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PERIOPERATIVE MANAGAMENT OF CYSTIC FIBROSIS IN PATIENTS UNDERGOING ORAL AND MAXILLOFACIAL SURGERY CARE

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Abstract

Cystic Fibrosis (CF) is an autosomal recessive disorder and is considered one of the most fatal hereditary diseases. The average survival age of CF patients has significantly increased over the past 60 years, particularly with advances in neonatal and pediatric care, along with modern preventive care methods. There is a large number of CF patients who require interventions in oral and maxillofacial surgery. This paper will discuss the diagnosis, pathophysiology, and systemic complications of CF and will provide relevant information regarding the management of CF patients in oral and maxillofacial surgery. Recommendations for preoperative, perioperative, and postoperative care of these patients will be presented.

Keywords: cystic fibrosis, premedication, protocol, surgery.

Introduction

CF is a generalized dysfunction of the exocrine glands. It is associated with abnormal chloride transport in the apical membrane of epithelial cells in CF, which leads to impaired secretion clearance in various organs. Abnormal secretion of thick mucus from glands leads to obstruction in the secretion pathways of the organs. The impairment in chloride transport is caused by mutations in the membrane protein called CF transmembrane conductance regulator. This mutation causes failure in the maturation of the CF transmembrane glycoprotein for conductivity regulation. The result is a limited transport of the protein to its normal cellular location for membrane insertion and abnormal kinetics in chloride transport. [1,2]

Clinically, this disorder is associated with high salt content in the sweat of affected patients, caused by impaired chloride reabsorption from the lumen of sweat gland ducts. High intraluminal chloride levels retain sodium, which leads to the characteristic "salty sweat." Apart from the sweat glands, the most commonly affected organ systems are the respiratory, gastrointestinal, and reproductive systems. [1]

Clinical aspects of cystic fibrosis

Early and Late Manifestations

CF manifests in various ways and may sometimes be diagnosed later in life. The earliest manifestation is intestinal obstruction in newborns – meconium ileus. This occurs in 10% of cases and tends to be inherited. It is often treated with therapeutic radiopaque enemas, though surgery may be needed. Most infants are diagnosed due to persistent, voluminous stools, failure to thrive, and/or recurrent pneumonia in the absence of meconium ileus or a family history of CF. Some patients may manifest few or no diagnostic symptoms for several years, although 70% of cases are now identified by age two. Mild respiratory symptoms may be mistaken for allergic disease, especially in 10-15% of patients who have normal digestive function. Other unusual manifestations include nasal polyps, rectal prolapse, recurrent abdominal pain, biliary cirrhosis, and fat-soluble vitamin deficiencies. Adults with mild symptoms may initially present due to infertility. [3]

Salivary Glands

The effects of CF on the major salivary glands range from mild to severe. Mucous-secreting glands are pathologically affected, but serous glands are not significantly involved. The parotid glands are purely serous, so their saliva is minimally affected. The submandibular glands are usually enlarged and easily palpable. Significant changes are observed in the submandibular, sublingual, and small salivary glands, along with alterations in saliva composition. The submandibular gland is mixed, containing both serous and mucous acinar cells, while the sublingual gland is almost exclusively mucous, making it more severely affected. Changes in normal parenchyma are evident with dilated acini and loss of cellular morphology. Ducts in the sublingual and submandibular glands are often blocked with cellular debris and fine filaments. Pathological changes in these glands are mainly related to ductal obstruction, although some may be secondary to the disease itself. Increased calcium levels and elevated pH and buffering capacity of saliva have been observed. [3]

