RESEARCH ARTICLE

Home intravenous antibiotic therapy in children with cystic fibrosis: clinical outcome, quality of life and economic benefit

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Abstract

Background: Pediatric home care has improved therapeutic options for children with chronic disease. Home intravenous (IV) antibiotic treatment against *Pseudomonas aeruginosa* (PsA) in cystic fibrosis (CF) patients has offered increased flexibility to these patients and family life. A prospective clinical study was conducted to compare safety, efficacy, and cost benefits of home versus hospital IV antibiotic treatment among CF children and adolescents.

Method: The clinical outcome, quality of life, and cost benefits of home versus hospital antibiotic treatment were assessed. The clinical outcome was evaluated with Forced Expiratory Volume in one second (FEV_1) and weight gain before and one month after antibiotic treatment, while the Quality of life was evaluated using the DISABKIDS questionnaire. Cost analysis was performed to calculate cost benefits from home IV treatment.

Results: Thirty-five stable patients with CF (mean age: 12.6 ± 7 years, 56 % male, mean FEV_1: 83.5 ± 26 %), colonized with PsA, were treated with IV antibiotics for two weeks either in the hospital (15 patients), or at home (20 patients) under supervision by a home care nurse. Lung function (FEV_1) and weight improved significantly in both groups (ΔFEV_1% =7.7 ± 6.1, $p < 0.001$; ΔWeight =1.2 ± 0.8, $p < 0.001$). Hospital treatment did not show a better clinical outcome, compared to home treatment (ΔFEV_1, $p = 0.606$; ΔWeight, $p = 0.608$). Both improvements in the quality of life and economical savings were substantial ($p < 0.001$) regarding patients treated at home. Also, patients treated at home did not report any significant side effects or complications.

Conclusions: Home IV antibiotic therapy monitored by a home care nurse, is a safe, efficient, and cost-saving therapeutic option in CF. Hippokratia 2016, 20(4): 279-283

Keywords: Cystic Fibrosis, homecare, *Pseudomonas aeruginosa*, quality of life, intravenous, antibiotic therapy

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Introduction

Cystic fibrosis (CF) is a common lethal inherited disease in the European population, affecting approximately 1: 2,500 children[1,2]. It is a complex genetic disease affecting many organs, although 85 % of the mortality is a result of lung infections. As a result of these infections, the patient's pulmonary disease is worsening by the time[3,4].

The basic genetic defect in CF predisposes and causes chronic airway infection with several bacterial pathogens. These bacteria are capable to eventually establish a chronic presence in the airways due to impaired innate immunity and are associated with a chronic inflammatory response[5]. The most common pathogenic bacteria in CF include *Pseudomonas aeruginosa* (PsA), *Staphylococcus aureus*, *Haemophilus influenzae*, *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans* and *Burkholderia* species[6,7].

Frequent and prolonged duration antibiotic treatment via different routes is the cornerstone in slowing down the progression of lung disease[8]. While oral and inhaled antibiotics provide sufficient treatment for many CF lung infections, intravenous (IV) antibiotic treatment is often needed especially in the treatment of PsA. Courses of at least two weeks are administered to treat the exacerbations of the respiratory infections. Intermittent antibiotic treatment of PsA infection is time-consuming and socially demanding if carried out in the hospital. Therefore, home antibiotic treatment has been introduced increasing flexibility for patients. Lung infections are often treated in hospital with IV antibiotics for many weeks. Besides been costly, this disrupts the lives of patients with cystic fibrosis. Treatment can be given at home if patients and their careers are given enough training and support[8].

In several countries the experience with, and the outcome of home IV antibiotic therapy are being reported since the 1980s; however, most publications concern adults[9-13]. Over the last three decades, several studies compared the efficacy and safety of home compared to hospital therapy, but there are only a few studies reporting pediatric data[14-22]. In Greece, home IV antibiotic therapy has just recently been introduced. In this study,

we evaluated the safety and effectiveness of home IV antibiotic therapy compared to hospital therapy, among children with CF.

