin treatment. One individual who took crystalline niacin had beneficial effects on lipid levels, while the other person who took a delayed release preparation had little lipid effect. The cause of these previously unreported side effects of niacin therapy is uncertain but may be related to prostaglandin-mediated vasodilatation, hyperalgesia of sensory nerve receptors, and potentiation of inflammation in the gingiva with referral of pain to the teeth. (CHEST 1998; 114:1472–1474)

Key words: dyslipidemia; niacin; side effects

Abbreviations: HDL = high-density lipoprotein; LDL = low-density lipoprotein; Lp(a) = lipoprotein (a)

Niacin has long been recognized to be a useful lipid-lowering drug. It is the most effective drug for raising high-density (HDL) lipoprotein cholesterol and the only lipid-lowering drug that has been shown to lower serum levels of lipoprotein (a) (Lp[a]). In patients with coronary heart disease its use has been associated with lack of progression or actual regression of coronary plaques and a reduction in all-cause mortality.

The usual dose of niacin recommended for lowering lipid is 1.5 to 6 g daily, but because of side effects, few patients can take the larger dose. The side effects of niacin are well known and have been described in detail. The most consistent side effect is cutaneous flushing and the most serious side effect is hepatitis. In long-term studies, the incidence of discontinuing the drug due to side effects has varied from 10% to 40% even when comparable doses have been employed. New side effects may appear after 1 or 2 years of incident-free therapy. Two cases of hitherto unreported side effects of niacin therapy, dental and gingival pain, are presented here.

CASE REPORTS

CASE 1

A 65-year-old white man, previously asymptomatic, developed unstable angina in September 1996. At angiography, he was found to have a 90% lesion in the left circumflex coronary artery that was dilated and stented. Aside from age and male sex, he had no other conventional risk factors. His lipid values appear in Table 1. His serum Lp(a) was found to be elevated at 0.67 mmol/L (26 mg/dL; Berkeley Heart Lab; San Mateo, CA). The median normal value for this laboratory value is 0.10 mmol/L (4 mg/dL). The median value is for the mid-50% distribution for nearest age category based on data for a white study population with an age range of 45 to 64 years. The numbers of subjects in age and sex groups ranged from 1,123 to 1,542 subjects.

Therapy was started with crystalline niacin in progressively increasing doses over a 4-week period, achieving a peak dose of 3 g/d (750 mg qid). He experienced flushing, mainly in the face and neck, following each dose of niacin. Following the nocturnal dose, he frequently awoke with a flushed feeling in the tongue and gingiva. He continued receiving this dose for 4 months, at which time his serum lipid values were determined again. The dose of niacin was increased to 4 g/d in an effort to lower the Lp(a) level even further.

After taking this dose for 10 days, he began to experience intense pain in the teeth and gingiva. The pain began with the post-dose flush but would persist for 2 to 3 h and would shift in location from the lower frontals to the right lower lateral and right upper lateral gingival area. A dental examination, including radiographs, revealed no abnormalities. The dose of niacin was decreased to 3 g/d, and the pain subsided. After 3 weeks with the lower dose, the pain recurred and was again temporally related to each niacin dose. The pain became even more intense, requiring the administration of a narcotic.

Attempts to prevent the pain by further decrements in dose were unsuccessful, and niacin therapy was discontinued. Serum lipid levels were measured (Table 1). Two weeks after discontinuance of niacin therapy, the dental and gingival pain had markedly diminished. After another 3 weeks, less intense dental pain returned. A dental examination revealed a periodontal lateral root abscess. During treatment with erythromycin over a 2-week period, the abscess resolved and the pain again subsided. Subsequently, the lower front teeth remained sensitive to touch and to temperature changes.

CASE 2

A 65-year-old white man, previously asymptomatic, developed chest pain consistent with unstable angina in April 1996. Angiography revealed a significant left circumflex coronary artery lesion that was dilated and stented. Because of a low high-density

*From the Medical College of Ohio, Toledo, OH (Drs. Leighton and Davis); Center for Heart Disease Prevention, St. Joseph’s/Candler Health System, Savannah, GA (Dr. Gordon); Department of Oral and Maxillofacial Surgery, University of Michigan, Ann Arbor, MI (Dr. Small); and the Department of Pharmacy Practice, Mercer University, Southern School of Pharmacy, Macon, GA (Dr. Ward). Correspondence to: Richard F. Leighton, MD, 5 Amberly Court, Savannah, GA 31411-2702
Table 1—Clinical Data for Case 1*

