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ORIGINAL SCIENTIFIC ARTICLE

Dental treatment for people with cystic fibrosis

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Abstract
Aim To describe the nature and consequences of the multi-system genetic condition cystic fibrosis with a view to ensuring optimal dental treatment planning for these patients.
Methods A literature search was conducted to identify the key medical and dental manifestations of cystic fibrosis. These findings are discussed and utilised to create recommendations for treatment planning in patients with cystic fibrosis for the practising dental practitioner.
Results Cystic fibrosis is a complex, lethal, multisystem autosomal recessive disorder resulting from mutations on chromosome 7 which result in dysfunction of an ion channel that sits on epithelial surfaces. Respiratory disease remains the leading cause of mortality. Survival has greatly increased in recent decades secondary to improved treatment and specialist care. Specific dental manifestations of the disease may result from the condition itself or complications of treatment. Modification of patient management may be necessary to provide optimum patient care.
Conclusion The pathophysiology and clinical manifestations are relevant to practicing dental practitioners and inform recommendations to be utilised to ensure optimal treatment planning for these patients.

Keywords Cystic fibrosis · Caries · Respiratory · Dental

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Introduction

First described in 1938 (Andersen 1938), cystic fibrosis (CF) remains the most common lethal genetic disorder amongst Caucasians worldwide. In the intervening time, better understanding of the pathological abnormalities associated with the condition and multi-disciplinary care based in specialist centres has transformed the condition from one of childhood mortality to one with an estimated life expectancy of greater than 40 years (Lewis et al. 1999; Stephenson et al. 2015). CF remains, however, a chronic, life-shortening condition requiring substantial medical intervention.

Cystic fibrosis is inherited in an autosomal recessive fashion. The gene responsible for the condition was localised in 1985 to the long arm of chromosome 7 and successfully sequenced in 1989 (Wainwright et al. 1985; Riordan et al. 1989). This gene encodes for a 1480 amino acid protein, named the cystic fibrosis transmembrane conductance regulator (CFTR) (Bear et al. 1992). The function of the CFTR protein is to act as an ion channel, which predominantly transports chloride, with resultant effects on extracellular fluid levels (see Fig. 1) (Mall and Galietta 2015). This ion channel sits on various epithelial cell surfaces including respiratory epithelium, salivary glands, the pancreas, liver, sweat glands and the reproductive tract. Gene mutations lead to dysfunction of the protein by different mechanisms and to varying degrees. The most common gene mutation is a deletion of the amino

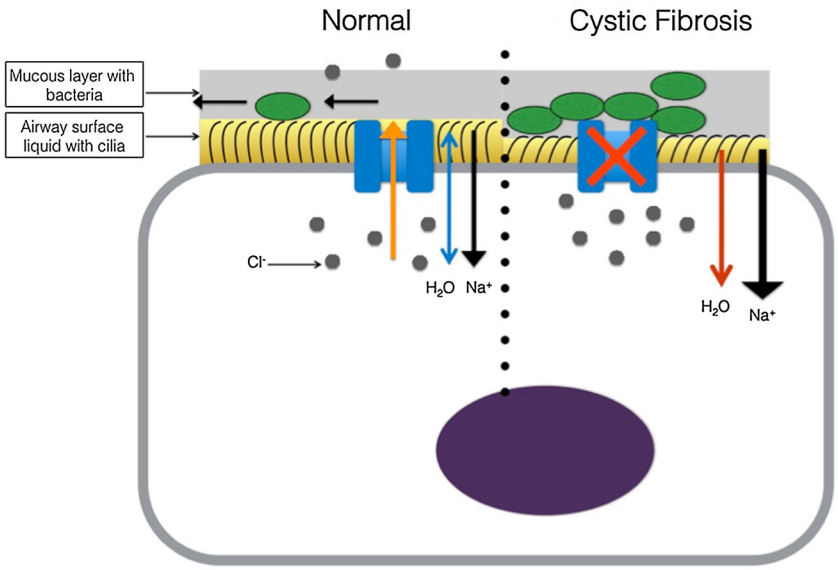

Fig. 1 Representation of an airway epithelial cell. In a normal cell, functioning CFTR protein (*blue channel*) allows the passage of chloride ions through to airway surface liquid. CFTR also exhibits a down-regulatory effect on sodium resorption through ENaC channels. Water transport is balanced according to ion concentrations permitting adequate airway surface liquid height for ciliary function to propel the mucous layer along the epithelial cell surface. In the CF cell, CFTR dysfunction impairs chloride transport and upregulates sodium and water resorption. This leads to dehydration of the airway surface liquid layer with resultant ciliary dysfunction and accumulation of thicker mucous layers

