Oral care for patients with cystic fibrosis

Précis

This clinical feature outlines the systemic manifestations, pharmacological management and dental management of patients with cystic fibrosis.

Abstract

Aim: To outline the systemic manifestations and pharmacological management of cystic fibrosis. Oral manifestations and considerations for the provision of dental care are also addressed.

Methods: A literature search was conducted to identify medical and dental manifestations of cystic fibrosis. These findings were then used to provide recommendations regarding the provision of dental care for people with cystic fibrosis.

Results: Cystic fibrosis is a multiorgan condition. There are no known disease-specific contraindications for the provision of dental treatment. However, dentists can implement protocols to facilitate and encourage regular dental attendance.

Conclusion: Further research should be conducted to assess the oral health of people with cystic fibrosis, notably caries and periodontal status, so that, if necessary, appropriate care strategies and guidelines can be developed.

Introduction

Cystic fibrosis (CF) is a chronic condition caused by a mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Ireland has the highest incidence of CF in the world, with one in 1,461 live births reported as CF positive and a carrier rate for the CFTR mutation reported at one in 19.[1] The pulmonary and gastrointestinal systems are primarily affected; however, disease manifestations are seen across multiple organ systems (**Table 1**).

Pathophysiology

Mutations of the CFTR gene affect chloride ion channel function, which leads to the dysregulation of epithelial fluid secretions. Hyperproduction of thick mucous secretions causes obstructions of organs. People with CF (PWCF) experience recurrent or chronic pulmonary infections due to impaired mucociliary clearance, which allows pathogens to accumulate.[2] Childhood pathogens responsible for pulmonary infections, such as *Haemophilus influenzae* and *Staphylococcus aureus*, are superseded by *Pseudomonas aeruginosa* in adolescence. This pathogen is the predominant cause of pulmonary mortality and morbidity in CF.[3]

Table 1: Manifestations of cystic fibrosis.

Pulmonary	Impaired mucociliary clearance Recurrent lung infection Diminished expiratory flow rate and volume Bronchiectasis Shortness of breath
Pancreatic	Pancreatic insufficiency Pancreatic cyst Pancreatitis Gastroesophageal reflux disease (GERD)
Gastrointestinal	Meconium ileus Distal intestinal obstruction syndrome Constipation Rectal mucosal prolapse
Hepatobiliary	Portal hypertension Cirrhosis Liver failure
Other	Salty skin and sweat Diabetes Osteoporosis Infertility

F. O'Leary, N. Coffey, M. Hayes, F.M. Burke

Cork University Dental School and Hospital, University College Cork

Corresponding author: Dr Fiona O'Leary, Restorative Dentistry, Cork University Dental School and Hospital, University College Cork E: fiona.oleary@ucc.ie T: 021-490 1100

Table 2: Causes of nutritional failure.

Laboured breathing
Inflammatory catabolism
Increased calorie requirements
Cystic fibrosis-related diabetes
Intestinal dysmotility
Pancreatic enzyme insufficiency

Table 3: Oral manifestations of cystic fibrosis.

Development defects of enamel
Tooth discolouration (tetracycline staining)
Xerostomia
Oral candida
Mouth breathing
Anterior open bite (associated with chronic nasal obstruction and sinusitis)

FIGURES 1: Routinely prescribed inhalation therapies.

FIGURE 2: CREON pancreatic enzyme replacement supplement.

Gastrointestinal (GI) complaints predominantly arise from mucous inspissation and dysmotility. Nutritional failure (**Table 2**) is a primary concern for PWCF, with multiple studies showing that nutritional status is a strong predictor of morbidity and mortality.[4] Pancreatic enzyme insufficiency affects approximately 85% of PWCF. It causes malabsorption and maldigestion of nutrients and fat-soluble vitamins A, D, E, and K.[5] CF-associated liver disease (CFLD) affects approximately 30-50% of patients, with symptoms generally developing before or during adolescence. CFLD is characterised by slow disease progression and manifestations can vary from mild asymptomatic high levels of liver enzymes to cirrhosis.[6] CF-related bone disease has been reported in up to 15% of PWCF. Causes include:[6]

- CFTR gene mutation;
- vitamin D deficiency;
- nutrition deficiency;
- diminished production of sex hormones;
- increased inflammatory cytokines; and,
- glucocorticoid therapy.

