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LONG TERM MANAGEMENT OF CYSTIC FIBROSIS

Mohammed Saeed Alghamdi[1], Osama Abduallah Alzahrani[1], Ali mohammed alghamdi[2], Abdullah solaiman m aloraini[2]

[1] King Fahad Armed Forces Hospital-Jeddah
[2] Prince Sultan Medical Military City

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Abstract

Introduction: *Cystic fibrosis (CF) is a lung disease that involves more than 80,000 people globally. It is a life-threatening genetic disorder characterized by the buildup of thick, viscous mucus secretions in various organ systems, most commonly the pulmonary, gastrointestinal, and genitourinary systems. This article reviews the long-term management of cystic fibrosis*

Aim of the study: *The review aims to understand clinical manifestations of cystic fibrosis, its diagnosis, and monitoring of patients, as well as guidelines for management and emerging pharmacologic treatments.*

Methodology: *The review is a comprehensive research of PUBMED from year to 1990 to 2008.*

Conclusion: *There is an immense improvement in the management of cystic fibrosis, especially after approval of CFTR modulators, but it is still in question since management of cystic fibrosis not only the protein rectifiers but also symptomatic treatment and intensive physiotherapy, which require concomitant therapies. The genotype myriad also poses a challenge, and most correcting drugs are for children older than 12 years of age. Most of these drugs have serious hepatic toxicity and other side effects. The psychological and social burden of disease should also need to be concerned.*

Keywords: Cystic fibrosis, antimicrobials, nutritional therapy, respiratory status

Corresponding author:
Mohammed Saeed Alghamdi,
E-Mail:M-al-ghamdi1990@hotmail.com

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INTRODUCTION:

Cystic fibrosis is an autosomal recessive disease that occurs due to mutations in the CFTR (cystic fibrosis transmembrane conductance regulator) gene. The most common mutation is the deletion of phenylalanine at codon 508 and is reported in nearly 70% of patients with cystic fibrosis. Regarding cystic fibrosis, 1600 mutations of the CFTR gene have been described. The genetic mutations of different genes have varying effects on CFTR function and lead to different phenotypes of the disease. Some mutations are known to cause milder forms of the disease, although there is not enough evidence about these, nor is the prognosis determined. The CFTR protein is expressed in many cells and has several functions, not all of which have been linked with disease. The main function of this protein is as an ion channel that regulates liquid volume on epithelial surfaces through secretion of chloride and inhibition of absorption of sodium. [1]

Diagnosis

A mutation in the CF transmembrane conductance regulator (CFTR) gene is responsible for cystic fibrosis. A protein produced by this gene known as CFTR protein regulates the movement of chloride and sodium ions across epithelial cell membranes; due to mutations in one or both copies of the gene, ion transport becomes defective and results in a buildup of thick mucus throughout the body which in turn lead to leading to respiratory insufficiency, systemic obstructions. This also leads to decreased mucociliary clearance and altered ion transport, allowing bacteria to colonize the respiratory tract, such as Pseudomonas, Haemophilus influenza, and Staphylococcus aureus, which invokes an inflammatory response and ultimately chronic infection.[2]

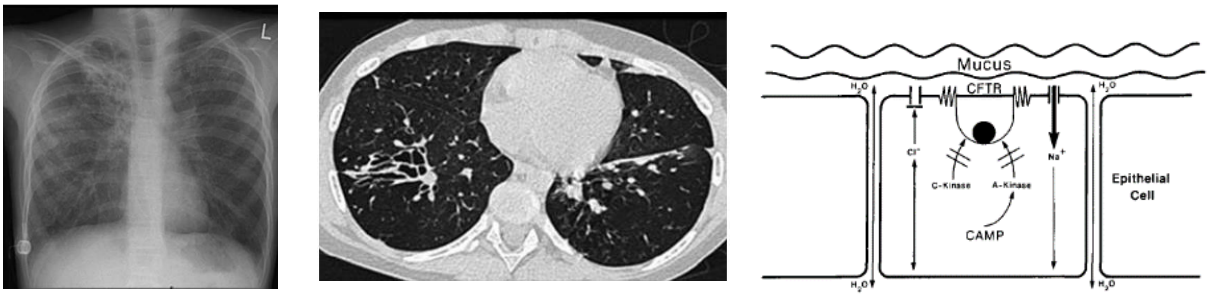

Figure showing Severe bronchiectasis in end-stage cystic fibrosis in chest radiograph (left), computed tomogram (middle), A defect in the ion transport system of cystic fibrosis patients' respiratory epithelia produces a block in the chloride channel preventing normal cellular chloride excretion and sodium reabsorption (right).[3,4]

The optimal level of a diagnostic test for cystic fibrosis is the measurement of sweat electrolyte levels. Patients with the disease have increased concentrations of sodium and chloride (>60 mmol/l, diagnostic; 40-60 mmol/l apart from this exocrine pancreatic insufficiency, chronic obstructive pulmonary disease, and familial history of cystic fibrosis is present. A minimum of two of these criteria is essential for diagnosis, in addition to a positive sweat chloride test.[3,4]

