ELSEVIER

Contents lists available at ScienceDirect

Paediatric Respiratory Reviews



Pro-Con debates in clinical medicine

Infection prevention and control in cystic fibrosis: One size fits all The argument against



Alan R. Smyth a,b,c,*, Sherie J. Smith a,b, Nicola J. Rowbotham a,b

- ^a School of Medicine, University of Nottingham, Nottingham, UK
- ^b Nottingham Evidence Based Child Health Group, School of Medicine, University of Nottingham, Nottingham, UK
- ^c Nottingham Children's Hospital, Nottingham, UK

Educational aims

The reader will come to:

- Appreciate that infection prevention measures in cystic fibrosis are based on theoretical benefit more than proven efficacy.
- Understand that to be successful, infection control measures need to be simple, universally applied and acceptable.

ARTICLE INFO

Keywords: Infection prevention Evidence Practise Cystic fibrosis

ABSTRACT

As awareness of the risks of cross infection has increased, infection prevention and control measures have become more draconian. Infection control measures can have a profound effect of the organisation and delivery of CF services and on the lives of people with CF outside the hospital. However, the consequences of inadequate infection control measures may be the permanent acquisition of a chronic infection which is virtually untreatable. Recommendations for infection prevention and control therefore must protect patients but should also be evidence-based and proportionate. This article will review the literature, juxtaposing evidence and popular practise.

© 2019 Elsevier Ltd. All rights reserved.

The last half century has seen a dramatic improvement in the life expectancy and quality of life for people with cystic fibrosis (CF) [1]. Much of the early improvement in these outcomes has been attributed to the frequent use of 14 day courses of intravenous antibiotics, particularly for those patients who have chronic pulmonary infection with *Pseudomonas aeruginosa* [2]. Furthermore, long term antibiotic regimens are used in CF such as oral azithromycin and inhaled antibiotics (e.g. colistimethate sodium, tobramycin and aztreonam). Each of these approaches will contribute to the selection of resistant organisms in the CF airway. Patients with CF may therefore develop chronic pulmonary infection with multi-drug resistant organisms including: *P. aeruginosa*; methicillin resistant *Staphylococcus aureus* (MRSA); *Burkholderia cepacia* complex and non-tuberculous mycobacteria, particularly *Mycobacterium abscessus* [3].

E-mail address: alan.smyth@nottingham.ac.uk (A.R. Smyth).

Since these infections were first described in CF, there has been concern that multi-drug resistant infection can be acquired by person to person spread between CF patients or from an environmental source (either in the CF centre or the home). Person to person spread has been proposed for multi-drug resistant P. aeruginosa [4], MRSA [5], B. cepacia complex [6] and M. abscessus [7]. Acquisition of both P. aeruginosa [8] and MRSA [5] from the hospital environment has been suggested. *P. aeruginosa* is present in the homes of CF patients with a new pulmonary infection but it has not been established whether the patient contaminates their environment or vice versa [9]. Uncertainty about the risks of acquiring infection either from other patients or from the environment has given rise to pervasive anxiety in the CF community [10]. In one survey, parents reported using a mean of 11 "hygienic measures" in the home, including ensuring their child had a different toothbrush for morning and evening and removing all pot plants from the house [11].

As awareness of the risks of cross infection has increased, infection prevention and control measures have become more draconian. Following reports of the transmission of *Burkholderia cepacia* complex by social contact, infection control guidelines

 $[\]ast$ Corresponding author. School of Medicine, University of Nottingham, Nottingham, UK.

were published advising against any social contact between people with CF and avoiding activities such as CF camps [12]. The first edition of the US CF Foundation consensus document on infection control [13] stated that: "No recommendation can be made for the routine wearing of masks by CF patients..." The most recent edition of the same guideline [14] states that: "All people with CF, regardless of respiratory tract culture results, should wear a surgical...mask when in a healthcare setting..." Infection control measures can have a profound effect of the organisation and delivery of CF services and on the lives of people with CF outside the hospital. However, the consequences of inadequate infection control measures may be the permanent acquisition of a chronic infection which is virtually untreatable. Recommendations for infection prevention and control therefore must protect patients but should also be evidence-based and proportionate.

So how robust is the evidence? That depends on how high we set the bar. Conventional clinical trials are designed to show a difference (improvement) in the group mean with an intervention. With cross infection, we are in pursuit of zero infection and so an improvement in the group mean may not be enough. A recent systematic review found only 2 randomised controlled trials of infection prevention and control measures in CF – the majority of studies being a "before and after" design [15].