Oral manifestations

Oral manifestations of CF are outlined in **Table 3**. The dysfunction of the CFTR gene, recurrent systemic infection and long-term antibiotic use have all been linked to the formation of developmental defects of enamel.[7] Clinical consequences of such defects include:

- hypersensitivity;
- aesthetic concerns;
- increased risk of erosion; and,
- increased risk of caries.

Up to 81% of adults with CF experience gastro-oesophageal reflux disease (GERD),[8] which further increases the risk of erosion and caries. Current research provides conflicting results regarding the caries and periodontal risk status of PWCF. Studies indicate a lower caries prevalence in children with CF, which has been attributed to paediatric antibiotic treatment reducing levels of cariogenic

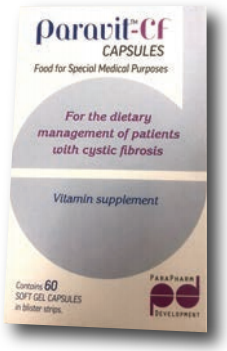

FIGURE 3: Paravit vitamin supplement often taken to combat malnutrition.

FIGURE 4: Desunin and Altavita D3, both used to prevent and treat vitamin D3 deficiency.

bacteria. Adolescents and adults show equal or higher caries incidence compared to non-CF patients.[9]

Multiple risk factors may predispose PWCF to oral candida. These include:

- impaired salivary gland function;
- inhalation antibiotic and steroid therapy; and,
- high carbohydrate diet.

Medical management

Medical treatment is a lifelong commitment involving a multidisciplinary team of healthcare professionals. Multifaceted developments in treatment have led to an improvement in quality of life and an increase in the median age of survival from 36.6 years to 44.4 years over the last decade.[10] Mainstay daily treatments for the symptomatic relief of CF include inhaled and oral medications (**Figure 1**), and airway clearance.

Malnutrition is prevented with pancreatic enzyme replacement supplements and increased calorie intake. Increased calories are met with nutritional supplements and grazing dietary habits, which in turn increase caries risk (**Figures 2**, **3** and **4**).

FIGURE 5: Kalydeco gene modulator therapy.

Gene therapy drugs such as Orkambi, Kalydeco and, more recently, Kaftrio, have significantly advanced CF treatment by targeting the underlying genetic mutation (**Figure 5**). Their indications and efficacy depend upon an individual's CFTR variant.[11]

Dental treatment

Dental treatment can be provided safely to PWCF in a general dental setting. Currently there are no disease-specific contraindications for the provision of dental care to these patients. However, dental practitioners should be aware of complications that may arise from comorbidities:

- vitamin deficiencies;
- liver disease; and,
- bone disease.

Prolonged postoperative bleeding can arise in cases of vitamin K deficiency and CFLD through disruption of hepatic synthetic function.[12] CF-related bone disease treated with bisphosphonate therapy is accompanied by the risk of medication-related osteonecrosis of the jaw post extraction.

Dental prescribing

Dental analgesia is essential for PWCF, with several studies reporting an explicit interaction between pain and a restriction to perform physiotherapy and exercise.[13] Local anaesthetic can be used in accordance with the usual precautions. In the absence of severe renal impairment and hepatic failure paracetamol is well tolerated for pain management. Non-steroidal anti-inflammatories (NSAIDs) such as ibuprofen have been used in the systemic pain management of CF; however, for the management of odontogenic pain they should be used prudently. Opioid analgesics for dental pain should be avoided due to their potential to cause pulmonary depression, reduced bowel movement and constipation. Caution should be exercised when prescribing antibiotics as allergic reactions are more common in PWCF than in the general population. This is due in part to increased exposure.[14]

Considerations for dental practice

As previously discussed, routine dental treatment offers few problems specific to CF. Nevertheless, dental practitioners can implement additional measures to facilitate and safeguard these patients. These measures include:

- appointment allocation to minimise patient-to-patient contact, e.g., first appointment of the day – this is particularly relevant amidst the ongoing Covid-19 pandemic and in an aerosol-laden environment;
- appointments for non-sibling PWCF should not be scheduled on the same day to minimise the risk of transmission of pathogens, notably *P. aeruginosa*, between patients;
- limiting treatment provision to a single allocated surgery;
- ensuring that all staff members do not have any transmissible illness, e.g., colds, coughs;
- enforcing meticulous cross-infection control and dental chair waterline disinfection;
- shorter appointment times and regular breaks during treatment; and,
- providing dental treatment with the patient in an upright or semi-upright position in the dental chair to facilitate the clearance of airway secretions (**Figure 6**).