acid phenylalanine in position 508 (Phe508del, previously deltaF508) on chromosome 7; although there are almost two thousand known CFTR mutations (Sosnay et al. 2013). Ultimately CF-causing mutations lead to dehydration of mucous and the formation of thick viscid secretions in the lungs and other organs.

The purpose of this review was to

1. Inform the practising dental surgeon of the nature and consequences of CF with a view to ensuring optimal treatment planning for these patients and
2. Identify the dental consequences of CF of which practising dental surgeons should be aware.

Epidemiology

Cystic fibrosis is a worldwide disease although the prevalence varies from country to country. It is more common in Caucasian populations, but has been recognised in almost all ethnic groups. The carrier frequency of CF mutations is estimated at 1 in 25 in the United Kingdom (UK), 1:4000–10,000 in Latin American, 1:15,000–20,000 amongst African Americans and 1:350,000 in Japan (O'Sullivan and Freedman 2009).

Clinical manifestations

Respiratory conditions

Respiratory disease remains the foremost cause of morbidity and mortality for people with CF (Davies et al. 2007). Thicker mucous lining the airways produces an ideal environment for the acquisition and persistence of pathogens in the respiratory tract. This in turn gives rise to a cycle of pulmonary inflammation and destruction, resulting in progressive structural lung disease most commonly manifested as bronchiectasis. Clinically this presents as a daily productive cough whilst increasing structural damage results in decreasing pulmonary function with increasing shortness of breath and exercise limitation over time. Episodic increases in respiratory symptoms associated with increased inflammatory response, termed pulmonary exacerbations, necessitate additional treatment with either oral or intravenous antibiotic therapy and may require hospital admission.

Cystic fibrosis lung disease requires an arduous regimen of targeted therapy with the aim of preventing or slowing decline. Treatment involves daily physiotherapy to clear thickened respiratory mucous and the nebulisation of solutions aimed at thinning out secretions (mucolytics-

dornase alfa, hypertonic saline, mannitol) (Mogayzel et al. 2013). In addition, most patient as they age become chronically infected with respiratory pathogens. Targeted nebulised and oral antibiotic therapy is utilised to suppress the levels of infection in the lung and prevent acute exacerbations (Döring et al. 2012). Ultimately lung disease is progressive, leading to respiratory failure and the need for supportive oxygen or ventilatory therapies and when suitable, lung transplantation.

Recently the development of novel therapies named CFTR modulators have been greatly heralded in the lay media and medical literature. CFTR modulators directly target the dysfunctional CFTR protein and aim to increase functional activity of CFTR protein channel on epithelial cell surfaces (Barry et al. 2015). These medications are to this point genotype specific. For example, the CFTR 'potentiator' ivacaftor increases the open probability of aberrant CFTR protein which has been transported to cell surfaces but exists in a predominantly closed state (Van Goor et al. 2009). This abnormality of CFTR mainly occurs in what is termed class III or 'gating' mutations. In class II mutations the aberrant protein is often misfolded and cannot be transported to the epithelial cell surface and is, therefore, degraded intracellularly. Targeting mutations of this class require a separate step to correct protein folding and enable its transport to the cell surface ('CFTR correction') with the subsequent use of potentiators to increase activity. Significant improvements in respiratory health have been achieved by restoring some CFTR activity for patients with certain gene mutations and patients have described a transformative effect of therapy in some cases (Ramsey et al. 2011). Continuing trials aim to broaden the applicability of these treatments and work has been completed to find therapies which are genotype independent utilising nebulised gene therapy (Alton et al. 2015) or stem cell approaches (Schwank et al. 2013).