Respiratory System

More than 95% of CF-related deaths are due to pulmonary complications. [4] Accumulation of dehydrated, viscous mucus followed by bacterial colonization leads to the characteristic respiratory complications of CF. Early pathogens involved in this process include Staphylococcus aureus and Haemophilus influenzae. The respiratory tract in most CF patients is colonized by Pseudomonas aeruginosa, which is responsible for 90% of morbidity and mortality in CF patients. [2] These pathogens stimulate an immune response in the host, resulting in infiltration of neutrophils, cytokine release, proteolytic enzymes, and high levels of antibodies. Chronic immune stimulation by Pseudomonas antigens causes the local release of proteases, such as elastase, and oxygen radicals from neutrophils and pulmonary macrophages. At birth, the lungs of CF patients are histologically normal, but bronchopulmonary obstruction increases as patients age. Initially, obstruction at the bronchial level causes air trapping, with abnormal mucus compromising mucociliary clearance and airway clearance. Extensive bronchiectasis is a common finding during adolescence. Bronchiectatic cysts, usually most prominent in the upper lobes, can occupy up to 50% of the cross-sectional area of the lungs. As the obstructive process progresses, peribronchial fibrosis follows, leading to restricted lung function. In advanced pulmonary disease, multiple cysts or bullae may appear, commonly in the upper lobes, and can lead to complications like pneumothorax.

Pulmonary Function

Pulmonary obstruction from secretions, edema, airway collapse, and bronchial hyperreactivity leads to gas trapping and increased residual volume. Total lung capacity is variably increased, and the residual volume/total lung capacity ratio is a useful prognostic indicator, showing progressive increase with worsening pulmonary function. Functional residual capacity is increased, while forced expiratory volume in one second (FEV1) and forced vital capacity are decreased. Ventilation-perfusion mismatch (V/Q) may be expressed early in the disease and lead to an increased arterial oxygen gradient. This results in decreased arterial oxygen tension (PaO_2). Arterial carbon dioxide tension ($PaCO_2$) is usually normal; elevated $PaCO_2$ typically indicates severe disease. [5]

Gastrointestinal system

Pancreatic Disease

Pancreatic insufficiency is another hallmark of CF, occurring in 80-90% of patients. This leads to maldigestion and malabsorption of nutrients. In children, it results in difficulties in weight gain, frequent large or liquid stools (steatorrhea), intolerance to fatty foods, excessive bloating, and abdominal cramps. Exogenous pancreatic enzymes, a high-calorie nutritional regimen (100%-130% of the recommended daily intake of calories), and vitamin supplements for fat-soluble vitamin deficiencies (A, D, E, and K) are part of the treatment modalities for pancreatic disease in CF. [2,4] Pancreatic lesions can progress with age. In some patients, pancreatic function may be preserved earlier in life but eventually declines, often accompanied by episodes of acute pancreatitis. [6]

The endocrine pancreas is also affected; 40-60% of CF patients test positive for glucose intolerance, although only a small percentage require insulin therapy. Unlike diabetes mellitus, the alpha and beta cells of the pancreas are equally affected by "strangulation" caused by pancreatic fibrosis, leading to low levels of both insulin and glucagon. The incidence of ketoacidosis and peripheral vascular complications is rare in CF patients. [4,6]

Intestinal Obstruction Symptomatic

CF may present at birth with meconium ileus in 10%-15% of patients. Generally, complications of intestinal obstruction are more common in older patients than in children. After pulmonary disease, intestinal obstructions account for the majority of diagnostic and therapeutic issues in adult CF patients. Thick mucus obstructions, along with maldigestion and pancreatic enzyme insufficiency, lead to solid fecal matter obstruction in the small intestine, which can result in initial complications of meconium ileus and intussusception. Intermittent obstruction of the small and large intestines and rectal prolapse can continue to pose problems throughout the patient's life. [6]

Other Gastrointestinal Complications

Gastroesophageal reflux is documented in 12% of adults and 20% of children with CF. This is important for anesthesia selection and technique. One-third of CF patients have positive tests for abnormal liver function, and 5% have cirrhosis. There is also a high prevalence of cholelithiasis (12%). Pancreatic insufficiency leads to lithogenic bile due to reduced reabsorption and excessive fecal loss of bile acids.[1,4,6]