Material and methods

Thirty-five stable pediatric patients with CF, chronically colonized with PsA participated in this prospective study. The study was conducted by the Pediatric Pulmonology and Cystic Fibrosis Unit of the 3rd Pediatric Department in Hippokration Hospital of Thessaloniki from January to December 2014.

Ethical approval was obtained by the Ethics Committee of the Medical School of Aristotle University of Thessaloniki (institutional review board file No 1; 18/12/2013). Two nurses trained the children and their parents how to administer IV antibiotics, for three days during their hospital stay. Then, the parents were asked whether they wanted to continue treatment at home under the supervision of a home nurse. Twenty of them agreed while the remainder 15 children completed their treatment in the hospital.

The care of these 20 children was continued at home with regular visits on a weekly basis by home nurses. In case of an adverse event or deterioration of the lung infection, the doctor was informed to decide whether the child should be referred to the hospital. All participants performed regular physiotherapy during the treatment intervals. The clinical outcome of the IV treatment was evaluated with the Forced Expiratory Volume (FEV_1) and weight measured at the initiation of home IV antibiotic therapy and one month later.

Quality of life (QoL) was measured with the DISABKIDS questionnaire, which is a validated questionnaire, completed both by children and their parents. The measures used for the current study were the DISABKIDS chronic generic measure (DCGM-37) and the DISABKIDS condition-specific module for cystic fibrosis[23]. The DISABKIDS chronic generic module (DCGM-37) consists of 37 rating-scaled items assigned to six dimensions: Independence, Emotion, Social inclusion, Social exclusion, Limitation, and Treatment. These six dimensions can be combined to produce a general score for health related QoL. The condition-specific cystic fibrosis questionnaire (DISABKIDS Cystic Fibrosis Module) consists of two domains: the impact domain (six items) concerning limitations and symptoms, and the treatment domain (eight items) concerning treatment limitations related to cystic fibrosis. In the study both DISABKIDS, the self-report version (child version) and the proxy version (completed by one of their parents) were used[23].

The economic evaluation was made by cost analysis which included cost estimates for the 35 patients before and after the IV antibiotic therapy. The cost at home included the IV drugs while the cost at the hospital was calculated according to the Diagnostic Related Groups (DRG), a system to classify hospital cases and determine how much a patient's hospital stay costs. The objective of the statistical analysis was to test whether there were statistically significant cost differences between two groups.

Statistical analysis

Descriptive statistics were used to describe the study population (mean ± standard deviation). Differences in lung function, weight parameters and QoL scores before and one month after antibiotic treatment were analyzed using paired t-tests. The Student's t-test was used to compare the FEV_1, weight and QoL scores values between the groups. The level of significance was set at $p < 0.05$. Statistical analysis was performed using the IBM SPSS Statistics software, version 20.0 (IBM SPSS, IBM, Armonk, NY, USA).

Results

The mean age of the thirty-five children with CF was 12.6 ± 7 years (56 % male), mean $FEV_1\% = 83.5$ (± 26), mean weight =37.7 (± 17) kg, and mean height =142.9 (± 26) cm. Twenty patients were treated with IV antibiotics for two weeks at home (Group A) and 15 patients received IV treatment in the hospital (Group B). The two groups did not differ in disease severity (Schwachman score), age, and lung function characteristics (Table 1).

The clinical outcome was beneficial in 92 % of the studied population. Lung function (FEV_1) and weight improved significantly in both groups ($\Delta FEV_1\% = 7.7 \pm 6.1$, $p < 0.001$; ΔWeight $= 1.2 \pm 0.8$, $p < 0.001$), (Table 2). Hospital treatment did not show a better clinical outcome, compared to home treatment (ΔFEV_1, $p = 0.606$, ΔWeight, $p = 0.608$), (Table 2). There were no complications among the patients treated at home, apart from a rash five days after drug administration in one patient. There were no differences in baseline QoL scores when the hospital and home groups were compared (Table 1), although changes achieved with treatment showed differences (Table 2 and Table 3). In the home group, there were statistically significant improvements in all quality of life domains, whereas in the hospital group there were significant improvements only in physical and impact domains (Table 3).