<table>
<thead>
<tr>
<th>Date</th>
<th>Total Cholesterol, mmol/L</th>
<th>Triglycerides, mmol/L</th>
<th>HDL Cholesterol, mmol/L</th>
<th>LDL Cholesterol, mmol/L</th>
<th>Lp(a), mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>October 1, 1996†</td>
<td>4.47</td>
<td>0.95</td>
<td>1.55</td>
<td>2.48</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>(173)</td>
<td>(84)</td>
<td>(60)</td>
<td>(96)</td>
<td>(26)</td>
</tr>
<tr>
<td>January 20, 1997</td>
<td>4.86</td>
<td>0.65</td>
<td>2.56</td>
<td>1.99</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>(188)</td>
<td>(58)</td>
<td>(99)</td>
<td>(77)</td>
<td>(12)</td>
</tr>
<tr>
<td>February 1997‡</td>
<td>3.96</td>
<td>0.62</td>
<td>2.07</td>
<td>1.60</td>
<td>0.31</td>
</tr>
<tr>
<td>April 4, 1997§</td>
<td>(153)</td>
<td>(55)</td>
<td>(80)</td>
<td>(62)</td>
<td>(12)</td>
</tr>
</tbody>
</table>

*Values in parentheses are given as mg/dL.
† Niacin, 3 g/d, was begun between October 1, 1996, and January 20, 1997.
‡ Niacin, 4 g/d for 10 d was begun in February 1997; patient had dental pain.
§ Niacin, 3 g/d, was begun between February and April 14, 1997; patient had dental pain. Niacin was discontinued after April 4, 1997.

Lipoprotein (HDL) cholesterol value (Table 2), in July 1996 therapy was started with 1.5 g/d of a delayed-release niacin preparation.

Lipid levels were measured again in November 1996, at which time the HDL cholesterol value remained unchanged, but the low-density lipoprotein (LDL) cholesterol had increased. As a result, the niacin dose was increased to 2.25 g/d. Within a month, he began to notice an ache in the upper teeth, more concentrated in the right-sided molar area. He consulted a dentist who could find no dental disease. He continued to receive the same niacin dose and continued to have aching in his teeth. A second dental examination was nonrevealing. Serum lipid levels were again determined in late March 1997. Because of a persistently elevated LDL cholesterol value, therapy with pravastatin, 20 mg/d, was started. He related his symptoms of dental pain to his physician, and the niacin dose was decreased to 1.5 g/d. His dental pain improved but was still present. One month later, serum lipid values were again determined. A decrease in the LDL cholesterol value was noted. Niacin was then discontinued, and within 2 days, he no longer had dental pain although his teeth remained sensitive to touch intermittently for another 3 weeks.

**COMPOSITION OF NIAcin PREPARATIONS**

The niacin preparations the two patients were taking were both produced by the same company (Goldline Laboratories; Fort Lauderdale, FL). In addition to nicotinic acid, the crystalline preparation contained dicalcium phosphate, microcrystalline cellulose, stearic acid, croscarmellose sodium, magnesium stearate, and hyroxypropyl-methylcellulose. The timed-release capsule contained titanium dioxide, methylparaben, propylparaben, and butylparaben, FD & C blue No. 1, FD & C blue No. 4, sucrose, gelatin, and starch in addition to nicotinic acid.

**DISCUSSION**

In spite of extensive descriptions of the side effects encountered with doses of niacin required for lipid lowering, dental and gingival pain have not been reported heretofore. A review of the medical literature on niacin side effects (through a Medline search) and a review of an adverse reaction database (Micromedex-1997) have revealed no such reports. In both cases, symptoms first appeared after the patient had been receiving the drug (crystalline niacin in case 1 and sustained release niacin in case 2) for 5 months and appeared to be related to an increase in dose. In each case, symptoms improved with a decrease in dose but did not subside completely until the drug was discontinued.

Table 2—Clinical Data for Case 2*

<table>
<thead>
<tr>
<th>Date</th>
<th>Total Cholesterol, mmol/L</th>
<th>Triglycerides, mmol/L</th>
<th>HDL Cholesterol, mmol/L</th>
<th>LDL Cholesterol, mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 14, 1996†</td>
<td>3.93</td>
<td>1.08</td>
<td>0.78</td>
<td>2.64</td>
</tr>
<tr>
<td></td>
<td>(152)</td>
<td>(96)</td>
<td>(30)</td>
<td>(102)</td>
</tr>
<tr>
<td>November 19, 1996‡</td>
<td>4.65</td>
<td>1.34</td>
<td>0.70</td>
<td>3.34</td>
</tr>
<tr>
<td></td>
<td>(180)</td>
<td>(119)</td>
<td>(27)</td>
<td>(129)</td>
</tr>
<tr>
<td>December 1996§</td>
<td>4.68</td>
<td>1.13</td>
<td>0.91</td>
<td>3.26</td>
</tr>
<tr>
<td></td>
<td>(181)</td>
<td>(100)</td>
<td>(35)</td>
<td>(126)</td>
</tr>
<tr>
<td>March 25, 1997‖</td>
<td>3.62</td>
<td>1.20</td>
<td>0.88</td>
<td>2.20</td>
</tr>
<tr>
<td></td>
<td>(140)</td>
<td>(106)</td>
<td>(34)</td>
<td>(85)</td>
</tr>
</tbody>
</table>

