Nasally Inhaled Dornase Alfa in the Postoperative Management of Chronic Sinusitis Due to Cystic Fibrosis

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Objective: To determine the benefit of nasally inhaled dornase alfa in cystic fibrosis (CF) sinusitis.

Design: Retrospective chart review comparing postsurgical course, radiographic studies, and pulmonary function test results in patients who were treated with nasally inhaled dornase alfa with those in patients who were not treated with dornase alfa.

Patients: Twenty consecutive patients with CF who underwent functional endoscopic sinus surgery from 1993 to 1997 were included in the study. Treatment with nasally inhaled dornase alfa was initiated in 5 of the 20 patients after they underwent functional endoscopic sinus surgery.

Setting: Tertiary care academic center.

Results: The dornase alfa–treated patients had less mucosal edema and no polyps at serial endoscopy over 3 years compared with the non–dornase alfa–treated patients. The patients who received nasally inhaled dornase alfa also underwent fewer revision functional endoscopic sinus surgical procedures (1.6 vs 3.2), even though there was essentially no change in pulmonary function test results in these patients.

Conclusions: Sinusitis continues to be a major cause of morbidity in patients with CF. Symptomatic patients frequently require multiple drug regimens, including long-term systemic antibiotic therapy, topical and systemic steroid therapy, and antibiotic nasal irrigations. This preliminary study indicates the potential impact of nasally inhaled dornase alfa in controlling postoperative symptoms in CF sinusitis.

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Cystic Fibrosis (CF) is an autosomal recessive disease characterized by an abnormal ion transport mechanism, which results in decreased chloride permeability of the cell. The lower chloride permeability leads to desiccation of the extracellular fluid, resulting in mucus that is 30 to 60 times more viscous than normal. Cystic fibrosis does not alter the actual mucociliary transport mechanism; however, this mechanism is unable to transport these thick secretions. The resultant mucostasis results in blockage of the sinus ostia, thereby contributing to chronic and recurrent sinusitis.

Since CF affects exocrine glands, including the lungs, pancreas, gastrointestinal tract, and paranasal sinuses, medical management has been the mainstay of treatment. Functional endoscopic sinus surgery (FESS) in CF has a defined role for patients with persistent nasal obstruction. Surgical intervention is necessary in patients with polyps, facial pain or headaches that affect quality of life, medialization of the lateral nasal wall on computed tomographic scan, or worsening pulmonary status despite aggressive medical management. Despite the need for surgical intervention, FESS has failed to demonstrate any correlation with pulmonary function or to affect the long-term incidence of chronic sinusitis.

Recent studies have focused on the use of recombinant human deoxyribonuclease 1 (dornase alfa) to decrease the viscosity of pulmonary secretions in patients with CF. Deoxyribonuclease is a human enzyme, normally found in urine, blood, and saliva. It is responsible for the digestion of extracellular DNA. In CF, extracellular DNA is released from leukocytes within the airways as a response to chronic bacterial infections, such as those caused by Pseudomonas aeruginosa. In phase 1 and 2 clinical trials, dornase alfa was administered via jet nebulizer, which resulted in a 14% improvement in forced expiratory volume in 1 second (FEV1) and was well tolerated. Phase 3 studies...
PATIENTS AND METHODS

The medical records of 20 consecutive patients with CF who underwent FESS from 1993 to 1997 were reviewed. Five of these patients began nasal inhalation of dornase alfa after their initial FESS. The remaining 15 patients did not receive dornase alfa in any form. Pulmonary function test (PFT) results; postoperative examinations, including findings of serial endoscopic examinations; and radiographic studies were compared between the 2 groups.

demonstrated a reduced risk of respiratory exacerbations by 28% and a mean improvement of 5.8% in FEV1. Patients who received dornase alfa also required significantly fewer days of antibiotic therapy and spent less time in the hospital.3

Five postsurgical patients with CF at our institution began taking dornase alfa via face mask to achieve nasal inhalation. The clinical outcome of these patients will be presented and compared with that of postsurgical patients with CF who have not used dornase alfa.

RESULTS

Twenty patients with CF (10 females and 10 males; age range, 11-29 years) underwent FESS. Of the 5 patients treated with dornase alfa, 4 were male and 1 was female (age range, 11-25 years). Pulmonary function tests were performed yearly from the time of initial FESS, and the results were compared from year to year. Over the 4-year period, PFT results in the control group were worse in 8 patients (53%), improved in 5 patients (33%), and unchanged in 2 patients (14%). In the dornase alfa–treated group, PFT results were worse in 4 patients (80%) and improved in 1 patient (20%). The non–dornase alfa–treated group averaged 3.2 sinus procedures (range, 1-8 procedures), and the dornase alfa–treated patients averaged 1.6 procedures (range, 1-2 procedures). Postoperative endoscopic examinations were performed at regular intervals on all patients, and the results were rated as follows: 0, normal results; 1, polypoid edema or purulence; and 2, polyps. At the 6-month follow-up visit after the last FESS, nasal endoscopy of the control group demonstrated 9 patients with stage 0 disease (70%), 3 patients with stage 1 disease (23%), and 1 patient with stage 2 disease (7%). Two patients were unavailable for follow-up. The 6-month follow-up visit of the dornase alfa–treated patients showed 3 with stage 0 disease (75%), 1 with stage 1 disease (25%), and 1 unavailable for follow-up. Postoperative computed tomographic scans, performed on 7 treated and 3 nontreated patients during the last year, revealed no significant change in the maxillary or ethmoidal sinuses when compared with preoperative scans. The following 2 case reports demonstrate the potential benefit of treatment with nasally inhaled dornase alfa.

