Original Article

Adherence to nebulised therapies in adolescents with cystic fibrosis is best on week-days during school term-time

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Abstract

Objectives: Treatment regimen for families of children with cystic fibrosis (CF) is considerable, particularly when nebulised therapies for chronic *Pseudomonas aeruginosa* airway infection are prescribed. Adherence to these regimens is variable, particularly in adolescence. Previously, we reported children to be more adherent in evenings compared to mornings, suggesting an association with time-pressure. The aim of this study was to determine whether adherence would be better in adolescent patients at weekends and during school holidays when time-pressures may be less.
Study design: 24 patients (14 male, median [range] age 13.9 [11.1–16.8] years) were enrolled from two regional paediatric CF centres in the United Kingdom. Data for a full scholastic year, were downloaded openly from a breath-activated data logging nebuliser (I-neb™). Adherence (% of doses taken ÷ expected number) was calculated during term-times, holidays, weekends and weekdays, for each patient.
Results: Large variations in adherence were seen between patients. However, adherence during term-time was significantly better than holidays ($p < 0.001$). Weekday adherence was better than weekend adherence in term-time but not holidays. Interestingly, patients prescribed three daily treatments took on average 1.4 treatments/day, a similar number to those prescribed two daily treatments.
Conclusion: Overall adherence to inhaled therapies was reasonable, but significantly reduced during holiday periods. This suggests a need for families to have not only time, but also structure in their daily routine to maintain optimal adherence to long-term therapies. It is important for CF teams to appreciate these factors when supporting families.
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1. Introduction

Families of children with cystic fibrosis (CF) face a considerable treatment burden, which is compounded by nebulised treatments for chronic *Pseudomonas aeruginosa* airway infection [1,2]. While it is known that adherence to all forms of treatment is an issue in any chronic disease, and particularly so during adolescence, very few studies have examined actual rates of adherence in this age group. This is partly because, until relatively recently, accurately measuring adherence to therapies was difficult.

The development of breath-actuated nebuliser devices incorporating built-in data-logging systems has provided a highly reliable mechanism for accurately recording and assessing adherence [3]. Using this technology, we have previously shown that adherence to inhalation therapies is often poor but that children of all ages are generally more adherent to therapy in the evenings than in the mornings [4]. This suggested that time-pressures in the mornings might adversely affect adherence and thus we speculated whether adherence would be better when time-pressures may be less [4,5].

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Consequently, the present study explored this further by examining weekday/weekend and term-time/holiday adherence data in a group of adolescents with CF over a full, UK scholastic year.

2. Methods

2.1. Study design

In this observational study, adherence to nebulised therapies during weekdays/weekends and term-time/holidays in young people attending secondary school was calculated based on data collected and analysed retrospectively during routine clinical practice over a full, UK, scholastic year.

2.2. Participants

Participants attended one of two regional paediatric CF clinics; Alder Hey Children's Hospital in Liverpool or Leeds General Infirmary. All patients with CF, aged between 11 and 17 years at or starting secondary school in September 2008, who were established on therapy through the I-neb™ (Respironics, Philips, Chichester, UK) using standard tidal breathing mode of inhalation, were included in the study. Patient demographics and clinical characteristics including pulmonary function tests were recorded.

2.3. Ethics

Clarification regarding the nature of the study was sought from the Alder Hey Research, Development and Ethics *Users Views Group*. Following methodological review, the opinion of this committee was that this study constituted service evaluation. All families were aware that nebuliser usage and adherence to treatment were being monitored routinely.

2.4. Device, drug delivery, monitoring and measurements

The I-neb™ adaptive aerosol delivery device has a data-logging facility which records the dates and times of treatments. Patients and their parents are encouraged to bring their handheld devices to clinic appointments and on average, bring them to half their clinic appointments. At clinic, the data-log is accessed via a reading cradle using dedicated computer software provided by the manufacturer. The data are discussed routinely with the individual patient and their family during the clinic visit. The *I-neb* has sufficient memory to record 5000 events allowing adherence to be calculated retrospectively if clinic appointments were missed or the device forgotten.

Over a full UK scholastic year, the number and date of all treatments were recorded, data routinely collected in both centres as part of service evaluation. Adherence was calculated as the percentage of the number of taken treatments/number of prescribed treatments. This information combined with the dates of school holidays for all patients in the two clinics allowed adherence to be calculated for weekdays and weekends, and term-times and holidays over the year. Overall and individual holiday adherence rates were calculated to investigate whether individuals and their families experienced difficulties over particular vacation periods.

This included 'half-term' breaks, which are normally week-long holidays mid-way through a school-term. Children from both centres spent on average 38 weeks (73%) of the year at school.

2.5. Treatments

Participants were prescribed a range of inhalation therapies (Colistin, Tobramycin and Dornase alfa but not hypertonic saline) with varying frequencies (1–3/day) during the study period. For patients taking Colistin, a commercial preparation was used (*Promixin®*, Profile Pharma Ltd., Chichester, UK), with the treatment dose being 1 mega unit (MU) diluted in either normal saline or sterile water and given either once or twice daily.

2.6. Statistics

Data were analysed and presented depending on whether they were normally distributed or not. Thus, adherence was expressed as mean (standard deviation [SD]) with differences for individual patients examined between different time points using a paired samples t test. Data were displayed graphically as mean (standard error of the mean [SEM]) or as line graphs. We used SPSS 18.0 and all statistical tests were two-tailed with a p value equal to or less than 0.05 considered statistically significant.

3. Results

3.1. Participants

Data from 24 patients (12 Liverpool; 12 Leeds) between 1st August 2008 to the 31st July 2009, were included in this study. Median (range) age was 13.9 (11.1–16.8) years and median (range) FEV_1 and FVC, 78 (43–105)% and 88 (52–110)% respectively.

Patients were prescribed one treatment (n=10), two treatments (n=5) or three treatments (n=9) every day. In two patients, treatment regimens were changed very soon after the start of the study from three to one treatment/day and so they were analysed as taking one treatment each day. Between the two centres, 7 different combinations of nebulised treatment were prescribed i.e. once daily colistin, or twice-daily colistin and once daily DNAse etc. Overall, 16 patients were prescribed Colistin, 13 patients DNAse and 3 patients Tobramycin. Over the study period, according to the Leeds criteria for *P. aeruginosa* infection [6], 8 patients were free of infection, 8 patients were intermittently infected and 10 patients were chronically infected. The median (range) duration of use of the *I-neb* prior to the study period was 20 (1–36) months. The mean (SD) percentage of treatments taken, which were successfully completed was 92 (14)% during term-time and 92 (15) during the holidays.

3.2. Adherence

Mean (SD) overall adherence over the 12 months of treatment through the *I-neb* was 65 (28)% with 12/24 patients achieving an