*Values in parentheses are given as mg/dL.
† Niacin, 1.5 g/d, was begun between May 14 and November 19, 1996.
‡ Niacin, 2.25 g/d, was begun between November 19 and December 1996.
§ Patient experienced dental pain in December 1996.
‖ Niacin, 1.5 g/d, and pravastatin, 20 mg/d, were begun between March 25 and April 25, 1997.
¶ Patient experienced dental pain and niacin was discontinued after April 25, 1997.
The cause of symptoms in these two patients is uncertain. Over time, niacin-induced, prostaglandin-mediated vasodilatation in the enclosed pulp chamber may have resulted in fluid accumulation and pressure on nerve endings. Prostaglandins can also cause hyperalgesia in local sensory nerve receptors and directly potentiate inflammatory activity. Neural irritation in the gingiva can result in localized pain as well as pain referred to adjacent teeth and to parodontal structures. The abscess formation in case 1 was probably enhanced by the local edema, predisposing to the entrance of bacteria. Whether any of the additives in the niacin preparations play any contributing role is uncertain. One may conclude that dental and gingival pain should be added to the list of side effects of which physicians should be aware when they prescribe niacin for lowering lipid levels.

REFERENCES

Bullous Sarcoidosis

A Report of Three Cases*

Marc A. Judson, MD, FCCP; and Charlie Strange, MD, FCCP

Three cases of pulmonary sarcoidosis presented as bullous emphysema with severe airflow obstruction,

and the diagnosis of sarcoidosis was unsuspected for at least 2 years. Potential mechanisms of bullous emphysema from sarcoidosis are discussed. The physician should suspect sarcoidosis as the cause of bullous emphysema when young patients who have smoked relatively few pack-years present with emphysema or severe airflow obstruction. Additional clues are the presence of mediastinal adenopathy on a chest radiograph or a CT scan and a history consistent with extrapulmonary sarcoidosis.

(CHEST 1998; 114:1474–1478)

Key words: airflow obstruction; bullae; emphysema; pathology; sarcoidosis

The presentation of pulmonary sarcoidosis is highly variable. Most patients present with mild or no pulmonary symptoms,1 minimal pulmonary dysfunction,1 and without evidence of fibrosis or fibrocystic disease on a chest radiograph.2–4 Three cases of pulmonary sarcoidosis presented as bullous emphysema with severe airflow obstruction, and the diagnosis of sarcoidosis was not suspected by pulmonary physicians for at least 2 years.

CASE REPORTS

CASE 1

A 37-year-old black man was referred for consideration of bullectomy or lung transplantation. He was a former smoker of 1/2 pack of cigarettes daily for 20 years (Table 1). He was an active runner 5 years previously until worsening dyspnea over 2 years limited exercise to walking less than 100 feet.

Physical examination revealed a hyperresonant chest, diminished breath sounds in all fields, and a prolonged expiratory phase. Pulmonary function tests (Table 2) revealed an obstructive ventilatory defect with significant trapped gas. A chest radiograph showed extensive bilateral bullous disease with adjacent lung contraction. A chest CT scan is shown in Figure 1.

The diagnosis of pulmonary sarcoidosis was entertained on the basis of the chest CT scan. A lung gallium scan failed to reveal pulmonary parenchymal or mediastinal uptake. Serum angiotensin-converting enzyme activity was normal.

The patient received a right single-lung transplant 9 months after referral, had an uncomplicated postoperative course, and is doing well. Characteristics of a postoperative pleural effusion have been reported elsewhere.5 Histologic examination of the excised lung revealed areas of extensive fibrosis with noncaseating granulomas (Fig 2). The walls of the bullae contained little fibrosis and rare noncaseating granulomas. Polarized light microscopy was nonrevealing. Endobronchial granulomas also were present.

CASE 2

A 40-year-old white man presented with 2 years of progressive dyspnea for which he had been given a diagnosis of emphysema.

*From the Division of Pulmonary and Critical Care Medicine, Medical University of South Carolina, Charleston, SC. Manuscript received October 15, 1997; revision accepted April 3, 1998.

Correspondence to: Marc A. Judson, MD, FCCP, Division of Pulmonary And Critical Care Medicine, Medical University of South Carolina, 171 Ashley Ave, Charleston, SC 29425; e-mail: judsonma@musc.edu

Downloaded From: http://journal.publications.chestnet.org/pdffacess.asx?url=/data/journals/chest/21874/ on 06/26/2017