Treatment, Progression, and Survival

After diagnosis, most of the patients respond well to nutritional therapy with pancreatic enzymes and vitamin supplementation. During the first year of life, special infant formulas, comprised of protein hydrolysates and medium-chain triglycerides, are used. Post that a regular diet is sufficient for most patients. Furthermore, evidence for the pulmonary disease is explored with microbial cultures, chest radiographs, and pulmonary function tests in older children. Antibiotics are administered aggressively by intravenous mode if required. Bronchodilators are given by aerosol inhalation or orally to patients with airway reactivity (asthmatic symptoms). The objective of initial treatment is to achieve as normal a status as possible. In combination with psychosocial support and education, this therapeutic approach has evolved, but the basic defect remains and is slow but progressive involvement continues, especially in the lungs. Compliance plays a very important role in the effectiveness of recommended therapy. In long-term care- family education, continued review, and support is important factors.[4]

Table 1: Management of cystic fibrosis [5-9]

Category	Components
Respiratory support.[5]	This determine baseline respiratory status Requires for clarifying code status and lung transplant candidacy Diagnostics include - chest imaging, blood gas assessment, clinical assessment to determine the severity of the respiratory failure. • Supplemental oxygen is given in mild hypoxia, no CO2 retention, or increased WOB • High-flow nasal cannula (increased WOB, minimal or mild CO Q30 2 retention) • Noninvasive ventilation (increased WOB, moderate CO2 retention) • Invasive mechanical ventilation (altered mental status, hemodynamic instability, or severe respiratory acidosis)
Airway clearance[6]	Inhaled therapy includes – • Albuterol • Hypertonic saline • Dornase alfa • Consider inhaled antibiotics • Chest physiotherapy - Numerous devices available; select based on the clinical situation and patient preference Typical treatment order- Albuterol > hypertonic saline >chest physiotherapy > dornase alfa > inhaled antibiotic
Sedation and analgesia [7]	Sedation – • Anticipate tolerance to sedatives • Propofol is the first-line treatment • Consider dexmedetomidine or low-dose ketamine if propofol is inadequate • Use daily SAT or SBT Analgesia – • Multimodal approach to pain treatment • Caution with opiates because of risk of DIOS
Infectious disease [7]	Obtain prior culture data Send new cultures on admission Use dual systemic coverage of Pseudomonas Ensure appropriate drug dosing for patients with CF
Nutrition[8]	Provide nutrition consultation Ensure adequate calorie and protein intake, lower carbohydrate content with severe hypercarbia Consider metabolic cart testing when caloric requirements unclear Provide enteral feeding if unable to meet needs with oral intake Use TPN if unable to feed enterally Ensure adequate pancreatic enzyme replacement therapy Consider antacid therapy
Diabetes[9]	Do not restrict calories Insulin is the mainstay of therapy Treatment can improve BMI and respiratory status
Physical Therapy [9]	Mobilization with physical therapy and occupational therapy
Psychological issues [9]	Screen for depression and anxiety and treat if found. Consider palliative care consultation to assist in symptom management and goals of care discussions

Gastrointestinal issues [9]	Treat GERD if present Monitor for constipation and DIOS Use osmotic laxative-based bowel regimen

Table 2: Antibiotics in cystic fibrosis patients [10]

Long- Term Antibiotic therapy	Dosage	Dosing Considerations
Antipseudomonals		
Piperacillin-tazobactam	4.5 g IV q6h	Extended infusion
Ceftazidime	2 g IV q8h	Preferred aminoglycoside because of less ototoxicity Check random levels after dosing and adjust based on pharmacokinetics Consider pharmacy assistance where available
Cefepime	2 g IV q8h	
Meropenem	2 g IV q8h	
Ciprofloxacin	400 mg IV q8h	
Levofloxacin	750 mg IV or po q24h	
Tobramycin	8-10 mg/kg IV q24h	Primarily used in NTM infection Check random levels after dosing and adjust based on pharmacokinetics Consider pharmacy assistance where available
Amikacin	20 mg/kg IV q24h	
Reserved for highly resistant Pseudomonas		
Ceftazidime-avibactam	2.5 g IV q8h	
Ceftolozane-tazobactam	3 g IV q8h	
Colistimethate sodium	2.5 mg/kg IV q12h	
Anti-MSSA		
Nafcillin	2g IV q4h	
Ceftriaxone	2 g IV q12h	
Vancomycin	Loading dose of 25-30 mg/kg IV, then 15 mg/kg IV q8-12h	
Linezolid	600 mg IV q12h 600 mg po q12h	
Ceftaroline fosamil	600 mg IV q12h	

CONCLUSION:

Cystic fibrosis patients who are critically ill are vulnerable to many complications in the long term and a high risk for mortality. Therefore, to provide optimal care, a multidisciplinary approach is required that addresses all the associated complications and problems and needs of this population for the same. Despite being a very challenging disease, cystic fibrosis poses favorable outcomes, which can be achieved in many of these patients. Early transfer of cases to health centers specializing in this field of care should control the complication. Long-term treatment is maintained with antimicrobials.

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