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Original article

Small intestinal absorption in patients with chronic obstructive pulmonary disease complicated by cor pulmonale – A pilot study

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SUMMARY

Background: Cor pulmonale is a common complication to Chronic Obstructive Pulmonary Disease (COPD), and may result in increased pressure in the inferior caval vein and stasis of the liver. The chronic pulmonary hypertension may lead to stasis in the veins from the small intestine and thereby compromise absorption of nutrients.

Aim: To investigate whether patients with pulmonary hypertension have reduced absorption capacity compared to COPD patients without cor pulmonale.

Methods: Absorption of D-xylose (25 g) and zinc (132 mg), administered as a single dose, was tested in 14 COPD patients, seven with and seven without cor pulmonale. The presence of cor pulmonale was determined by echocardiography. The concentration of D-xylose and zinc were measured in peripheral blood one, two and three hours after ingestion and used as markers of absorption. Furthermore, urine was collected for five hours to determine the amount of excreted D-xylose.

Results: No significant difference in absorption of D-xylose ($p = 0.28$) or zinc ($p = 0.51$) was found between the two groups. However, a trend towards a delay in D-xylose absorption, as assessed by time-to-peak concentration, was observed in patients with cor pulmonale ($p = 0.08$). There was no significant difference in the amount of excreted D-xylose in the urine between the groups ($p = 0.52$). No correlation was found between the tricuspid regurgitation gradient and the absorption of both test-markers ($rs = 0.34$ and $rs = -0.25$). Likewise, no correlations were found between the inferior caval pressure during the in- and expiration phases and the absorption of D-xylose ($rs = -0.09$ $rs = 0.23$) or zinc ($rs = -0.39$, $rs = -0.39$).

Conclusion: We found no indications that small intestinal absorption is affected in a clinically relevant degree in patients with cor pulmonale.

1. Introduction

Comorbidity is common in patients with chronic obstructive pulmonary disease (COPD), and weight loss and malnutrition are often seen in advanced COPD [1,2]. Weight loss, due to some combination of increased resting energy expenditure, potentially reduced small intestinal absorption capacity and lower food intake, increased age is associated with a poor prognosis, not least with regard to mortality, in this group of patients with severe COPD [3,4].

As a complication to more severe COPD, some patients develop cor pulmonale (CP) defined as changes in the morphology of the right ventricle and/or reduced function caused by pulmonary hypertension leading to liver stasis and potentially reduced venous flow from the upper intestine. If stasis develops in the bowel, this may reduce the absorption capacity further, which in turn will further compromise nutritional status in this vulnerable group of

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patients. This phenomenon is indicated by the finding of a reduced uptake of isotope-marked amino acids known to be only slightly extracted in the liver in patients with moderate to severe COPD compared to healthy controls [5]. The difference between intravenous and oral intake was used as an indicator of splanchnic extraction, and could be explained by hampered absorption or retention in the liver. We wanted to explore this finding further using two different compounds with different absorption kinetics in patients with severe COPD and cor pulmonale.

2. Materials and methods

2.1. Participants

The study was conducted April to July 2016. Patients were recruited from the pulmonary out-patient clinic, Hvidovre Hospital, and were eligible for the study if they fulfilled the following criteria: 1) A diagnosis of COPD [2], 2) 60+ years, 3) Clinically stable and 4) Unchanged medication for COPD for at least 6 months; and none of the following criteria: 1) Unable to understand Danish, 2) Other clinically important heart-disease than chronic right heart changes presumably due to lung disease, 3) Clinically significant gastro-intestinal or kidney disease and 4) Diabetes and/or treatment with systemic corticosteroids for the last 6 months. By using participants above 60 years old, we ensure a comparable test group by limiting outliers of young COPD-patients, with atypical COPD.

Written informed consent was obtained from all participants. Based on the echocardiographic findings, the participants were divided into two groups – COPD patients with CP and without CP.

Table 1
Baseline characteristics.