Infection control and prevention of the acquisition of new respiratory pathogens is an important tenet of modern CF care. The acquisition and persistence of certain pathogens most notably *Pseudomonas aeruginosa* and *Burkholderia cenocepacia* have been associated with an accelerated decline in pulmonary function (Qvist et al. 2015). Robust evidence now exists that transmission of these bacteria may take place between patients, and 'outbreaks' of certain transmissible pathogens have been recorded worldwide in CF clinics (LiPuma et al. 1990; Jones et al. 2001). This has altered the design of modern CF care in an effort to minimise patient-to-patient contact, a factor that all health care professionals who care for people with CF should be cognisant of.

Ear, nose and throat disease

Cystic fibrosis additionally impacts on the upper respiratory tract with nasal polyposis and sinusitis being common (Gysin et al. 2000). Chronic sinusitis may manifest as facial pain, nasal congestion and the inability to breathe through the nose. Sinuses may become chronically colonised with pathogens similar to those that are isolated in the lower respiratory tract. Due to chronic aminoglycoside exposure for the purpose of treating respiratory infections, patients are at risk of sensori-neural hearing loss and vestibular problems (Farzal et al. 2016).

Gastro-intestinal manifestations

Liver disease is a classical manifestation of CF disease but varies in its prevalence. Cholestasis due to abnormal bile may lead to biliary fibrosis, cirrhosis, portal hypertension and ultimately hepatic failure. It is estimated that up to 35 % of CF patients will have clinically apparent CF-related liver disease; however, substantially fewer will have severe disease (Colombo 2007). Liver disease may result in liver synthetic dysfunction with a resultant coagulopathy. In some cases this dysfunction can become sufficiently profound enough to warrant liver transplantation.

Dysfunction of the pancreas is present in the majority of patients, with exocrine pancreatic insufficiency invariably seen. Thick pancreatic secretions block the pancreatic duct and the activation of pro-enzymes within the pancreatic duct result in auto-destruction of the pancreas (Gibson-Corley et al. 2016). Ultimately, this presents as deficiency of normal pancreatic enzymes with resultant malnutrition. Replacement pancreatic enzyme supplements are utilised to ensure adequate absorption of fats. Replacement of the fat soluble vitamins A, D, E and K are necessary if patients are pancreatic insufficient. Again a potential for coagulopathy exists due to the malabsorption of vitamin K. Pancreatic endocrine function may also be disturbed and is increasingly evident with ageing, resulting in CF-related diabetes mellitus (Brennan and Beynon 2015).

Viscid secretions in the bowel lumen may also compromise absorption of nutrients from the gut. CF patients can suffer from chronic constipation, bowel obstruction, intussusception and gastro-intestinal reflux.

Patients with CF require a highly calorific diet due to a combination of malabsorption and hypermetabolism. Resting energy expenditure is increased potentially due to the increased work needed for breathing and chronic inflammation (MacDonald 1996). This may be exacerbated by poor appetite as a consequence of pulmonary disease (Borowitz et al. 2002). Food intake is often maximised by

the intake of larger and more frequent meals, sugary drinks and high-calorie, nutrition dense, sugary dietary supplements and supplemental enteral feeding (Moursi et al. 2010). It is important to note that nutritional status is paramount to the health and long-term survival of the patient with CF and it is inappropriate for the dental team to suggest a reduction in volume of intake of high-calorie foods and drinks.

Other manifestations

Bone disease has been recognised as one of the challenges of CF management. Osteopaenia and osteoporosis can occur secondary to malnutrition, vitamin D deficiency and the use of systemic glucocorticoids (Plant et al. 2013). Osteoporosis may result in low-impact fractures and even rib fractures induced by coughing alone. Treatment for osteoporosis in this population may include the use of bisphosphonate therapy, (Conwell and Chang 2014) and dental practitioners should be aware of the concomitant risk of osteonecrosis of the jaw.

