Effect of different treatment regimens of CFRD on clinical status: A register study

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Objective: CFRD is the most common comorbidity in CF. The recommended treatment of CFRD is insulin, but other options are also in use. Only few data exist related to other treatment options. Therefore we analyzed the German CF-register for the documented therapy of CFRD.

Methods: Data from the German CF-register were used from patients with CFRD in 2010 in a retrospective observational study. Delta FEV1% and delta BMI-Z-score from 2 years before diagnosis of CFRD to year of diagnosis and from year of diagnosis to 2 years after were calculated for each treatment group (insulin, oral anti-diabetic drugs, no therapy with drugs) and compared using ANOVA-analysis.

Results: 798 patients with CFRD were documented in 2010. 51.9% were female; age (mean±SD) at diagnosis 23.8±9.3 years; CFRD duration 5.8±4.5 years. Treatment: 57.6% insulin, 9.8% oral anti-diabetic drugs, 2.1% with both and 30.2% without any drug treatment. The mean (±SD) CFRD duration in the non-treated patients was 5.0±4.0 years. ANOVA tests showed no differences between treatment groups regarding changes in FEV1% and BMI-Z-score from 2 years before to the year of diagnosis and delta FEV1 and delta BMI-Z-score from year of diagnosis to 2 years later.

Conclusions: The percentage of patients treated with oral anti-diabetic drugs is in the international published range. We know the weakness of retrospective studies. Nevertheless the numbers are high and the observation time is long. Our data point to the question if insulin is the only successful initial treatment of CFRD in all CF patients. At least a part of patients with CFRD seems to be well treated with other regimes.

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Detection of autonomic neuropathy in adult cystic fibrosis patients – It is not all about hyperglycaemia!

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Objectives: Autonomic dysregulation of the nervous system is known to exist in Cystic Fibrosis for reasons that are unclear. Hyperglycaemia has an added impact on the development of autonomic neuropathy (AN). We examined the prevalence of AN in 49 adult CF patients attending the All Wales Adult CF Centre.

Methods: We investigated autonomic abnormalities by undertaking Ewing’s test. Data of the baseline clinical characteristics of patients was studied.

Results: Of the 49 patients studied (31 male) 27 patients had Cystic Fibrosis Related Diabetes (CFRD), 8 had CF-impaired glucose tolerance (CFIGT) and 14 had CF with normal glucose tolerance (CFNGT). The mean FEV1 percentage predicted was 63% in CFRD, 44% in CFIGT and 54% in CFNGT groups. Evidence of autonomic neuropathy was prevalent in all 3 groups of patients regardless of their glycaemic status. Definite parasympathetic dysfunction was present in 71% and 29% of the CFRD and CFIGT groups respectively. 31% of patients with signs of early autonomic dysfunction were in the CFNGT group. A positive correlation was noted between age and abnormalities detected by Valsalva manoeuvre and deep breathing, p =0.001 and p =0.000 respectively.

Conclusion: Our data suggests that other factors such as inflammation, more prominent with increasing age, rather than glycaemic status exerts a greater influence on the development of AN in CF. It is possible that patients classified as having NGT in CF may have longstanding dysglycaemia which has not been uncovered by the conventional method of testing in CF and therefore contributing to the development of early AN.

Glucose tolerance in cystic fibrosis patients: The DIAMUCO study

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Objective: The aim of DIAMUCO study is to describe the natural history of the glucose tolerance (GT) and to identify predictive factors of the changes in GT in cystic fibrosis (CF) patients for a four-year period. We present the patients’ characteristics at inclusion.

Patients and Methods: We used a cross-sectional study design and included a total of 228 patients, 111 children (between 10 and 18 years) and 117 adults between 2009 and 2011. All patients had an annual screening. Patients were classified as having normal glucose tolerance (NGT), impaired glucose tolerance (IGT), or CF-related diabetes mellitus (CFRD) using the 2-h oral glucose tolerance test (OGTT).

Results: Mean age was 20.1±8.1 years old (min.: 9.7 and max.: 48.7) and mean weight z-score was -0.5±1.5. Of all, 56.5% were homozygous for the F508del-CFTR mutation. All the patients were pancreatic insufficient. 48.6% of patients were colonized with Pseudomonas. The mean FEV1 was 75.4±24.1%. None received antidiabetic therapy.

On OGTT, 67.5% patients were classified as NGT, 25.0% as IGT and 7.5% as CFRD. CFRD but not IGT have insulinopenia. Differences in weight z-score (-0.36 and -0.88); insulin 2-h (22.8 and 41.6); C peptide 2-h (2.34 and 3.54) and glycosylated haemoglobin (5.71 and 5.87) were significant between NGT vs. IGT together with CFRD groups respectively.

Conclusion: The prevalence of abnormal glucose tolerance in our CF population was 32.5%. IGT together with CFRD correlated with nutritional status while only CFRD correlated with age and was associated with insulinopenia. The four-year period study will provide information about natural evolution of GT and its predictive associated factors.

Determinants of bone loss in cystic fibrosis

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Objectives: Bone disease is now well described in cystic fibrosis adult patients. CF bone disease is multifactorial but many studies suggested the crucial role of inflammation and chronic pulmonary infection. The objectives of this study were to assess the prevalence of osteoporosis in a current adult CF population and to examine its relationship with infections and inflammation.

Methods: Patients were recruited in the adult CF Lyon centre and assessed in clinically stable period, later during an exacerbation, and finally 14 days after the end of antibiotic therapy. At each time points, we performed a clinical evaluation, lung function tests and biochemical tests: markers of inflammation (CRP, IL-6, TNFα), serum markers of bone turnover (serum CTX), and serum RANK-L and OPG. Absorptiometry and dorso-lumbar radiographs were also performed. We enrolled 56 patients (29 men, mean age of 26). Bone Mineral Density (BMD) values indicated osteopenia in 41% and osteoporosis in 14% of patients. We found in 2 patients 1 or 2 vertebral fractures on radiographs without any history of previous fracture. After antibiotic treatment, serum RANK-L and OPG were increased (+24%, p =0.08 and +13%, p =0.04 respectively), with a stable ratio. This increase was delayed in comparison to the increase of inflammation markers. Serum CTX were stable during pulmonary exacerbation. No significant correlation was found between serum inflammation markers, CTX and RANK-L.

Conclusion: In this study, bone disease seemed to be less severe than previously described. We found a mild increase of serum RANK-L levels, delayed compared with the pulmonary exacerbation, and independent from the bone resorption level.