Antibiotic therapy and fat digestion and absorption in cystic fibrosis

Aleksandra Lisowska1,2, Andrzej Pogorzelski3, Grzegorz Oracz3, Wojciech Skorupa4, Szczepan Cofta5, Jarosław Szydłowski5, Jerzy Socha3 and Jarosław Walkowiak1,7

11st Chair of Pediatrics, Department of Pediatric Gastroenterology & Metabolism, Poznań University of Medical Sciences, Poznań, Poland; 2Department of Bronchology & Cystic Fibrosis, National Institute for Tuberculosis & Lung Diseases, Pediatric Branch, Rabka, Poland; 3Department of Pediatric Gastroenterology, Hepatology & Immunology, Child Memorial Health Institute, Warszawa, Poland; 41st Clinic of Lung Diseases, National Tuberculosis and Lung Diseases Research Institute, Warszawa, Poland; 5Department of Otorhinolaryngology, Poznań University of Medical Sciences, Poznań, Poland; 6Department of Dietetics, Chair of Human Nutrition & Hygiene, Poznań University of Life Sciences, Poznań, Poland

Antibiotic therapy in the cystic fibrosis (CF) mouse model has been shown to result in reduced bacterial load of the intestine and significant body mass gain. The effect was suggested to be linked to the improvement of intestinal digestion and absorption. Therefore, we aimed to assess the influence of routinely applied antibiotic therapy in CF patients on fat assimilation. Twenty-four CF patients aged 6 to 30 years entered the study. Inclusion criteria comprised confirmed exocrine pancreatic insufficiency and bronchopulmonary exacerbation demanding antibiotic therapy. Exclusion criteria comprised: antibiotic therapy six weeks prior to the test, liver cirrhosis, diabetes mellitus, oxygen dependency, the use of systemic corticosteroids. In all enrolled CF subjects, 13C-labelled mixed triglyceride breath test (13C MTG-BT) was performed to assess lipid digestion and absorption, before and after antibiotic therapy. Sixteen subjects were treated intravenously with ceftazidime and amikacin, eight patients orally with ciprofloxacin. Cumulative percentage dose recovery (CPDR) was considered to reflect digestion and absorption of lipids. The values were expressed as means (medians). The values of CPDR before and after antibiotic therapy did not differ in the whole studied group [4.6(3.3) % vs. 5.7(5.3) %, p = 0.100] as well as in the subgroup receiving them intravenously [4.6(3.2) % vs. 5.7(5.3) %, p = 0.327] or in that with oral drug administration [4.6(3.4) % vs. 5.7(5.4) %, p = 0.167]. In conclusion, antibiotic therapy applied routinely in the course of pulmonary exacerbation in CF patients does not seem to result in an improvement of fat digestion and absorption.

Keywords: cystic fibrosis, antibiotic therapy, malabsorption, stable isotope breath test

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INTRODUCTION

Cystic fibrosis (CF) is an inflammatory and destructive disease with differentiated clinical expression. Bronchopulmonary disease is the major clinical manifestation which frequently demands antibiotic therapy. Available data suggests that such treatment applied in CF patients improves not only respiratory function but also nutritional status, which has been related to increased energy intake and decreased energy expenditure (Vic et al., 1997; Castro et al., 2002; Hankard et al., 2002; Béghin et al., 2003). Interestingly, antibiotic therapy in the CF mouse model resulted in the reduction of bacterial load of the small intestine, decreased intensity of intestinal inflammation and significant body mass gain. The effect was suggested to be linked to the improvement of intestinal digestion and absorption (Norkina et al., 2004a; 2004b). Therefore, we aimed in the present study to assess the influence of routinely applied antibiotic therapy in CF patients on fat digestion and absorption.

MATERIAL AND METHODS

The study comprised 24 CF patients (14 females and 10 males) (Table 1). Diagnosis of CF was based on history, clinical manifestation and increased sweat chloride concentrations and confirmed by the CFTR gene analysis. The genotypes of the studied patients were as follows: F508del/F508del (n = 11), F508del/CFTRdele2,3 (21 kb) (n = 2), F508del/R553X (n = 1), F508del/2143delT (n = 1), CFTRdele2,3 (21 kb)/CFTRdele2,3 (21 kb) (n = 1), 1717-1G-A/N1303K (n = 2), 1717-1G-A/N1303K (n = 1), F508del/1282X (n = 1), 1717-1G-A/N1303K (n = 1), F508del/unknown mutation (n = 2), unknown mutation/unknown mutation (n = 1).