The cost of home IV therapy was significantly lower than the cost of hospital treatment (2100€ vs 3360€, respectively, $p < 0.001$).

Discussion

Provision of health care in Europe is constantly reforming. There has been recently a change towards management of chronic conditions at home[24]. Home administration of high-technology treatments, such as IV antibiotics has become feasible because of the development of improved venous access devices and portable infusion pumps[20]. In CF patients, home IV antibiotic therapy is evolution providing solution to both increasing demands for hospital beds, and the necessity to minimize interference of treatment to individual's normal lifestyle and QoL. Home IV therapy may also reduce costs by avoiding frequent hospital admission or reducing the length of stay. Hospitalization may be hazardous for patients with CF, especially children, because of the risk of acquiring *Burkholderia cepacia*, Methicillin-resistant *Staphylococcus aureus* (MRSA), and other multi-resistant organisms[25].

Most CF patients tend to prefer home IV treatment,

Table 1: Baseline characteristics of the 35 stable pediatric patients with cystic fibrosis that participated in this prospective study. Twenty patients were treated with intravenous (IV) antibiotics for two weeks at home (Group A) and 15 patients received IV treatment in the hospital (Group B). The two groups did not differ in baseline disease severity (Schwachman score), age, lung function and quality of life.

Group characteristics	Group A (Home care) n =20	Group B (Hospital) n =15	p value
Shwachman score	76 (46-100)	74 (42-94)	0.46
Age, years	12.6 (±7)	12.7 (±6)	0.85
BMI (kg/m²)	18.32 (±3.42)	18.98 (±3.2)	0.58
FEV1 (%)	87.2 (±8.1)	78.83 (±7.2)	0.54
DISABKIDS (QoL) score	51.8 (±10)	53.2 (±11)	0.35

Values are given as median (with range in brackets) or mean (± standard deviation in brackets), FEV_1: Forced Expiratory Volume in one second, BMI: body mass index, QoL: quality of life.

Table 2: Change in clinical outcome (weight gain and FEV_1) and quality of life (QoL) score after intravenous antibiotic treatment of the 35 stable pediatric patients with cystic fibrosis that participated in this prospective study. Both groups show significant improvement in weight gain, FEV_1, and QOL. Hospital treatment showed a higher improvement in QoL, compared to home treatment.

	Change in clinical outcome after iv treatment						
	Whole study group n =35		Group A (Home care) n =20		Group B (Hospital) n =15		Group A vs Group B
	Change after iv	p value whole study group	Change after iv	p value Group A	Change after iv	p value Group B	p value Group A vs Group B
ΔWeight, kg	1.2 (± 0.8)	0.001†	1.1 (±0.8)	0.001†	1.5 (±0.7)	0.001†	0.608
ΔFEV_1 (%)	7.7 (± 6.1)	0.001†	7.0 (±6.0)	0.001†	9.0 (±5.4)	0.001†	0.606
ΔQoL score	6.1 (± 3.9)	0.001†	7.4 (±3.7)	0.001†	3.8 (±2.6)	0.07	0.04*

Values are given as mean (± standard deviation in brackets), IV: intravenous, QoL: quality of life, ΔWeight: weight gain, ΔFEV_1: % change of the Forced Expiratory Volume in one second, ΔQoL: change in total QoL score, †: p ≤0.001, *: p <0.05.

Table 3: Baseline characteristics and change in the quality of life (QoL) dimensions. Comparison of the change in QoL parameters among the two groups after intravenous (IV) treatment. In the home group, there were statistically significant improvements in all QoL dimensions, whereas in the hospital group there were significant improvements only in physical and impact parameters.

