ACHROMOBACTER XYLOSOXIDANS: FOLLOW-UP OF 20 PATIENTS WITH CHRONIC INFECTION

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Background: A. xylosoxidans (Ax) is capable of persistent infection of the respiratory tract of Cystic Fibrosis patients although its contribution to pulmonary decline in this population is not clear.

Aim: To evaluate pathogenic role of Ax studying lung function and nutritional status in CF patients with chronic Ax infection.

Methods: Data (FEV1, FVC, BMI, sputum and number of IV therapy) of 20 CF patients in our centre were studied retrospectively at the time of establishment of infection (T0), one year after T0 (T-1) and one year after T-1 and were then compared. Statistical analysis was performed by Student’s T test. Mean age of the 20 (13 females) patients was 14.5 (range 6–23.3) at T0.

Results: Lung function showed a slight decrease in the year before the acquisition of Ax both in FVC (91 ± 2.0 vs 86.1 ± 12.6 % predicted, p = 0.22) and FEV1 (84.4 ± 20.5 vs 79 ± 11.6 % predicted, p = 0.09), without reaching statistical significance. Respiratory data showed no deterioration in the year after infection: FVC (88.4 ± 18.1 vs 86.1 ± 12.6 % predicted, p = 0.47) and FEV1 (82.9 ± 23.2 vs 79 ± 11.6 % predicted, p = 0.26). However, the number of respiratory exacerbations was much higher in the year after colonisation as demonstrated by the i.v. treatment mean days per patient (12.1 ± 15.5 vs 3 ± 1.6 ± 5, p = 0.03).

Nutritional status remained unchanged during the study period as demonstrated by BMI of T1 vs T0 (18.1 ± 2.9 vs 18.1 ± 3.1 p = 0.07) and T0 vs T+1 (18.1 ± 3.1 vs 18.7 ± 2.9 p = 0.07).

Conclusion: The pathogenic role of chronic infection by Ax seems to be relevant in terms of therapeutic burden for patients in the short-term. A key factor would be monitoring the evolution of the patients chronically infected by Ax.

CYTOKINE PROFILES IN DIFFERENT MATRIXES (SERUM, SPUTUM AND EXHALATE) OF CYSTIC FIBROSIS PATIENTS

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The hallmarks of cystic fibrosis (CF) lung disease are bacterial infections by opportunistic pathogens and chronic inflammation, characterized by polymorphonuclear neutrophil predominance, progressing to obstructive lung disease and bronchiectasis.

High levels of sputum tumor necrosis factor (TNF)-α and interleukin (IL)-8 and serum IL-6 have been found in CF patients. The aim of this study was to analyze the major cytokines such as IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-10, interferon (IFN)-γ, the chemokines IL-8, monocyte chemoattractant protein-1 ( MCP-1) and the growth factors epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF) before and after antibiotic therapy in serum, sputum and exalate in order to clarify the process involved in the CF inflammation and to evaluate which cytokine or growth factor are the most important.

In the group that developed CFRD, baseline glucose concentration was increased indexes (HOMA and QUICKI).

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OXIDATIVE STATUS CHANGE IN CYSTIC FIBROSIS (CF) AND ORAL ADDITION WITH WHEY PROTEIN ISOLATE WITH HIGH CONTENT OF CYSTEINE: PRELIMINARY OBSERVATIONS

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Oxidative status has a role in the progressive lung damage in CF. Glutathione is the amino acid that gives to glutathione antioxidant status. The objective of this study is to reduce the oxidative status in CF with oral addition of whey protein isolate with high content of cysteine (PROther). We recruit CF patients older than 6 years, with a FEV1<70%, with a BMI <21 kg/m2 in adults and with a weight <-2SD centile in children. Oxidative status is estimated on a blood sample with different markers. The PROther test can measure oxidative stress and antioxidant status respectively. The study has started in May 2007 and will last for 12 months. Patients will be checked every three months. We have planned the enrolment of 50 patients at least. During the follow-up at every examination we will control oxidative status, clinical conditions (nutritional status, growth, lung function), compliance to the administration of PROther, alimentary intake and Quality of life. We recruited 32 patients still now. All cases show a pathological condition of oxidative status. Oxidative stress is increased in all patients and in 52% of cases is very serious. Antioxidant status is normal in 46% of cases and 14% show a high deficiency. Four patients deserted the study for a bad compliance to the administration of PROther not related to the product. In 6 patients we have done the first control after three months from the recruitment. All these cases show an improved oxidative status.

In conclusion, antibiotic therapy in CF patients could be monitored by cytokine profiles in sputum and serum, while exalate levels are too low to be useful. VEGF, a growth factor involved in tissue remodeling, needs further studies.

CYSTIC FIBROSIS RELATED DISEASES IS ANTICIPATED BY REDUCED INSULIN SECRETION DURING OGTT

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Diabetes in Cystic Fibrosis (CFRD) is increasingly common with advancing age because of a combination of insulin resistance and insulin secretory defects. Many patients are normoglycemic or even hypoglycemic after overnight fast, and there are repeated changes of glucose tolerance status from normal to diabetes and vice versa, for many years and for unclear reasons. These features render difficult the prediction of CFRD development.