Musculoskeletal abnormalities include CF-related arthropathy and chronic joint pain. CF-related vasculitis may also become apparent with typical vasculitic skin rashes and often associated arthralgias. Loss of excessive chloride from the skin has long been noted and constitutes one of the key diagnostic tests for CF, but the excessive salt losses may also present with heat prostration as noted in one of the earlier descriptions of CF during a heat wave in New York (Kessler and Andersen 1951). Infertility occurs in the vast majority of male patients due to the congenital absence of the vas deferens preventing the inclusion of spermatozoa into semen. Modern medical techniques have assisted in making parenting a possibility for males with cystic fibrosis via the surgical extraction of spermatozoa (McCallum et al. 2000).

Dental manifestations of cystic fibrosis

It had been assumed that people with CF would be at significantly increased dental risk due to their high-calorie diet, the potential for use of sugar-containing medications (Barry et al. 2009) and an increased prevalence of gastro-oesophageal reflux disease (Scott et al. 1985). Evidence to date, however, has not been consistent with this assumption.

Dental caries

Many papers have reported on low caries rates in patients with CF. Jagels and Sweeney (1976) found a significantly decreased caries levels in children with CF when compared with their near-aged healthy siblings. Similarly, Kinirons (1983) reported lower caries prevalence in a group of 116 children with CF, compared with healthy sibling controls. In contrast, Aps et al. (2001) did not find a significant difference in caries levels between patients with CF and controls and a more recent study indicated that patients with CF have high caries prevalence (Dabrowska et al. 2006). A qualitative systematic review suggested that although children with CF may have a lower caries risk, this is not necessarily the case for adolescents (Chi 2013).

A reduced caries risk may have a number of possible explanations. It may be that patients with CF are more compliant with oral hygiene regimes, but this theory has not been addressed in the literature (Chi 2013). Pancreatic enzyme replacements have been associated with salivary gland hypertrophy (Mangos et al. 1969) and caries reduction (Sweeney and Shaw 1965) in animal models. Human studies have suggested that pancreatic enzyme supplementation may lead to a reduction in plaque levels (Jagels and Sweeney 1976) and reduced caries risk (Narang et al. 2003). Additionally, patients with CF have significantly higher mean values of salivary pH and buffering capacity as a direct effect of the dysfunctional CFTR protein that is found in salivary glands. This potential aetiological factor may have additional relevance with the advent of the aforementioned medications that directly increase the activity of CFTR protein and the relative protective dysfunction of the protein in caries aetiology may be reversed.

Another proposed factor for reduced caries risk is antibiotic exposure. Kinirons (1992) examined a group of 164 children with CF and matched controls of similar age, gender and socioeconomic status. He reported significantly lower caries rates in the CF group, the greatest difference occurring in the groups with “high” and “medium” antibiotic exposure. He concluded that antibiotic usage may be a major factor in the reduction in caries levels in the CF group. It has been proposed (Chi 2013) that the increase in caries in adolescence may in fact be attributable to a change in antibiotic regime. Previous studies have described reduced caries risk in patients being treated with beta-lactam antibiotics such as penicillin. Children are prescribed regular ‘prophylactic’ flucloxacillin to target *Staphylococcus aureus*, the main respiratory pathogen in children with CF. Flucloxacillin is also active against *Streptococcus mutans* and may, therefore, explain the apparent protection against dental caries for younger children with CF. However, chronic antibiotic prescription often alters in older ages, sometimes due to the isolation of gram-negative bacteria such as *Pseudomonas aeruginosa*. This often results in a change in antibiotic prescription away from penicillin-based therapy to the macrolide azithromycin, which may potentially have less effect against pathogenic oral bacteria. Additionally, the

utilisation of chronic nebulised antibiotic therapy targeted at gram-negative organisms may result in altered intra-oral ecology, favouring the gram-positive *S. mutans* and possibly leading to increased caries risk (Chi 2013).

The bulk of evidence points to a lower caries risk for people with CF. In the context of significant risk factors for caries including a cariogenic diet and regular intake of potentially sugar-containing medications, even a similar caries risk is remarkable. The reason for this remains unclear and may be related to direct effects of the CFTR protein dysfunction, pancreatic enzyme supplementation or antibiotic exposure and further research in this area would be beneficial to prevent significant dental morbidity as life expectancy increases.

