Impact of insulin treatment of Cystic Fibrosis Related Diabetes (CFRD) on BMI and respiratory function

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Background
Cystic fibrosis related diabetes (CFRD) is one of the main complications of cystic fibrosis (CF), occurring in the 40-50% of CF patients, following inflammatory-degenerative damage of the pancreas. The secretion of altered pancreatic juice, more acid and rich in protein, leading to the obstruction of the pancreatic ducts, determines an increase of intraductal pressure, inflammation, amyloid deposition, fatty infiltration, pancreatic damage, and parenchymal atrophy. These alterations cause damages ranging from pancreatic insufficiency to insulin and glucagon deficiency. The onset of diabetes in CF patients worsens the patient’s overall clinical condition, affecting nutritional/weight status, pulmonary function, infectious exacerbations and short- and long-term microvascular complications. Moreover, CFRD causes neuropathy, gastropathy, retinopathy and diabetic nephropathy, similarly to other forms of diabetes

Patients and methods
We selected a sample of 17 insulin treated patients (Group T) and a sample of 17 controls with CF but normal glucose metabolism (Group C). Group T was in turn subdivided into overt diabetics patients and pre-diabetics patients (impaired glucose tolerance -IGT or indetermined glucose tolerance-INDET) on the basis of glycated hemoglobin and OGTT. For each patients in Group T an observation period was established starting with the first insulin administration and ending after 12 months. For Group C patients, a compatible year of observation was chosen to compare with the year of study of the first sample. Data regarding Body Mass Index (BMI), Forced Vital Capacity (FVC), Forced Expiratory Volume (FEV1) and Peak Expiratory Flow (PEF) were collected at time 0, and at time 12. The number of respiratory infectious episodes during the year of observation and during the preceeding year were recorded for Group T; the same parameters were studied in the sub-groups in the early stages of glucose alteration (IGT, INDET).

Results

Group T vs Group C

Group T BMI significantly increased after one year of insulin treatment (P < 0.001); Group C BMI after one year of observation was not significantly changed.

Figure 1-2: Group T and group C BMI and Delta BMI comparison

Figure 3: time 0-time 12 respiratory indexes comparison

Comparing the Delta values observed between 0 time vs 12 months time for the respiratory indexes, we confirmed the positive change in Group T vs Group C, significantly different only for PEF, the main effort-dependent respiratory index.

Figure 4: Group T- group C Delta respiratory indexes comparison

Pre-diabetics vs Diabetics

BMI showed a greater increase in diabetic vs prediabetic patients, with a p value close to significance (P=0.0547).

There were no statistically significant differences in respiratory indexes between the two subgroups after 12 months insulin treatment.

Evaluation of infectious episodes revealed a reduction of the number of episodes in treated patients more evident in those with pre-diabetes.

Figure 5: pre diabetes-diabetes Delta BMI comparison

Figure 6-7: pre diabetes-diabetes infectious episodes comparison

• BMI is lower in diabetic and prediabetics CF patients compared to CF patients with normal glucose metabolism and can improve after insulin treatment
• Insulin deficiency could contribute to aggravate the restrictive component of CF, through the inadequate development of the thoracic muscles necessary to perform a maximal forced expiration
• Insulin treatment of prediabetics could reduce the number of infectious episodes in CF patients
• Early insulin treatment of CF patients with diabetes or prediabetes could improve patients’ quality of life, reducing the number of admissions and comorbidity