- Segregation. When patients attend their CF centre, it is no longer proposed that they are cohorted together with other patients who have the same organism but rather individual segregation is recommended. These changes have been driven by the observation that an epidemic strain of *P. aeruginosa* can cross-infect patients with less pathogenic strains [16] and by the unquantifiable risk of a new transmissible pathogen appearing within a cohort who are mixing freely. Only one study (before and after) has evaluated individual segregation of CF patients and this found no significant difference in acquisition of *P. aeruginosa* after segregation was introduced [17]. A post hoc subgroup analysis of these data suggested that acquisition of *P. aeruginosa* was reduced in children.
- Hand hygiene is practised universally in health care settings and is acceptable to patients and staff. One before and after study has examined the efficacy of hand hygiene in CF but did not demonstrate a reduced risk of transmission with hand hygiene measures [18].
- Gowns and gloves. A systematic review, looked at 23 studies of glove use in health workers and found that, although gloving can reduce acquisition of microorganisms on the hands, inappropriate glove use is frequent and can increase the risk of transmission of infection by health workers [19]. An observational study on a medical ward and intensive care unit documented that frequently gloves were neither discarded nor hand hygiene performed after patient contact [20]. A study in 4 US hospitals found that skin contamination of the health worker occurred during gown and glove removal in 46% of cases [21]. Current CF infection control guidelines recommend that gowns and gloves are worn for all patient contact [14].
- Face masks. Perhaps one of the most contentious issues is the question of whether face masks should be worn by all CF patients when attending the CF centre. A randomised controlled trial of face mask use found that air contamination during CF clinic visits was infrequent and was not reduced by the use of masks [18]. In contrast, studies of air contamination in CF adults using a "cough rig" have shown that face masks reduce the gen-eration of *P. aeruginosa* aerosols [22] and that the density of organisms is reduced for wear periods of up to 40 minutes [23].
- High-efficiency particulate air (HEPA) filters and air changes. Performing spirometry has been shown to increase room air contamination [24] and it is recommended that a HEPA filter is

used in the spirometry room (equivalent to 12 air changes per hour) or else 30 minutes should elapse before the room is used by the next patient [14]. However, differences in the number of air changes per hour have not been shown to affect air contamination [24].

None of these recommendations will be effective if they are not implemented consistently by patients and staff. A recent survey of paediatric CF centres in Ireland showed that only one centre adhered to the recommendation on gowns and gloves and no centres followed the recommendation on use of face masks or room ventilation [25]. There is some evidence which suggests that infection control measures can compromise patient care [26].

So does infection prevention and control allow room for pragmatism? Hand hygiene and individual segregation should be practised in every CF centre. However HEPA filtration may work best when it is part of the design of new-build CF facilities. In the meantime, many centres will have to opt for leaving spirometry rooms vacant and ventilated for 30 minutes after use. Glove use may add little to infection prevention through simple hand hygiene. Indeed gloves may give false reassurance and may lead to appropriate hand hygiene being omitted after patient contact. Face masks remain controversial and their efficacy in children has not yet been demonstrated. Some paediatric centres may await further evidence before deciding on the use of face masks. There is little evidence on how to reduce environmental acquisition in the home and CF centres should restrict their advice to measures which are evidence-based and readily implemented. Careful pragmatic implementation of infection control should aim to protect patients whilst avoiding stigmatisation and anxiety.

DIRECTIONS FOR FUTURE RESEARCH

- Provide evidence for or against simple measures such as masks, gowns and gloves as the centrepiece of infection prevention.
- Justify the role of highly expensive frequent air cycling in clinical rooms.

References

- [1] Dodge JA, Lewis PA, Stanton M, Wilsher J. Cystic fibrosis mortality and survival in the UK: 1947–2003. Eur Respir J 2007;29(3):522–6.
- [2] Frederiksen B, Lanng S, Koch C, Hoiby N. Improved survival in the Danish center-treated cystic fibrosis patients: results of aggressive treatment. Pediatr Pulmonol 1996;21(3):153–8.
- [3] UK Cystic Fibrosis Trust. UK CF Registry. Annual Data Report 2017. London: Cystic Fibrosis Trust; 2018.
- [4] Cheng K, Smyth RL, Govan JRW, et al. Spread of β-lactam-resistant Pseudomonas aeruginosa in a cystic fibrosis clinic. Lancet 1996;348 (9028):639–42.
- [5] Harik NS, Com G, Tang X, Melguizo Castro M, Stemper ME, Carroll JL. Clinical characteristics and epidemiology of methicillin-resistant Staphylococcus aureus (MRSA) in children with cystic fibrosis from a center with a high MRSA prevalence. Am J Infect Control 2016;44(4):409–15.
- [6] Govan JR, Brown PH, Maddison J, et al. Evidence for transmission of Pseudomonas cepacia by social contact in cystic fibrosis. Lancet 1993;342 (8862):15–9.
- [7] Bryant JM, Grogono DM, Rodriguez-Rincon D, et al. Emergence and spread of a human-transmissible multidrug-resistant nontuberculous mycobacterium. Science 2016;354(6313):751–7.
- [8] Smyth A, Heaf D, Corkill J, Hart T, Sisson P, Freeman R. Transmission of Pseudomonas-cepacia by social contact in cystic-fibrosis. Lancet 1993;342
- [9] Schelstraete P, Van Daele S, De Boeck K, et al. Pseudomonas aeruginosa in the home environment of newly infected cystic fibrosis patients. Eur Respir J 2008;31(4):822–9.
- [10] Palser SC, Rayner OC, Leighton PA, Smyth AR. Perception of first respiratory infection with Pseudomonas aeruginosa by people with cystic fibrosis and those close to them: an online qualitative study. BMJ Open 2016;6(12). https://doi.org/10.1136/bmiopen-2016-012303.