Xerostomia

Xerostomia is common in the CF patient (Fox 1996) possibly as a result of salivary gland dysfunction and medication effects. Mucous-secreting glands including the submandibular, sublingual and minor salivary glands express CFTR protein with resultant alteration of salivary gland architecture and function (Mandel et al. 1967; Wiesmann et al. 1972) while the serous parotid glands appear to be unaffected (Di Sant'Agnese and Davis 1976). This has been associated with a high mean pH and increased buffering properties of stimulated saliva (Kinirons 1983). Xerostomia may be aggravated by mouth breathing due to chronic rhino-sinusitis (Brihaye et al. 1997).

Oral hygiene

Oral hygiene in the CF patient has been investigated with some conflicting results. Wotman and Kinirons have separately reported on higher calculus levels in CF children predominantly affecting the lower anterior teeth. These findings are thought to be secondary to an altered salivary composition, with increased calcium composition of the submandibular saliva (Wotman et al. 1973; Kinirons 1989). Ferrazzano et al. (2012) reported on lower plaque and gingivitis prevalence in the CF group. In contrast, Jagels and Sweeney (1976) noted minimal calculus deposits in CF patients. They did, however, confirm earlier reports of a low debris index in this cohort. Blacharsh (1977) reported similar findings and attributed this to the lifelong antibiotic regimen and digestive enzyme supplementation in the CF group.

Adherence rates to oral hygiene in CF patients are unclear. There exist potential barriers to adherence including time constraints due to arduous treatment regimens and potentially more permissive parenting styles in children with chronic illnesses (Mattsson 1972).

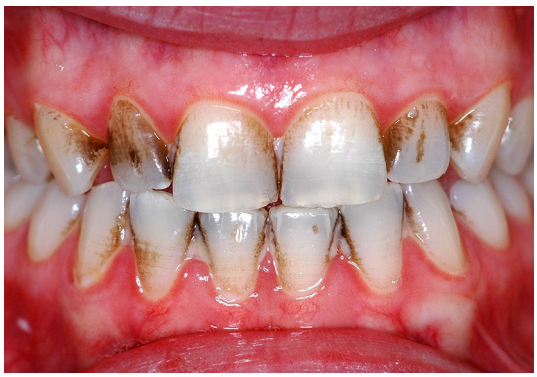

Fig. 2 Black discolouration of teeth following the utilisation of the carbapenem antibiotic meropenem

Dental staining

Coronal staining of permanent teeth has been reported in children with CF (Schuster and Shwachman 1956). These findings appear to be historical, linked to the intake of tetracycline antibiotics during dental development. Acknowledgement of this side effect led to a move to alternative antibiotic prescription for all children including those with CF, thus reducing the risk of dental hard tissue discolouration (Fernald et al. 1990). Other antibiotics including doxycycline and linezolid have also been associated with tooth discolouration and may be utilised in CF. Nebulised antibiotics, particularly the off-label utilisation of the carbapenem antibiotic meropenem, have been associated with marked black tooth discolouration (see Fig. 2).

Dental anomalies

Dental anomalies may be more common in people with CF. Narang et al. (2003) reported a significant increase in dental enamel defects in the permanent teeth of 6- to 9-year-old children with CF. These results were confirmed in a later small study (Azevedo et al. 2006). CFTR has been shown to play an important role in pH regulation during enamel development in CF (CFTR knockout) mice with loss of CFTR expression leading to enamel hypomineralisation (Sui et al. 2003). It has been postulated that enamel defects in CF patients may result from secondary effects of the disease such as metabolic disturbance and infection (Azevedo et al. 2006).

Other oral findings in CF patient

Tongue discolouration can occur in CF for a variety of reasons. Oral antibiotics have been associated with the development of black hairy tongue (Khasawneh et al. 2013). Due to the use of antibiotics and inhaled corticosteroids the development of oral candidiasis is common and

can often be troubling for CF patients (Balfour-Lynn and Welch 2014).

