

INFORMED CONSENT FOR THE PARTICIPATION IN THE CLINICAL STUDY:

Vitamin D and  $\Omega$ 3 fatty acids role in the "honeymoon" of the child's Type 1 diabetes

Dear Parents,

you are asked to participate in a clinical study to assess whether the administration of vitamin D and Omega 3 can benefit in the first months / years from the onset of type 1 diabetes (T1D) in terms of honeymoon extension and increase of insulin sensitivity.

Type 1 diabetes is caused by the destruction of the  $\beta$  cells of the pancreatic islets, which produce insulin. Symptoms of diabetes (weight loss, increased diuresis and thirst) begin when most  $\beta$  cells are destroyed. Approximately 10-20% of  $\beta$  cells, often residual at the time of diagnosis. The preservation of these islets and their regeneration would be fundamental for the effective treatment of the disease.

After the initial clinical presentation of T1D, often begins a remission phase of the disease, called "honeymoon", during which the glycemic control is guaranteed with reduced doses of insulin (<0.5 U / kg / day). This phase, due to the restoration of an insulin production by  $\beta$  residual cells, is then destined to run out in variable times, often of months or sometimes years, with a slow increase in insulin requirements. In the proposed study we would like to try to stop this progressive loss of residual  $\beta$  cells, through the administration of vitamin D, and Omega 3 (EPA/DHA).

In the literature, some studies have shown that children with diabetes mellitus in childhood had taken fewer amounts of cod liver oil, rich in vitamin D and PUFA  $\Omega$ 3 (EPA, DHA) compared to healthy children. In addition, administration of cod liver oil in the first year of life would appear to be associated with a reduced risk of T1D appearing in the first 15 years. In addition,  $\Omega$ 3 fatty acids and vitamin D have anti-inflammatory and immunomodulatory properties, suggesting a protective role of  $\Omega$ 3 and / or vitamin D in type 1 diabetes. Maintaining a good ratio AA (arachidonic acid) / EPA (eicosapentanoic acid) < 3 would seem to guarantee the best anti-inflammatory effect.

In the present study we would like to investigate a possible protective role of vitamin D, and of the polyunsaturated fatty acids  $\Omega$ 3 (EPA/DHA) administered in your child in the first years of illness, focusing attention on insulin needs, metabolic parameters, the entity and the duration of the "honeymoon" remission period to evaluate possible benefits given by the current supplementation.

There are no side effects given by supplementation at the recommended dosages.

We ask for your consent to: We be able to carry out supplementation with Vitamin D and omega 3 in the first months of the onset; We carry out a food questionnaire in order to obtain the dietary intake of fatty acids, We collect data in the folder related to personal data and metabolic parameters (insulin needs, Hb Glycated, glycemic variability, etc) to make a comparison between before and after supplementation. The duration of the study is 12 months. Blood tests (coagulation, triglycerides, C-peptide, fasting glycaemia, vitaminemia D, ratio AA / EPA) are expected at the time of enrollment and at 3, 6, 12 months after supplementation. In particular, a comparison will be made before and after the supplementation at different times and the data will be compared with those of other children of the same age and sex not supplemented. A case-control study is conducted by Camillo Ricordi in Miami (Florida US) with vitamin D and omega 3 with high doses with the same intent (Poseidon study). You can refuse participation or abandon it at any time without compromising in any way the relationship with the doctors responsible for the study.

**INTEGRATION:**

Preliminary data from the study shows that the group undergoing omega $\omega$ 3 intake has lower insulin needs (U / Kg / die) and better glycosylated hemoglobin (HbA1c%) compared to the control group without omega $\omega$ 3 supplement, so it is requested to be able to integrate in the context of the aforementioned levies, also examinations aimed at the understanding of the "Determinants of persistent remission in the Child's Type 1 Diabetes". These tests consist of: i) Collection for HLA determination of exposure to type 1 diabetes, without preservation of DNA sample in addition to the duration of the study; ii) sampling for determining T $\omega$  lymphocyte subpolymers markers of activation or deactivation of beta $\omega$ cell oriented autoimmunity; iii) collection of incretins, or hormones secreted by the digestive system, capable of reducing glycemia; iv) quantitative dosage of omega $\omega$ 3 (EPA, DHA) and omega $\omega$ 6 (Arachidonic Acid).

Personal data will not be made available or accessible to third parties, with the exception of communication to the Health Authorities, required by law. The dissemination of data for scientific publications will take place exclusively anonymously.

**His rights**

As an interested party to the processing of personal data, you may at any time avail of the rights granted by Article 13, Law 675/1996, and more precisely: be informed with reference to the person in charge of processing, methods and purposes of processing;

- oppose, for legitimate reasons, the processing of personal data;
- oppose the processing of personal data for commercial purposes.
- obtain from the Data Processor without delay:
- communication in an understandable form of data concerning it
- cancellation of data processed in violation of the law

**Responsible for the study**

Prof. Gianni Bona, Department of Medical Sciences, Pediatrics, C.so Mazzini 18, University of Eastern Piedmont (Telephone 0321/3733350, fax: 0321/3733598).

**Possible risks**

Our study presents no risk. Coagulation alterations are possible for doses > 5g / day, not provided for this study. In addition a coagulation assay will be performed at different times as a control.

**For the minor**

Dear child, boyfriend,  
we ask you to help us to understand if vitamin D and omega 3 can be used to better control your disease in terms of longer duration of the honeymoon (the time when you will do little / no insulin therapy) and better control of your values of blood sugar. For this you will need to take every day of the capsules or the omega 3 syrup and once a week some drops of vitamin D. Vitamin D helps us to increase your immune system. Omega 3 fatty acids fight inflammation and hopefully can reduce what is present in your pancreas.

our clinical data (weight, height, etc) and your blood values (blood sugar, c $\omega$ peptide, etc) will be compared before and after supplementation and compared to other unsupported children.