QoL dimensions	Group	Baseline score Mean (SD)	Mean Δscore	p #	p ##
Independence	**Home**	71.2 (15)	9	0.001†	0.001†
	Hospital	69.4 (12)	2	0.09	
Physical	**Home**	47.1 (11)	15	0.001†	0.03*
	Hospital	52.5 (19)	9	0.001†	
Emotion	**Home**	45.4 (14)	13	0.001†	0.001†
	Hospital	48.7 (11)	2	0.09	
Soc. Exclusion	**Home**	31.2 (12)	6	0.001†	0.04*
	Hospital	33.7 (15)	3	0.08	
Soc. Inclusion	**Home**	54.6 (16)	28	0.001†	0.001†
	Hospital	52.4 (16)	3	0.08	
Medical	**Home**	50.3 (14)	12	0.001†	0.01*
	Hospital	48.1 (12)	4	0.07	
Impact	**Home**	43.6 (14)	5	0.04*	0.02*
	Hospital	45.3 (15)	11	0.001†	
Treatment	**Home**	51.3 (16)	11	0.001†	0.02*
	Hospital	47.8 (13)	5	0.04*	
TOTAL score	**Home**	51.8 (19)	7	0.001†	0.04*
	Hospital	53.2 (19)	4	0.07	

Values are given as mean (± standard deviation in brackets), SD: standard deviation, QoL: quality of life, #: comparison of the change in QoL parameters after intravenous treatment, ##: comparison of the change in QoL parameters among the two groups (home vs hospital) after intravenous treatment, †: p ≤0.001, *: p <0.05.

instead of being hospitalized. Treatment in the hospital is considered to be disruptive for patients, especially children, and their families, deprive them of school or work activities, and their social lives for considerable amounts of time. Also, there are financial strains on patients due to earning losses, due to absence from work; and expenses for traveling to and from the hospital, especially if the referral center/hospital is at a considerable distance from patient's home. After numerous admissions throughout their lives, patients and their families become acquainted with many aspects of IV drug administration and often want to start self-administration of these medications, avoiding hospital admissions[22].

Our study showed that there was a statistically significant improvement in lung function and weight, after IV antibiotic therapy in 35 stable children with CF, treated either at home or in hospital. Moreover, children on home care showed a significant improvement in their QoL and also substantial economic savings, compared to patients treated in the hospital.

Over the last thirty years, studies from several countries reported conflicting results regarding the benefits of home versus hospital IV antibiotic administration for CF lung infections[20]. The evaluated outcomes in these reports included changes in lung function, duration of therapy, QoL, anthropometric measures, and cost-effectiveness. These studies enrolled mainly adult patients, and their comparison could be problematic due to differences in enrolled patients' age, outcome measures, study designs, treatment indications, and length of treatment periods. Our study examined the clinical outcomes, QoL, and economic cost of pediatric patients treated with IV antibiotics either in the hospital or their home environment.

Furthermore, lung function, particularly FEV_1 is the most important objective clinical outcome measure in CF. The main aim of treatment with IV antibiotics is to achieve and maintain the patient's best lung function[21]. In our study, lung function and weight improved significantly in both groups ($p = 0.001$). Hospital treatment did not show a better clinical outcome, compared to home treatment (ΔWeight, $p = 0.608$; ΔFEV_1, $p = 0.606$). These results are in agreement with the results of other studies which showed that although there were some changes from baseline, mean improvements in body weight, FEV_1 and FVC were not statistically significant between home and hospital groups[26,27]. The study of Wolter et al, reported that there were significant differences over time in changes from baseline noted for FEV_1 ($p = 0.006$) and FVC ($p = 0.002$) although, there was no statistical difference between home and hospital arms in the overall improvement in the lung function (FEV_1, $p = 0.27$; FVC, $p = 0.30$)[26]. Additionally, Termoz et al, compared changes in FEV_1, FVC and weight among patients with CF who were treated in the hospital or at home. A total of 153 patients were analyzed (51 inpatients matched to 102 patients treated at home). The two groups had no significant differences in any outcome variable compared to baseline. The mean variation per year in FEV_1 was greater ($p = 0.003$) in the hospital group versus the home group[28].