Inclusion criteria for subjects comprised the willingness to participate in the study and exocrine pancreatic insufficiency (fecal elastase-1 concentration <100 μg/g and the presence of steatorrhea) (Walkowiak, 2004; Walkowiak et al., 2005). Exclusion criteria comprised: intravenous and oral antibiotic therapy six weeks prior to the test, liver cirrhosis, diabetes mellitus, oxygen dependency, the use of systemic corticosteroids.

In all enrolled CF subjects, 13C-labelled mixed triglyceride breath test (13C MTG-BT) was performed to assess lipid digestion and absorption, before and after antibiotic therapy (on the day preceding antibiotic therapy and on the last day of antibiotic administration). Sixteen patients were treated intravenously with ceftazidime and amikacin, in respective doses: 150–250 mg/kg per 24 h and 20–35 mg/kg per 24 h, the remaining eight subjects were given ciprofloxacin orally in a dose of 35–50 mg/
Sciences, Poland.

Bioethical Committee of Poznań University of Medical

STATISTICA 8.0. (StatSoft Inc. 2008).

210, 240, 270, 300, 330 and 360 minutes after test meal

mixed on a slice of bread. Breath samples were collect-

ted triglyceride with 0.25 g butter per kg body mass

days.

DISCUSSION

The values of CPDR before and after antibiotic thera-

y did not differ in the whole studied group or in either of

the subgroups differing in the mode of drug administra-

tion (Table 2).

RESULTS

The values of CPDR before and after antibiotic ther-

apy were set at

p

< 0.05. Statistical analysis was performed using

STATISTICA 8.0. (StatSoft Inc. 2008).

The protocol of the investigation was approved by the

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DISCUSSION

No significant influence of the antibiotic treatment ap-

plied on lipid digestion and absorption was observed in

the present study. To the best of our knowledge this is

the first study assessing such a relationship in humans in

a reliable way.

Reilly et al. (1999) made an attempt to assess the ef-

fect of an acute respiratory exacerbation on energy bal-

ance. The exacerbation was associated with a significant

reduction in energy intake. A trend towards lower total

energy expenditure was observed. No statistical differ-

ences in fat absorption and resting energy expenditure

as well as body mass and composition were documented.

However, the power of the study was rather low, as only

14 children were studied. The data on the effectiveness

of fat digestion and absorption (coefficient of fat ab-

sorption — CFA) were available for ten of them. CFA

was better during exacerbation in seven subjects and

worse in one patient. The authors attributed some CFA

changes to a better compliance with the pancreatic en-

zyme replacement therapy under supervision. However,

they finally concluded that the changes were negligible.

With the methodology applied in their study it is diffi-
cult to determine the reliability of the findings. Fat in-
take was assessed during exacerbation for 6–7 days and

for one weekend and two week days during the stable

period. Fecal fat output was calculated from a three-day

stool collection made during each period. Nevertheless,

the relationship between the timing of food intake and

stool collection as well as between stable period, antibi-

otic treatment and exacerbation was not precisely. Ac-
cording to the authors’ discussion they aimed to assess

the difference in CFA between well-being and exacerba-
tion. In contrast to their study, we assessed the effect of

both oral and intravenous antibiotic therapies. In addi-
tion, we determined fat assimilation on fixed days before

and after antibiotic treatment (reflecting in a reliable way

appropriate time points) to assess its potential influence

on the efficacy of digestion and absorption.

There is a strong association of bacterial infection

and inflammation in CF, at least in the airways. Accu-
mulating evidence indicates that susceptibility to inflam-
mation may be inherent to the tissue involved even in

the absence of specific pathogenic microbial colonization

(Muhlebach et al., 1999). The CFTR-null mouse model
does not express CFTR and is not expected to have

inherent inflammation due to protein misfolding. The

observed inflammation in the CF mouse intestine most

likely occurs as a result of altered luminal environment

with subsequent bacterial overgrowth (Norkina et al.,
2004a; 2004b). The body weight of CF mice at the end of

3-week antibiotic treatment (ciprofloxacin and met-
ronidazole) was significantly increased compared to un-
treated CF mice and not significantly different from that

of wild-type animals. The antibiot-
ic treatment had no effect on the

body mass of control wild-type

animals (Norkina et al., 2004b).