FIGURE 6: Provision of dental treatment with patient in an upright position.

Continuity of care

Despite major advances in the medical management of CF, solid organ transplantation remains a viable treatment option for end-stage pulmonary disease. Dental assessment and appropriate treatment are considered in most transplant centres to be a compulsory prerequisite for solid organ transplantation. Continuity of dental care throughout a patient's life is incredibly important as an exacerbation or flare-up of an odontogenic or periodontal infection can lead to the postponement or cancellation of

transplant surgery. A comprehensive understanding of the primary disease, disease complications and disease management will allow dental practitioners to provide dental treatment in a safe, effective and reassuring environment for patients with CF.

References

1. **Lenihan, M., Mullane, D., Buggy, D., Flood, G., Griffin, M.** Anesthesia for lung transplantation in cystic fibrosis: retrospective review from the Irish National Transplantation Centre. *J Cardiothorac Vasc Anesth* 2018; 32 (5): 2372-2380.
2. **Saint-Criq, V., Gray, M.A.** Role of CFTR in epithelial physiology. *Cell Mol Life Sci* 2017; 74 91): 93-115.
3. **LiPuma, J.J.** The changing microbial epidemiology in cystic fibrosis. *Clin Microbiol Rev* 2010; 23 (2): 299-323.
4. **Yen, E.H., Quinton, H., Borowitz, D.** Better nutritional status in early childhood is associated with improved clinical outcomes and survival in patients with cystic fibrosis. *J Pediatr* 2013; 162 (3): 530-535.e.1.
5. **Ghodeif, A.O., Azer, S.A.** Pancreatic Insufficiency. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, January 2021.
6. **Kobelska-Dubiel, N., Klincewicz, B., Cichy, W.** Liver disease in cystic fibrosis. *Prz Gastroenterol* 2014; 9 (3): 136-141.
7. **Ferrazzano, G.F., Sangianantoni, G., Cantile, T., Amato, I., Orlando, S., Ingenito, A.** Dental enamel defects in Italian children with cystic fibrosis: an observational study. *Community Dent Health* 2012; 29 (1): 106-109.
8. **Robinson, N.B., DiMango, E.** Prevalence of gastroesophageal reflux in cystic fibrosis and implications for lung disease. *Ann Am Thorac Soc* 2014; 11 (6): 964-968.
9. **Chi, D.L., Rosenfeld, M., Mancl, L., Chung, W.O., Presland, R.B., Sarvas, E.,** *et al*. Age-related heterogeneity in dental caries and associated risk factors in individuals with cystic fibrosis ages 6-20 years: a pilot study. *J Cyst Fibros* 2018; 17 (6): 747-759.
10. **CF Registry of Ireland.** 2018 Annual Report. Available from: https://cfri.ie/annual-reports/.
11. **Donnelley, M., Parsons, D.W.** Gene therapy for cystic fibrosis lung disease: overcoming the barriers to translation to the clinic. *Front Pharmacol* 2018; 9: 1381.
12. **Harrington, N., Barry, P.J., Barry, S.M.** Dental treatment for people with cystic fibrosis. *Eur Arch Paediatr Dent* 2016; 17 (3): 195-203.
13. **Rosella, D., Papi, P., Giardino, R., Cicalini, E., Piccoli, L., Pompa, G.** Medication-related osteonecrosis of the jaw: clinical and practical guidelines. *J Int Soc Prev Community Dent* 2016; 6 (2): 97-104.
14. **Parmar, J.S., Nasser, S.** Antibiotic allergy in cystic fibrosis. *Thorax* 2005; 60 (6): 517-520.