Nazer et al showed that the percent change in FEV_1 was greater in-hospital group versus home group ($p = 0.04$). In this study, patients were not stable, as in our study; they were treated for a pulmonary exacerbation and they reported that hospital therapy resulted in a significantly better improvement in FEV_1 and required less duration of treatment as compared to home treatment in children with CF[20].

QoL has been used as a synonym for a subject-centered perspective on health. Despite the increase in "quality of life" research in adults, there are few studies on "quality of life" in children. While generic measures begin to emerge now, methods to assess the QoL of children with chronic conditions are still in development. The design of such an assessment tool for different age groups and varying levels of disabilities was the objective of a European Union-funded study: the DISABKIDS project. The purpose of DISABKIDS questionnaire was to assess the general QoL and the level of distress caused by the chronic disease. The questionnaire is relatively simple and fast to complete, and it is composed of 56 items which are divided to six dimensions: Independence, Emotion, Social inclusion, Social exclusion, Limitation, and Treatment[23]. QoL measurements are reported as important in many studies. A review suggested that QoL seems to be better when IV treatment is administered at home [16]. The benefits of home treatment for patients include shorter hospital stays, reduction in hospital-acquired infections, and improved health-related QoL[16]. Our study also showed that the children receiving home IV antibiotic therapy improved in all scales of QoL. This result is in agreement with the conclusion of Esmond et al, that the patients who undertook their treatment at home had improvements in their QoL[29]. One possible explanation for these results is the familiarity most patients have with the home environment, as there is minimal interruption to their everyday lifestyle and less disruption of their social relationships. Furthermore, as shown in our study, the pediatric patients who were better educated by the nurses, were more confident and able to self-manage their treatment at home, under the scheduled visits of nurses.

Additionally, comparative studies have shown that home IV antibiotic therapy is cost saving, reducing the economic burden on patients and health care providers[24]. A study by Elliott et al recorded that patients who had over one year 60 % of courses at home, had a mean cost of £13,528 compared with £22,609 for patients who had more than 60 % of courses in the hospital, and a mean cost of £19,927 for patients who had an equal mix of home and hospital care ($p = 0.001$)[21]. Thornton et al, also reported the cost of the hospital treatment to be higher than home treatment (mean difference £9,005, $p < 0.001$)[16].

Various studies revealed that home intravenous antibiotic treatments had a similar clinical outcome, provided a better QoL and were less costly than hospital interventions. In many European centers; patients with CF are given IV antibiotics on a regular basis even in the absence of acute pulmonary exacerbations, as recommended by the European guidelines[20,30,31]. Home treated patients are better select-

ed and prepared for home care and additionally many of them had visiting nurse support on regular base providing assistance with the IV administration of medications[10-15].

Finally, more studies are needed with the inclusion of more participants, longer follow-up period and more outcome measures. Especially, the small number of subjects included in most existing studies explains their inability to reach statistical significance as they are underpowered to detect differences between hospital and home IV antibiotic administration and thus defining the superiority of one intervention versus the other. Until further studies provide definitive answers, treatment at home, should be reserved for properly selected patients and be individualized, depending on the policy of each center and the needs of each patient[20]. In conclusion, although in certain countries most healthcare centers have established protocols for home IV treatment, few of them audit the outcome of their home IV antibiotic service[32]. Possible limitations of the current study include the small sample size, and the absence of randomization, as the groups were selected according to the patients' needs. Our prospective study, the first among CF pediatric Greek patients, adds additional evidence that home IV antibiotic treatment is an effective and safe alternative treatment for CF children as it provides potential benefits that include significant clinical outcomes, better QoL and more cost savings.

Conflict of interest

Authors declare no conflict of interest.

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