Cystic fibrosis (CF) is a lethal autosomal recessive disease affecting predominantly the Caucasian population. Defects in membrane conductance regulator protein (CFTR), which is due to mutation of the q31 region of the chromosome 7, leads to abnormal electrolyte concentration in exocrine secretions. Multi-system disease involves the upper and lower airways, pulmonary ducts, hepatobiliary ducts, and male reproductive tracts. Involvement of the sinonasal mucosa is observed in all CF patients either by clinical and radiological examination.

Management of CF chronic rhinosinusitis (CRS) includes both medical and surgical therapy. Medical therapy has evolved over the past few decades and includes nasal toilet, antimicrobial and anti-inflammatory medications (both systemic and topical forms), and newer recombinant enzymes – dornase alfa (Pulmozyme). Although medical therapy is the mainstay of therapy, surgical therapy is considered with significant disease burden that fails to respond to maximal medical therapy.

The objective of this study was to systematically review the literature to provide evidence-based recommendations regarding the effectiveness of medical treatment for CRS in CF patients.

METHODS AND MATERIALS

We searched PubMed, Embase, and the Cochrane CENTRAL Database for relevant publications within the 25-year time period of 1/1/1987 through 2/28/2012. A principal electronic search strategy was designed for use in PubMed and then tailored for the other electronic databases. The initial search included combined key terms and exploded Medical Subject Headings (MeSH) for the subject of interest. Only English language studies with original data were included. Exclusion criteria included: Published prior to 1987, no abstract present, written in a language other than English, review articles, technical reports, editorials, cadaver and animal studies, containing fewer than 5 patients with CF, no or poorly-measured outcomes, and experimental therapies (i.e. gene therapy).

The study selection process is illustrated in Figure 1. Two team investigators independently reviewed the titles and abstracts for initial inclusion. Full publications were obtained following initial selection of titles and abstracts. Each article was reviewed for study design and assigned a Level-of-evidence based on published guidelines by the Oxford Centre for Evidence-based Medicine Levels of Evidence. Quality assessment of each研究报告 article was utilized using the Cochrane Collaboration Tool for Assessing Risk of Bias and the Newcastle-Ottawa Quality Assessment Scale.

RESULTS

The systematic review included 12 studies with a total of 701 adult and pediatric patients (Table 1). Two of the studies were Level 1 evidence; one was Level 2 evidence; one was Level 3 evidence; and eight were Level 4 evidence. Three of the 12 studies used statistical analysis to assess outcomes, with all of these showing a significant difference in at least one of the outcomes measures.

Medical management included topical steroids (4/12), antibiotics (4/12), dornase alfa (3/12), and high-dose ibuprofen (1/12). Outcome measures included symptom scores (7/12), endoscopy findings (7/12), radiographic findings (4/12), pulmonary function testing (4/12), rhinomanometry (2/12), basic laboratory tests (1/12), microbial cultures (1/12), and saccharine clearance testing (1/12). Assessment of outcome improvement for the different medical therapies is show in Table 2. Topical steroids and dornase alfa had the strongest evidence, showing improvement in multiple outcome measures.

Risk of bias in the Level 1 to 2 evidence studies was assessed using a modified Cochrane Collaboration Tool for Assessing Risk of Bias. All three studies in this category demonstrated low risk of bias. The Newcastle-Ottawa Quality Assessment Scale was used to review the quality of the remaining studies (Table 3). The majority of case-control and case series was 5.0 out of 9 possible stars and 2.25 out of 3 possible stars, respectively.

DISCUSSION

This is the first systematic review in the English literature of the medical management of CF CRS. There is a relatively small number of articles identified and included in the review, considering all the literature. Many studies did not have a clear definition of disease or lacked measurable outcome measures. The preponderance of evidence is based on Level 3 to 4 evidence studies. The only Level 1 evidence studies have examined betamethasone and dornasa alfa, and showed improvement primarily in symptom and endoscopic scores. There is no strong evidence that antibiotics improve clinical outcomes. One of the major causes of mortality and morbidity in CF is pulmonary deterioration. There is inconclusive evidence of whether medical therapy improves PFT or modifies lower airway function in this progressive disease.

CONCLUSIONS

Dornase alfa and topical steroids showed significant benefit in the medical treatment of CF CRS. There was a lack of evidence to support antibiotic therapy in the outcomes assessed. High quality studies with clearly defined outcome measures are needed to determine the efficacy of various medical therapies for CF CRS. Overall Evidence Grade B-.