Considerations for the dental practitioner when treating patients with cystic fibrosis

The maintenance of oral health is important in patients with CF. Appropriate dental treatment should be offered to all patients to optimise their general health (see Table 1). Dental practitioners will be in particular requested to review patients prior to listing for lung transplantation to ensure optimal oral health and reduce the potential for the oral cavity to become a source of peri-operative sepsis in the setting of the profound immuno-suppression used to prevent graft rejection. In those patients with severe disease, treatment sessions should ideally be short and performed in the absence of sedation, unless express approval has been gained from a patient's respiratory specialist. Depending on the respiratory status of the patient,

Table 1 Items to elicit from a clinical history when assessing and planning treatment for the person with cystic fibrosis

Checklist for the dental treatment of the patient with cystic fibrosis
Keep appointments as short as possible and appointment time should be mid-morning to allow for chest physiotherapy and nebuliser morning routines
Treatment planning—if sedation required or indicated liaise with medical team
Be vigilant regarding infection control and list only one person with CF per list
Respiratory
Current clinical status—exacerbation or at baseline?
What is the patient's predominant respiratory organism—note in particular MRSA
Regular bronchodilator use—is pre-treatment indicated?
Current or recent corticosteroid use? Is there a requirement for steroid cover?
Baseline FEV_1?
History of respiratory failure?
Current or past supplemental oxygen use?
Current or previous non-invasive ventilation (NIV/BiPap) use?
History of lung transplantation?
If history of current pulmonary exacerbation, low baseline FEV_1 (<40 % predicted), current supplemental oxygen or non-invasive ventilation use or history of lung transplantation—advise liaison with medical team
Bleeding
Is the patient pancreatic insufficient? (Clue—use of supplemental pancreatic enzymes)
Are they prescribed and taking supplemental vitamin K?
History of liver disease?
Use of anticoagulant therapy?
Advise liaison with medical team if significant liver disease/or history of bleeding
Post-procedure analgesia
Is there a history of significant renal disease?
Is there a history of significant liver disease?
Is there a history of broncho-spasm secondary to non-steroidal anti-inflammatories?
Note previous analgesic dosing if available, higher doses may be necessary secondary to hypermetabolism or adjusted for renal/hepatic disease
If considering opioid analgesia—note respiratory history as above. Caution regarding risks of constipation/bowel obstruction
Post-procedure antibiotics
Are post-procedure antibiotics indicated?
Note patient allergy status as there is a higher rate of antibiotic allergy in CF patients
Advise liaison with medical team regarding appropriate antibiotic choice
Considerations for sedation/general anaesthesia
Liaise with medical team prior to any procedure requiring sedation or general anaesthesia
One patient with cystic fibrosis per procedure list
Is pre-operative optimisation of respiratory status advisable—contact medical team to assess requirement for pre-procedure antibiotic/physiotherapy management?

prolonged procedures may be preferentially performed in a hospital setting. Due to the chronic nature of the condition, people with CF are cared for in specialist paediatric or adult centres. In cases where a dentist requires additional information, those responsible for care will provide invaluable background information and advice. Certain considerations should be borne in mind when treatment planning for CF patients (see Table 1).

Cross infection control

As previously outlined segregation of patients with CF is essential in any healthcare setting to prevent the potential transmission of detrimental respiratory pathogens. The dental clinic may additionally present a risk for the acquisition of new respiratory organisms. *Pseudomonas aeruginosa* has been isolated from water samples from dental triple function syringes, contra-angle hand pieces and ultrasonic scalers (de Oliveira et al. 2008). In a prospective study in Denmark, water contamination with *P. aeruginosa* was noted in 2.9 % of water samples during dental visits not involving CF patients and 5.5 % of samples from those involving CF patients. Although only identified for one patient, a genotypically identical strain of *P. aeruginosa* was found in water samples and the sputum of the patient. The mode of transmission of this organism was unclear, but it establishes that dental equipment may harbour organisms following treatment of patients with CF and could pose further risk to subsequent patients (Jensen et al. 1997). A further concern is that once dental units are colonised with bacteria, it is difficult to completely eradicate them. A recent paper describing a case series of patients with possible surgical acquisition of organisms has called for the development of guidelines for minimising these risks (Mainz et al. 2015). Any such guidelines should be inclusive of dental practice.