	Non-CP group Median (min–max)	CP-group Median (min–max)	p-value
Number of patients	7	7	–
Sex			
- Male	4	3	–
- Female	3	4	
Age (year)	71 (62–85)	63.5 (60–81)	0.25
BMI	24.2 (17.2–26,0)	28.7 (20.3–46.3)	0.06
Height (cm)	163.0 (152–180)	174.6 (160–186)	0.31
Weight (kg)	60 (42–83)	80 (65–141)	0.02
GFR (ml/min)	66 (43–83)	70 (55–70)	0.47
Zinc supplement			
- Yes	4	2	
- No	3	5	
FEV1 (L)	0.73 (0.40–1.34)	0.65 (0.51–1.20)	0.69
Tobacco Pack years	45 (0–60)	40 (30–52)	0.56
TR-gradient [mmHg]	32 (22–36)	45 (40–50)	0.004
Pacc [ms]	70 (55–129)	69 (54–80)	0.37
PRV [mmHg]	36 (25–49)	48 (48–53)	0.04

A total of 14 responders out of 45 invited patients were included and completed the trial. Overall the groups were comparable, though there was a significant difference in body weight ($p = 0.02$) and a borderline significant difference in BMI ($p = 0.06$).

2.2. Echocardiography

An two-dimensional echocardiography was performed using a Vivid E95 scanner (version BT12; GE Vingmed Ultrasound, Horten, Norway) according to international scientific recommendations [6,7]. The systolic pulmonary arterial pressure was determined by the sum of the peak right ventricle (RV)-right atrium (RA) gradient (TR-gradient) and the estimated RA pressure. All images were stored digitally for subsequent analysis. To minimize variability, all examinations and analyses were performed by the same experienced cardiologist.

2.3. D-xylose and zinc absorption test

After 12 h of fasting, voiding to empty the urine bladder, and baseline blood sampling, the patients were orally administered 25 G D-xylose dissolved in 250 ml water, 6 tablets (132 mg) zinc and a protein shake containing 42 G Bodylab Whey100 protein powder, 100 ml water and 100 ml whole milk. Blood sampling was repeated after one, two and three hours. After one and two hours, each patient was given 200 ml of water to ensure sufficient urine production. The total urine production during the study period (5 h) was collected. All blood and urine samples for measurements of D-xylose were stored at −80° and analysed using a D-xylose Assay Kit (D-(+)-Xylose X1500-500G) in a Pentra 400 analyzers (HORIBA ABX, 34184 Montpellier, Cedex 4 France). Plasma-zinc was analysed immediately by routine photometry.

In order to ensure the quality of the D-xylose Assay Kit, a standard curve were made ($r^2 = 0.996$). Furthermore, one blood sample was measured 10 times to test for the precision (range: 3.27–3.43 μmol/L).

The protein shake was administered to compensate for the 12 h of fasting prior to baseline blood sampling, also because the studied group of patients is likely to have a higher basal metabolic rate. The protein shake did not contain phytic acid and had an osmolality of 335 mOsmol/L.

2.4. Statistical analysis

The primary endpoint was the amount of absorbed D-xylose in plasma during the three-hour study period expressed as Area Under the Curve (AUC). The secondary endpoints were the amount of D-xylose excreted in the urine during a five-hour period and the total amount of zinc absorbed during a three-hour period expressed as AUC.

Table 2
Results of D-xylose uptake in COPD patients with and without cor pulmonale.

D-xylose	Non-CP group Median (min–max)		CP group Median (min–max)		p-value
AUC_{DX}	n = 7	8.65 (3.38–10.57)	n = 7	6.90 (4.27–8.32)	0.28
Baseline (mmol/L)	n = 7	0,04 (0.01–0.09)	n = 7	0,00 (0.00–0.05)	0.04
1. hour (mmol/L)	n = 7	3.60 (1.54–4.48)	n = 7	2.57 (0.60–3.23)	0.06
2. hours (mmol/L)	n = 7	3.39 (1.38–4.80)	n = 7	3.18 (2.12–3.88)	0.57
3. hours (mmol/L)	n = 7	3.23 (1.19–4.58)	n = 7	2.92 (1.79–4.34)	0.75
Time-to-peak (hours)	n = 7	1 (1–2)	n = 7	2 (1–3)	0.08
Urine (L)	n = 6	0.51 (0.23–0.82)	n = 4	0.39 (0.25–0.65)	0.39
DX-excreted (g)	n = 6	5.47 (1.27–10.16)	n = 4	4.41 (0.59–8.28)	0.52