Reproductive system

Although sexual function is preserved and active spermatogenesis is present, more than 98% of adult men with CF have secondary azoospermia and underdevelopment of mesonephric derivatives such as the vas deferens, epididymis, and seminal vesicles. Similarly, 75% of women with CF are infertile. The thickened and dried cervical mucus acts as a barrier to sperm penetration, preventing pregnancy. CF patients with this condition can undergo in vitro fertilization, though the status of egg cell and semen carriers should be assessed to prevent disease transmission to offspring. [1,2]

Diagnosis

A preliminary guideline issued by the Cystic Fibrosis Foundation defines the CF diagnosis as the identification of at least 2 of the following clinical criteria (numbers 1 to 3) and 1 of the 2 positive laboratory criteria (numbers 4 and 5):

- Chronic mucous obstruction of the airways with recurrent respiratory infections (affecting nearly 100% of patients).
- Insufficient function of the exocrine part of the pancreas (occurs in 85% to 90% of patients), leading to steatorrhea and azotorrhea, and resulting in nutritional consequences of malabsorption.
- Reproductive complications leading to a fertility rate of less than 2% in men and approximately 25% in women.
- Two positive chloride sweat test values of 60 mEq/L obtained through the quantitative pilocarpine iontophoresis test (QPIT), according to the Bethesda, MD Cystic Fibrosis Foundation guidelines. (These elevated electrolyte levels in sweat are observed in almost 100% of patients with this disease.)
- Two alleles consistent with the CF diagnosis. The CF gene, located on the long arm of chromosome 7 and known as delta F508, involves a deletion of 3 base pairs resulting in the loss of phenylalanine at position 508 of the gene's amino acid chain. [7]

Preoperative recommendations

Evaluation

Before any surgery, whether under general anesthesia or conscious sedation, a thorough evaluation of the CF patient is crucial to minimize potential complications. The preoperative assessment should identify any acute pulmonary changes, assess the nutritional status, ensure good control of blood glucose levels, and rule out coagulation abnormalities. A chest X-ray is an invaluable tool for evaluating chronic pulmonary changes and ruling out any acute conditions. [8]

Nasal polyps are found in 26% of CF patients and may present with signs causing nasal obstruction symptoms. [9] Nasal polyps can pose a challenge for nasal intubation, especially for orthognathic surgeries in maxillofacial surgery. In the presence of nasal polyps, oral intubation or polypectomy may be necessary.

Timing

An important consideration when evaluating surgical interventions in CF patients is the timing of the procedure. In these patients, respiratory function follows a course of exacerbations and progressive deterioration. There are "optimal" periods when sputum levels are at a minimum, and pulmonary function test values are favorable. Surgical interventions should ideally be performed at a specially chosen time. Some patients may require considerable time in the morning to clear the secretions accumulated during sleep. Sputum clearance should continue until the patient enters the operating room. To this end, scheduling should be in the morning. [1] Procedures are preferably performed early in the week to ensure full medical and physiotherapy staff availability for postoperative care.

Premedication

Because these patients need to actively clear secretions before arriving in the operating room and should continue doing so as soon as possible postoperatively, premedication with heavy sedatives is contraindicated. Routine doses of antibiotics, cardiotonic drugs, and bronchodilators should continue throughout the perioperative period. Due to the already thick mucus, routine use of antisialogogues may be potentially harmful.[11] The use of opioids should be assessed based on the expected pain level associated with the surgical procedure, considering side effects like delayed recovery from anesthesia and constipation. Abdominal bloating from constipation may compromise respiratory function, and laxatives should be considered. Due to the high incidence of gastroesophageal reflux, H2 receptor antagonists are recommended.

Perioperative considerations

Monitoring the CF patient during surgery is crucial, involving ECG and pulse oximetry. Pre-oxygenation is an important step before induction, whether or not rapid induction is used. Intravenous induction is preferred over inhalational induction due to high functional residual capacity and low minute volume, which leads to slow induction times.