Coagulopathy

Patients with CF may be at a higher risk of bleeding. Vitamin K deficiency resulting from exocrine pancreatic insufficiency may be subclinical and is common. It has been reported that 50 % of children with CF in Canada showed low vitamin K levels (Drury et al. 2008) and 7 % of pancreatic insufficiency patients showed a prolonged prothrombin time. However, this was not associated with clinical bleeding (Rashid et al. 1999). CF-related liver disease with its potential to disturb hepatic synthetic function may also have a negative effect on normal clotting in CF. Additional risks include hypersplenism related to portal hypertension with resultant thrombocytopenia and the potential for medication-induced marrow suppression particularly in the context of acute antibiotic treatment. The overall risk of excessive bleeding is low and risk factors can usually be accurately assessed during history taking.

Treatment under sedation

Any planned treatment under oral, inhaled or intravenous sedation should be performed only after liaising with the patient's specialist team to ensure the suitability of such techniques. Pre- or post operative optimisation of respiratory status including, but not limited to, bronchodilation, antibiotic treatment or admission to hospital may be necessary. In general, subjects without evidence of respiratory failure or previous hypercarbia (raised carbon dioxide) should be suitable for such procedures; however, the important aspects of each case should be discussed with the treating medical team. Oral pre-medication with benzodiazepines may risk hypoventilation with resultant hypoxia and hypercarbia. In addition, the risk of prolonged sedative effects on an ability to clear respiratory secretions needs to be accounted for. A risk with nitrous oxide includes the potential for high concentrations of supplementary oxygen to lower respiratory drive.

General anaesthesia

General anaesthesia for dental treatment should be planned carefully with the patient's respiratory physician. Fitness for general anaesthesia will depend on a number of factors but most notably current respiratory condition. Some patients may benefit from pre- or post operative antibiotic courses with accompanying chest physiotherapy to optimise their respiratory status prior to any planned procedures.

For elective procedures patients may be booked into morning appointments early in the week to aid further management by a specialist CF team. Lists must be managed to avoid the placement of two CF patients with different respiratory pathogens on the same list. An in-depth review of peri-operative procedures and anaesthesia is beyond the scope of this review but is excellently described elsewhere (Huffmyer et al. 2009).

Post-operative analgesia

Appropriate post-operative analgesia can be an area of concern for dental practitioners when treating patients with CF. Appropriate analgesia is essential to prevent any effect of post-operative pain limiting the clearance of respiratory secretions. A number of factors may influence the pharmacokinetics of drugs in CF, including malabsorption, a hypermetabolic state and significant renal or hepatic dysfunction. Some patients may require higher doses of

analgesics to attain adequate pain relief (Molloy and Nichols 2015).

In the absence of significant liver disease the use of paracetamol is generally well tolerated and not associated with adverse events. Similarly, non-steroidal anti-inflammatory drugs may be used judiciously when required, but omitted in those patients with co-existent renal disease or known broncho-reactivity to these agents. Opioid analgesics are in general less suitable due to their potential to lower respiratory drive in patients with severe disease. A more significant factor for all patients, however, is the negative effect of opiates on bowel motility, which places patients at risk of bowel obstruction. It is imperative if the use of these agents is required that appropriate advice is provided to patients to prevent this potentially serious adverse event.

Conclusion

Cystic fibrosis is a complex, multi-system disease requiring careful multi-disciplinary management. It is imperative that the dental surgeon is aware of the possible systemic and dental manifestations of the disease. Despite conflicting results in the literature regarding caries risk in patients with CF, it is clear that these patients represent a group of high dental priority and should receive regular review with enhanced prevention. Treatment planning before any procedures accounting for the co-morbidities of each individual is essential for successful outcomes.

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Compliance with Ethical Standards

Conflict of interest PB has received honoraria and financial support for educational activities from Vertex pharmaceuticals Ltd.
This article does not contain any studies with human participants or animals performed by any of the authors.

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