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CLINICAL COMMUNICATION TO THE EDITOR

Gabapentin in the Treatment of Intractable Idiopathic Chronic Cough: Case Reports

To the Editor:

Cough remains the most common reason for seeking medical care in America. Intractable cough resolved when one patient was placed on gabapentin for migraine headaches. Our subsequent experience with this treatment is reported.

Patients were approached using Irwin and colleagues' "anatomic diagnostic" approach to cough.[1,2] Recent recognition of eosinophilic bronchitis, eosinophilic tracheobronchitis, and esophageal dysmotility was taken into consideration. Gabapentin was approved for use in 1993 as adjunctive therapy for partial seizures.[3] Currently, it is estimated that gabapentin is prescribed for off-label uses in 80% of cases.[3]

Case A is a 33-year-old woman with a history of celiac disease, hyperthyroidism, and porphyria. She was diagnosed with idiopathic chronic cough. In June 2003, the patient started taking gabapentin for migraine headaches; this coincided with complete resolution of cough with no recurrence to date. She remains on gabapentin.

Given the limited therapeutic options in patients with severe idiopathic chronic cough, it was believed reasonable to try gabapentin because it is well tolerated, has a wide margin of safety, and has no significant drug interactions.[3,4]

Known side effects were explained to patients who had a diagnosis of severely symptomatic idiopathic chronic cough and patients willing to accept the risks participated.[5] Gabapentin was given to 6 patients with idiopathic intractable chronic cough beginning at 100 mg twice per day and titrated until either improvement was manifest or a 1600-mg daily dose was reached. Response was assessed clinically by the attending physician. There was no formal cough-response instrument applied. After 1 year, the results in all patients who had been placed on gabapentin were analyzed.

Clinical details for all patients are summarized in Table 1.

Overall, the treatment was successful in 5 of 6 patients, with either complete resolution or substantial improvement in cough. The duration of improvement ranged from 6 months to ongoing. One patient relapsed on therapy and gained control by an increase in dose.

Although gabapentin was designed as a GABA-mimetic agent capable of crossing the blood–brain barrier, the effects of gabapentin in epilepsy do not seem to be mediated through interaction with GABA receptors and the exact mechanism of action remains controversial.[4] There is no explanation for its effect on chronic cough.

It is not surprising that there is variability in the response to gabapentin, because it is probable that there are many different causes for "idiopathic" chronic cough.

Each patient was screened for side effects mentioned in controlled and uncontrolled studies of gabapentin for neuropathic pain, and few side effects noted in Table 1 occurred.[6] One patient discontinued gabapentin temporarily because of fatigue. Another patient had transient drowsiness that resolved after 1 week. This parallels the experience in gabapentin treatment for epilepsy and neuropathic pain in which side effects commonly resolved within 2 weeks of initiating therapy and approximately 10.5% of patients quit controlled studies of gabapentin because of side effects.[3,5]

There is evidence that chronic cough is more common in women and that women are more likely to seek medical attention for cough than men because they are more adversely affected by cough.[6] Of note, all of the patients seen for intractable cough in this report were women and nonsmokers.

It is important to follow systematic practice when dealing with chronic cough.[2,7] Nevertheless, there will be a few patients in whom chronic cough persists. It is the opinion of some clinicians that there are "currently no effective treatments for controlling the cough response with an acceptable therapeutic ratio."[8] This report suggests that gabapentin may have a role in idiopathic chronic cough. Larger, placebo-controlled studies are necessary to elucidate this potential.

Sheldon Mintz, MD
Sunnybrook and Women's College Hospital
University of Toronto
Toronto, ON, Canada

Jason K. Lee, MD
University of British Columbia
Vancouver, BC, Canada

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Table 1 Patient Characteristics

Case/ age/sex	Comorbidities	Medications at Initial Evaluation	Cough duration (mo)	Bronchoscopy	Serology or Other Investigations	Upper GI Series	↑ MCT	*PND Workup by ENT	Therapeutic Trials	Dose of Gabapentin/Result of Therapy
A/34 y/ female	Celiac disease, porphyria	Hydrochlorothiazide Salbutamol PRN	18	Normal: negative for TB, fungus, routine cultures, and malignancy	*Bordetella pertussis* IgG EIA, reactive *B. pertussis* IGA EIA, nonreactive	0	0	0	1. Formoterol × 5 wk 2. Advair × 3 wk 3. Budesonide × 8 wk 3. Prednisone × 2.5 wk 4. Omeprazole 1 mo	**800 mg bid** Complete resolution of cough Duration of therapy: 1 y
B/64 y/ female	Chronic cystitis	Estrogen Progesterone Amitriptyline Alendronate	180	Normal bronchial biopsy: no eosinophils. BAL: no malignancy, no eosinophils	ANA negative; immunoglobulin levels N; negative for acid-fast bacilli	0	N	N	1. Omeprazole 2. Prednisone × 1 wk 3. Cholestyramine resin 4. Azithromycin	**300 mg tid** Greatly decreased cough. Thought it was ineffective after 3 mo, but got much worse after stopping. Probably improved. Total duration of therapy: 6 mo.
C/53 y/ female	Hypertension, dyslipidemia, hypothyroidism, osteoarthritis	Atorvastatin Estrogen Eltroxin Trazodone Tussionex Hydrochlorothiazide	192	0	*B. pertussis* IgG EIA, reactive *B. pertussis* IgA, nonreactive	Mild GERD + small sliding reducible hiatus hernia	0	N	1. Esomeprazole 2. Prednisone × 1 wk	**400 mg bid** Decreased frequency and intensity of cough Duration of therapy: 4 mo
D/53 y/ female	Nasal allergies	Venlafaxine Esomeprazole	48	0	Immunoglobulins, α-1-antitrypsin, sweat chloride, and esophageal motility all normal	N	N	N	1. Fluticasone × 3 2. wkNasonex × 3 wk	**200-300 mg bid** Stopped after 3 wk because of fatigue. Restarted, same dose. Fatigue left, cough is "10%-15% better"

E/73 y/ female	Mitral valve prolapse, tonsillectomy, hysterectomy, partial thyroidectomy, scoliosis	Atenolol Estrogen Thyroxine Etidronate Ca++ Vitamin D Indapamide Quinine	168	Normal: no fungus, no eosinophils, no malignancy	Aspergillus immunodiffusion, N; immunoglobulin levels, N; esophageal motility, slightly hypotensive lower esophageal sphincter	N	0	0	1. Beclomethasone 2. Fluticasone nasal 3. Advair 4. Omeprazole 5. Pizotifen 6. Desloratadine 7. Tegaserod 8. Cholestyramine resin 9. Zafirlukast	**400 mg PO bid** Complete resolution of cough Duration of therapy: 8 mo
F/77 y/ female	Polymyalgia rheumatica	Prednisone Fluticasone	48	0	Hematology	N	0	0	1. Prednisone high dose 2. Omeprazole	**100 mg bid** Complete resolution for 3 mo, then required 200 mg bid Total therapy 3 mo

PND = postnasal drip; MCT = methacholine challenge test; N = no abnormality found, 0 = not performed; Ig = immunoglobulin; PO = by mouth; bid = twice per day; tid = three times per day; GI = gastrointestinal; ENT = ear, nose, and throat; PRN = as needed; TB = tuberculosis; ANA = antinuclear antibody; BAL = bronchoalveolar lavage; GERD, gastroesophageal reflux disease; BAL = bronchoalveolar lavage.

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