In oral and maxillofacial surgery, infiltration of the surgical site with long-acting local anesthetics will reduce the need for postoperative narcotic use. Short-acting non-depolarizing muscle relaxants should be used to ensure quick recovery and avoid the need for antagonistic agents, which may cause drying effects on the respiratory system. It is important to note that aminoglycoside antibiotics used for treating infections may prolong the neuromuscular blocking effect. Coagulopathies due to vitamin K deficiency may increase intraoperative and postoperative bleeding. Nitrous oxide may cause pulmonary expansion and distension. Anesthesiologists should take appropriate measures for airway humidification and precise perioperative hydration.

Postoperative considerations

Recovery

Transferring the patient to the intensive care unit (ICU) postoperatively should be a decision made collectively by the anesthesiologist, surgeon, and respiratory care team. Returning the patient to the respiratory care team, who are familiar with their health condition, should be a priority. Vigorous pulmonary toileting and chest physiotherapy with postural drainage should be routine in postoperative care and must begin immediately after extubation and continue throughout hospitalization. Humidified oxygen is beneficial for postoperative patients and is well tolerated by them.

Antibiotic Therapy

Almost all patients with CF (Cystic Fibrosis) receive regular antibiotic treatment as part of their routine therapy. The type and dosage of these antibiotics are adjusted to achieve the desired effect. It is imperative for the oral and maxillofacial surgeon to discuss the planned surgical procedure with the physician treating the CF patient and decide on the correct type and dose of postoperative antibiotics.

The typical dosage regimen used in other populations may be inadequate for CF patients due to altered pharmacokinetics. In general, higher doses are necessary for CF patients to achieve similar peak and trough serum concentrations of antibiotics. It is important to note that some antibiotics, such as gentamicin and tobramycin, may have adverse effects, especially with the use of high doses.

Due to the potential for nephrotoxicity and ototoxicity from excessive tissue accumulation, serum trough concentrations exceeding 2 mg/L should be avoided. [1]

Another alternative for postoperative care of CF patients is aerosolized antibiotics. According to recent studies, the delivery of antibiotics in aerosolized form has many advantages, such as ease of administration, high concentrations in sputum, and a low potential for systemic side effects. In most cases, more than one antibiotic may be used for pulmonary exacerbations or postoperative care.

Dental Management

Mouth breathing and an open bite are associated with chronic nasal and sinus obstruction and are often observed in CF patients. Delayed dental and skeletal maturation in CF patients generally resolves if survival extends into the second or third decade. The severity of the systemic disease and the prognosis for life expectancy must be considered before starting orthodontic therapy. Additionally, due to the increased areas for bacterial plaque formation associated with orthodontic appliances, a well-defined caries prevention program, including improved oral hygiene and fluoride use, is essential before initiating any orthodontic therapy.

The frequency of consuming sugar-containing foods is generally higher in children with CF due to their need to maintain an increased intake of calories and salt. Despite these dietary guidelines, the incidence of caries among these patients has been noted to be lower than in a healthy age-matched population. It has also been observed that there is less dental plaque and gingivitis in CF patients. The reduced caries rate may be related to the effects of long-term antibiotic use and pancreatic enzyme replacement therapy on oral flora. The increased calcium content and buffering capacity of whole saliva provide further explanation for the reduction in dental caries. This favors remineralization of teeth and is also consistent with an increased prevalence of dental calculus.[3]

When performing oral surgical interventions, it is recommended that patients be maintained in an upright position during treatment, as it is often necessary to clear bronchial and tracheal secretions with frequent coughing.

Conclusion

Ongoing efforts to improve early diagnosis and treatment of CF should further extend the lifespan of the affected population, although CF remains a leading cause of death in the first decade of life. Families can expect to be asked more frequently for regular dental check-ups and to view this disease as a long-term challenge for treatment. Persistent treatment limitations highlight the importance of aggressive prevention of dental diseases. Regular professional care and good home oral hygiene habits are crucial for CF patients.

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