- [11] Ullrich G, Wiedau S, Schulz W, Steinkamp G. Parental knowledge and behaviour to prevent environmental P. aeruginosa acquisition in their children with CF. J Cys Fibros 2008;7(3):231–7.
- [12] UK Cystic Fibrosis Trust Infection Control Group. Pseudomonas aeruginosa infection in people with cystic fibrosis. Suggestions for prevention and infection control. Bromley: UK CF Trust; 2004.
- [13] Saiman L, Siegel J, Cystic Fibrosis Foundation Consensus Conference on Infection Control. Infection control recommendations for patients with cystic fibrosis: microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission. [Review] [395 refs]. A J Infect Control 2003;31(3 Suppl):S1–S62.
- [14] Saiman L, Siegel JD, LiPuma JJ, et al. Infection prevention and control guideline for cystic fibrosis: 2013 update. Infect Control Hosp Epidemiol 2014;35(Suppl 1):51–567
- [15] Rowbotham NJ, Palser SC, Smith SJ, Smyth AR. Infection prevention and control in cystic fibrosis: a systematic review of interventions. Expert Rev Respir Med 2019:1–10.
- [16] McCallum SJ, Corkill J, Gallagher M, Ledson MJ, Hart CA, Walshaw MJ. Superinfection with a transmissable strain of Pseudomonas aeruginosa in adults with cystic fibrosis chronically colonised by P aeruginosa. Lancet 2001;358:558–60.
- [17] van Mansfeld R, de Vrankrijker A, Brimicombe R, et al. The Effect of strict segregation on Pseudomonas aeruginosa in cystic fibrosis patients. PLoS ONE 2016:11(6):e0157189.
- [18] Zuckerman JB, Zuaro DE, Prato BS, et al. Bacterial contamination of cystic fibrosis clinics. J Cyst Fibros 2009;8(3):186–92.

- [19] Picheansanthian W, Chotibang J. Glove utilization in the prevention of cross transmission: a systematic review. JBI Database Systematic Rev Implement Rep 2015;13(4):188–230.
- [20] Girou E, Chai SH, Oppein F, et al. Misuse of gloves: the foundation for poor compliance with hand hygiene and potential for microbial transmission? J Hosp Infect 2004;57(2):162–9.
- [21] Tomas ME, Kundrapu S, Thota P, et al. Contamination of health care personnel during removal of personal protective equipment. JAMA Internal Med 2015;175(12):1904–10.
- [22] Wood ME, Stockwell RE, Johnson GR, et al. Face masks and cough etiquette reduce the cough aerosol concentration of Pseudomonas aeruginosa in people with cystic fibrosis. Am J Respir Crit Care Med 2018;197(3):348–55.
- [23] Stockwell RE, Wood ME, He C, et al. Face masks reduce the release of Pseudomonas aeruginosa cough aerosols when worn for clinically relevant periods. Am | Respir Crit Care Med 2018;198(10):1339–42.
- [24] Zuckerman JB, Clock SA, Prato BS, et al. Air contamination with bacteria in cystic fibrosis clinics: implications for prevention strategies. Am J Respir Crit Care Med 2015;191(5):598–601.
- [25] Breen C, Finn D, Greally P, O'Connell G, Elnazir B. A national paediatric survey of infection control measures in cystic fibrosis. Ir J Med Sci 2015;184(Suppl 7): \$278.9
- [26] Saint S, Higgins LA, Nallamothu BK, Chenoweth C. Do physicians examine patients in contact isolation less frequently? A brief report. Am J Infect Control 2003;31(6):354–6.