The obtained results suggest that

antibiotic therapy may have a sig-
nificant impact on digestion and

absorption in CF patients, there-

by influencing the energy balance
during treatment of pulmonary exacerba-
tions. The doses used in the

animal model are not easy to be
translated into a human study.

Moreover, ciprofloxacin doses

used in bronchopulmonary exacer-
bation in CF are well established.

Therefore, we applied its typical

Table 1. Basic epidemiological and clinical data of cystic fibrosis patients (n = 24)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
<th>Mean (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10–32</td>
<td>19.8 (18)</td>
</tr>
<tr>
<td>Body mass (Z-score)</td>
<td>–2.42–1.02</td>
<td>–0.89 (–0.94)</td>
</tr>
<tr>
<td>FEV1* (%)</td>
<td>55–105</td>
<td>78 (77)</td>
</tr>
<tr>
<td>Fecal elastase-1 (µg/g)</td>
<td>BDL–88</td>
<td>12 (7)</td>
</tr>
<tr>
<td>ALATc (U/l)</td>
<td>8–52</td>
<td>24.4 (24)</td>
</tr>
<tr>
<td>GGTPc (U/l)</td>
<td>6–98</td>
<td>18.9 (14)</td>
</tr>
</tbody>
</table>

*forced expiratory volume in 1 s; †below detection limit; ‡alanine transaminase (EC 2.6.1.2); †‡α-glutamyltransferase (EC 2.3.2.2)

13C MTG-BT was performed after overnight fast. Each of the studied subjects received 150 mg of 13C
mixed triglyceride with 0.25 g butter per kg body mass

mixed on a slice of bread. Breath samples were collect-
ed at baseline (fasting) and at 30, 60, 90, 120, 150, 180,
210, 240, 270, 300, 330 and 360 minutes after test meal

ingestion. The samples were analyzed with an IRIS 13C-

Analyser System (Wagner, Bremen, Germany). Cumula-
tive percentage dose recovery (CPDR) was considered to

reflect digestion and absorption of lipids.

Values are expressed as ranges, means and medians.

The statistical significance of differences in CPDR be-

fore and after antibiotic therapy was determined with the

use of Wilcoxon-rank test. The level of significance was

set at

p

< 0.05. Statistical analysis was performed using

STATISTICA 8.0. (StatSoft Inc. 2008).

The protocol of the investigation was approved by the

Bioethical Committee of Poznań University of Medical

Sciences, Poland.

Table 2. Lipid digestion and absorption in cystic fibrosis (CF) patients undergoing
antibiotic therapy based upon cumulative 13C dose recovery (CPDR)

<table>
<thead>
<tr>
<th>Studied group (n)</th>
<th>CPDR Parameter</th>
<th>Before</th>
<th>After</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF (24)</td>
<td>Mean (median)</td>
<td>4.6 (3.4)</td>
<td>5.8 (5.3)</td>
<td>( p = 0.100 )</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0–20.2</td>
<td>0.8–12.8</td>
<td></td>
</tr>
<tr>
<td>CF-IV* (16)</td>
<td>Mean (median)</td>
<td>4.6 (3.2)</td>
<td>5.7 (5.3)</td>
<td>( p = 0.327 )</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0–20.2</td>
<td>1.8–11.4</td>
<td></td>
</tr>
<tr>
<td>CF-PO** (8)</td>
<td>Mean (median)</td>
<td>4.7 (3.4)</td>
<td>5.7 (5.4)</td>
<td>( p = 0.167 )</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0–9.5</td>
<td>0–12.8</td>
<td></td>
</tr>
</tbody>
</table>

*CF-IV, subjects receiving antibiotics intravenously; **CF-PO, subjects receiving antibiotics orally
doses. Although intravenous therapy in such cases is more commonly used, we also assessed the effects of oral antibiotic administration on lipid assimilation. The observed changes did not reach the level of significance. However, a tendency towards an improvement of fat absorption was noted.

In conclusion, routinely applied antibiotic therapy in the course of pulmonary exacerbation in CF patients does not seem to result in an improvement of fat digestion and absorption.

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The authors declare no conflict of interest.

REFERENCES