REPORT OF CASES

CASE 1

A 10-year-old boy with CF underwent bilateral middle meatal antrostomies and endoscopic anterior ethmoidectomies in January 1992, with findings of polypoid mucosa and mucopurulence. Dornase alfa therapy was begun via face mask in March 1994, and the patient underwent nasal endoscopy in April 1996 during a tonsillectomy, with findings of no purulence or polyps. A computed tomographic scan in February 1996 showed mucosal thickening in both maxillary sinuses and the right sphenoidal sinus. Pulmonary function tests were performed yearly, and in December 1993 the patient’s FEV1 was 1.14 (92% predicted), his forced vital capacity (FVC) was 1.34 (96% predicted), and his FEV1/FVC was 0.85. The results of PFTs in January 1997 demonstrated an FEV1 of 1.95 (99% predicted), an FVC of 1.60 (90% predicted), and an FEV1/FVC of 0.82. At his last endoscopic examination, in December 1996, he had mild edema, no polyps, and trace purulence (stage 1). He is currently receiving pancrease, triamcinolone acetonide, albuterol jet nebulizers, and dornase alfa and has no symptoms of chronic sinusitis.

CASE 2

A 25-year-old man with extensive bilateral polyps and purulence underwent bilateral middle meatal antrostomies, anterior ethmoidectomies, a right frontal sinusotomy, and bilateral nasal polypectomies in September 1992. He began nasal inhalation of dornase alfa immediately after surgery. He underwent revision middle meatal antrostomies and ethmoidectomies in August 1994 and October 1995 for bilateral recurrent polyps, which primarily affected the right side. A computed tomographic scan obtained before the October 1995 procedure showed hypoplastic frontal sinuses, partial opacification of both maxillary and ethmoidal sinuses, and an antrochoanal polyp. In August 1994, PFTs showed an FEV1 of 2.98 (71% predicted), an FVC of 3.82 (79% predicted), and an FEV1/FVC of 0.78. In March 1996, PFTs showed an FEV1 of 2.73 (65% predicted), an FVC of 3.95 (80% predicted), and an FEV1/FVC of 0.69. His last endoscopic examination in November 1996 revealed no mucopurulence or polyps bilaterally (stage 0). He is currently being treated with dornase alfa, cisaipride, fluticasone propionate, tobramycin irrigations, pancrease, albuterol jet nebulizers, and ranitidine and is asymptomatic.

COMMENT

Cystic fibrosis is the most common lethal autosomal recessive genetic disorder in the white population, with a prevalence of 1 in 2000 live births and a carrier rate of 1 in 25. Primary causes of death in this population are respiratory failure and cor pulmonale.15 The rate of nasal polyposis ranges from 6% to 48%,1,2 and there is a high recurrence rate after nasal polypectomy.

The use of topical antibiotics has demonstrated some clinical efficacy in improving pulmonary function, decreasing intranasal bacterial counts, and resolving mu-
cosal inflammation.\textsuperscript{8} The studies in which these antibi-
otics were tested focused on altering the infection rate,
and did not address the primary problem of mucosal vis-
cosity. Dornase alfa directly alters the consistency of mu-
cosal secretions in CF, leading to improved pulmonary
function independent of chest physiotherapy.\textsuperscript{9} Al-
though no significant change in airflow obstruction or
mucociliary clearance could be demonstrated, the reduc-
tion of viscoelasticity might in itself be responsible for
the improvement in FVC.\textsuperscript{10}

This preliminary study was performed to deter-
mine whether nasally inhaled dornase alfa in postsur-
gical patients with CF leads to improvement in sino-
nasal symptoms as well as in the results of endoscopic
examinations. Although PFT results were actually
worse over time, this trend applied to both treated and
nontreated groups. Endoscopic examination results
were improved at 6 months after surgery in both
groups of patients. Perhaps the most encouraging find-
ing was the lower revision rate among the dornase
alfa–treated patients. All the patients with CF peri-
dically continued to require multiple drug therapies,
including nasal steroids, antibiotic irrigations, and sys-
temic antibiotics.

\section*{CONCLUSIONS}

The retrospective nature of this study prevents any defi-
nite conclusions; however, our findings suggest that na-
sally inhaled dornase alfa via face mask may help con-
trol postoperative symptoms in patients with CF. Future

Appendix A: References

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