The study aimed to detect predictive factors of CFRD development in patients routinely undergoing yearly Oral Glucose Tolerance Test (OGTT) evaluations. Starting from 2002, all patients followed at the CF Center in Milan aged >10 years and without established CFRD underwent OGTT yearly. Among those who received their first OGTT between 2002 and 2004 had developed definitive diabetes by April 2007. Each of them was matched with patients of same sex and age, who underwent an OGTT in the same month and year but did not develop CFRD (n = 21). Logistic regression, controlled for age, sex and follow-up time, was used to identify CFRD predictors among factors including glucose, insulin and c-peptide concentrations and area under the curve (AUC) during OGTT, insulin sensitivity indexes (HOMA and QUICKI).

In the group that developed CFRD, baseline glucose concentration was increased (92 ± 2.2 vs 72 ± 3 mg/dl, mean ± SEM, p = 0.034) whereas insulin and c-peptide concentrations were similar (5.4 ± 0.61 vs 7.8 ± 1.4 μU/ml, and 1.4 ± 0.11 vs 1.4 ± 0.2 ng/ml). Glucose (p = 0.010) and insulin AUCs (p = 0.030) were the most important
predictive variables, respectively directly and inversely related to CFRD development (pseudo R² for the model: 0.581, p < 0.001). Glycated hemoglobin and baseline glucose concentrations were directly related with outcome at univariate analysis whereas c-peptide concentrations were inversely related. In contrast, no relationship emerged between insulin-sensitivity indexes and outcome. Anthropometric (weight, height z-score, BMI) and pulmonary function indexes were also unrelated.

Conclusions: Defects in insulin secretion are determinants of subsequent CFRD development. The evaluation of insulin concentrations during OGTT may be helpful in CFRD prediction.

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Continued Subcutaneous Glucose Monitoring in Cystic Fibrosis (CF) Patients

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Objectives:

1. To study the effectiveness and reliability of the continuous monitoring of blood glucose (CGMS) in CF patients, to be able to identify at an early stage any condition of glycemic intolerance (IGT) or even diabetes.

2. To evaluate if the pre-diabetic treatment with insulin may lead to an improvement of CF pts glyco-metabolic control and of other clinical parameters such as BMI and FEV1.

Materials and Methods: We evaluated 10 CF pts (5 M and 5 F) with standard OGTT or altered baseline glycemic values. These pts had also shown a decrease in FEV1 and BMI values during the 2 years before the beginning of the study.

A microdialysis fiber was inserted subcutaneously into the periumbilical region and perfused with a buffer solution. Glucose concentrations in the dialysate were measured every 3 minutes by the glucose sensor over a 48-h period, during which 6 capillary blood samples were also collected before and after the 3 meals to evaluate the correlation between CGMS and traditional methods. The pts diagnosed for Cystic Fibrosis Related Diabetes (CFRD) as a result of monitoring, began insulinic therapy. After a follow-up period of 14 months glycaemia, FEV1 and BMI were evaluated again for each of them.

Results: Both the insertion of the fiber and the wearing of the device were well tolerated by the pts. Subcutaneous glucose levels were well correlated with capillary glucose measurements (r = 0.88, P < 0.001) over a wide range (45–250 mg/dl) for up to 48h. An analysis of 120 revelations showed a linear relationship between the CGMS and serial capillary blood glucose levels, and 98.33% of the data fell in the A and B regions of the error grid analysis. The results of CGMS for 48 hours confirmed the presence of IGT in all pts and identified early CFRD in 6 pts who had glycemic peaks > 200 mg/dl. After they were given insulinic therapy they showed an improvement of the glyco-metabolic control and an increment of 6% of BMI values during the 14 months of follow up. FEV1% values were unchanged.

Conclusions: The CGMS demonstrated high reliability and provided much more informations about glycemic excursions and glucose trends than the traditional diagnostic methods, making it possible to identify easier the CFRD in CF pts and begin as soon as possible an individual insulinic treatment.

Bile Duct Cholangiole Infection with Burkholderia cepacia complex in Cystic Fibrosis


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Objective:

To determine the effectiveness of FESS through the reduction of symptoms and the improvement of related clinical parameters in children and young adults with CF and sinusonal disease (SND).

Materials and methods: 12 children and young adults (15 years median age, range 7–38) with medically refractory SND were examined before and after FESS.

The main outcome measures were sinusonal symptoms, spirometric values (forced expiratory volume in 1 second, FEV1), and peak expiratory flux, PEF, and number of hospitalizations. The extent of polyposis was graded endoscopically and on computer tomography images. The sinusonal symptoms were inquired through a questionnaire pre- and postoperatively.

Results: The mean follow up time after surgery was 15.1 months. Postoperatively, polyp recurrence was seen in 5 pts of 12. Before surgery, bilateral nasal polyposis was an endoscopic finding in 11 pts of 12, and 50% of them had polypos occluding the middle meatus (grade 2 polyposis). 4 pts had undergone previous polyectomy, which was significant contributor to the survival of the patient.

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