MyCyFAPP Work Package 3: Development of the enzyme replacement predictive model

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Ethical review	Approved WMO
Status	Pending
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON46193

Source
ToetsingOnline

Brief title
MyCyFAPP PERT model

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Exocrine pancreas conditions

Synonym
Cystic Fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Kindergeneeskunde
Source(s) of monetary or material Support: Europese Unie;Horizon 2020

Intervention

Keyword: CF, Enzymes, Prediction, Therapy

Outcome measures

Primary outcome

The main study parameter is to assess, how much the final fat in stools

deviates from the normal concentration (6g/24h) after applying the ICF.

Secondary outcome

NA

Study description

Background summary

In the paediatric age, secondary malnutrition to Cystic Fibrosis (CF) has a negative impact in the patients* clinical evolution for its repercussion, among others, on the digestive and absorptive functions and the appetite. Maintaining an adequate nutritional status is an indispensable aspect of the CF treatment, since it directly affects the quality of life, the lung function and the survival.Pancreatic insufficient patients require supplementation with exogenous pancreatic enzyme therapy (PERT), with the aim to reduce the fecal losses of fat, protein and biliary acids and the deficit of fat-soluble vitamins associated to this disease. It is crucial that the administration of pancreatic extracts is in the correct dose and, moreover, adapted to each moment and each meal.

Study objective

It is a two-step approach study: The main objective in the first approach is to obtain a mathematical predictive model (MPM) adapted to each patient*s gastrointestinal conditions that calculates the optimal amount of enzymatic supplements for the optimal fat digestion of any food or meal. So for each patient an individual correction factor (ICF) will be obtained. Afterwards, in a second step, the objective is to validate the MPM by assessing how much the final fat in stools after applying the ICF deviates from the optimal value (<6g of fat/24h).
The MPM would be eventually implemented into a mobile APP, and together with an enzyme requirements database for different food products and meals digestion,

will be able to, through a calculation algorithm, predict the amount of PERD required for a specific meal, and taking into account individual needs for correction of the dose. This will allow the patients* self-management of this essential therapy regardless of time and place.

Study design

A prospective multicentre interventional study among paediatric CF patients in five reference paediatric CF units of the European Union: Valencia (Spain; Hospital Universitari i Politècnic La Fe), Madrid (Spain; Hospital Universitario Ramón y Cajal), Rotterdam (the Netherlands, Erasmus Medical Center), Leuven (Belgium; University Hospitals Gasthuisberg) and Milano (Italy; Ospedale Maggiore Policlínico).

The study consists of 3 parts
Part A:
- Follow a test diet with a fixed PERT dose (theoretical dose).
- Collection of feces that is marked by intake of color capsules.
- Keeping a nutritional diary.

After results of part A were analyzed, it was concluded that only one weekend was necessary in the coming stages, since in those patients that were compliant with the protocol, no differences were found between the two weekends.

Part B)
During the second part (February * March 2017), initially, patients would repeat the process with a different study dose, which would have been re-adjusted according to the results of faecal fat amount obtained during the first stage. However, due to the low degree of compliance with the test menu and with the stool collection schedule in stage A, results did not allow for a robust calculation system of the individual correction factor.
Therefore it was agreed upon conducting stage B with the theoretical optimal doses again including some amendments:
* Change in the test meals (more appealing)
* a *wash-out* period before and after the colorimetric markers intake
* Change in the stools collection schedule: to make it easier for the participants all the stools will be collected, in individual plastic bags instead of in one container.
All these updates are expected to increase adherence and compliance with the protocol and therefore, to enhance the quality of the samples and the accuracy of the analyses. After updated stage B, the model to calculate the individual correction factor will be constructed. It will be used to run the mathematical predictive model in Stage C.

Part C)
Finally, during the third stage (April * May 2017) patients will follow a semi ad-libitum diet while they complete a food record during one weekend. The diet

will consist of a set of foods that will be characterized for TOD. The PERT study doses will correspond to the dose predicted by the individual MPM. Dyed feces will again be collected, as described above. If the ICF can not be calculated by any means after the end of the present study, the model will be simplified and only the TOD will be used to predict the optimal dose of enzymatic supplement.

The 3 parts will take place during a period of 9 months.

Intervention

The interventions consist of following a test diet, the use of PERT (own capsules, test dose), the collection of feces that is marked by the intake of color capsules and keeping a nutritional diary. .

Study burden and risks

The burden of the study for participating patients consists of following a test menu (1 x 1 weekend for part B) and a semi free menu (1x 1 weekend for part C) adjusted to age and nutritional habits of the child and the collection of feces after taking color capsules to mark the feces corresponding to the menu. (can take up to 2 days after following the test menu before last colored feces are produced)

The participation in the present pilot study supposes no risk for the patient, provided that it does not include any additional medicament or treatment, but a slight change in the enzymatic supplements dose as compared to the current patterns.
Participation kan give more insight into the current use do food and PERT. The personal dose of PERT that we obtain in this study can lead to a decrease in abdominal pain, flatulence and diarrhea and may improve growth, nutritional status and quality of life in the longer term. We believe that the results of this study can contribute to improve the treatment both for participating patients and other patients with the same disease.

Contacts

Public
Selecteer

Wytemaweg 80
Rotterdam 3015 CN
NL
Scientific

Selecteer

Wytemaweg 80
Rotterdam 3015 CN
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Diagnosis of CF as evidenced by one or more clinical feature consistent with the CF phenotype or positive CF newborn screen AND one or more of the following criteria:
a) A documented sweat chloride * 60 mEq/L by quantitative pilocarpine iontophoresis (QPIT)
b) A documented genotype with two disease-causing mutations in the CFTR gene
2. Informed consent by parent or legal guardian; assent for children from age 12 years on
3. Having pancreatic insufficiency (stool elastase < 200 mcg/g stool) and using PERT
4. Age * 12 months and < 18 years at Screening visit
5. Stable clinical status at least two weeks before signing the informed consent.
6. Patients* capacity and willingness to fulfil the meal test and the faeces collection during the weekend.

Exclusion criteria

1. Acute infection associated with decreased appetite or fever at time of run-in visit
2. Acute abdominal pain necessitating an intervention at time of run-in visit
3. Severe cholestasis
4. FEV1 <40% for age, gender, weight and height.
5. Severe hypoalbuminemia (albumin in blood <2.5g/mL).
6. Hospitalisation or intravenous antibiotics <2 weeks before signing the informed consent.
7. Changes in the usual treatment (prokinetics, antiacids, H2 blockers and antibiotics) < 2

weeks before signing the informed consent.
8. Presence of alterations that, according to the investigator consideration, could jeopardise the safety of the patient.
9. Hypersensibility or adverse reactions to the enzymatic supplements.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	13-03-2016
Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO Date:	12-07-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24050
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL55266.078.16
OMON	NL-OMON24050