Trial to Reduce IDDM in the Genetically at Risk

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TRIGR Family News

Editor's corner

Dear Study families,

Professor Olga Kordonouri, TRIGR Co-Investigator from Germany wrote our leading article about prevention of type 1 diabetes in those children who are genetically at risk. Last year she was appointed also as a member of the TRIGR International Executive Committee (IEC).
Associate professor Anne Ormisson, *TRIGR Estonian National Investigator* tells us about Estonia, especially the early times of the TRIGR study.
European Study Monitor Mila Hyytinen wrote an article about Vitamin D intake during early pregnancy. Alissa from Australia tells us the things she likes.

Matti Koski
Chief Editor

Is there a way to prevent type 1 diabetes in those children who are genetically at risk?

Ten years ago the full-scale international Trial to Reduce IDDM in Genetically at Risk (TRIGR) started enrolling babies from families with members affected by type 1 diabetes with the aim to give a definitive answer whether weaning to a highly hydrolyzed formula is capable of reducing the frequency of diabetes. The first results of a pilot study in 242 children from Finland (230 children), Estonia (8 children) and Sweden (4 children) were very promising, so that scientists in 15 countries worldwide decided to perform the largest ever international study on type 1 diabetes in childhood, the TRIGR. Since that time 2159 families, our TRIGR families, are participating in this unique trial worldwide. Meanwhile, the TRIGR babies have become active preschoolers and self-confident schoolchildren, friendships between families or even families and study staff have developed, and the TRIGR scientists look forward to their annual meetings.

Among the first International TRIGR meetings in Wroclaw, Poland April 2003

These meetings are very helpful for the TRIGR staff. Not only do they get to meet other TRIGR Study Group members from different countries, they receive information regarding the current status of the study, new information about TRIGR procedures, ideas or tips for study visits and have discussion and problem solving if there are any issues or concerns.

The TRIGR staff has not only to ask children to take part in the study. They too have tasted the Study Formula, tested their own blood sugar and sampled the glucose drink for the OGTTs.

Participating in the largest and longest study for the primary prevention of type 1 diabetes in childhood is not only a unique situation for every TRIGR family, but sometimes also a challenge.

For our families, study examinations have become a yearly routine. The phone call from the study team around the child's birthday reminds them it is time to coordinate the study visit. Most of our TRIGR children have had their first oral glucose tolerance test (6-year OGTT) and starting this spring, some are having their second (10-year OGTT). This test shows us how well your child absorbs and uses glucose.

Children have to fast for this test and that means no food for at least 10 hours. At the study visit they are given a glucose drink to drink within 5-10 minutes. The blood sugar is measured before the test begins and then again 120 minutes later. The OGTT must begin before 10 in the morning. For some children this means that they have to miss school for at least 3 hours on that day. TRIGR-staff do their best to be flexible and offer study visits on weekends, during school breaks and will do a home visit if necessary.

It is very important to get the information provided by the OGTT not only for the scientists doing the study but also for the kids and their families, who will get the results after the visit. HbA1c is a very reliable parameter reflecting the average blood glucose levels over the preceding 10-12 weeks under routine nutritional conditions, but the OGTT can reveal mild disturbances of the body's capacity to metabolize carbohydrates.

Parents are often anxious or concerned prior to the yearly study visits about getting the results of the blood tests and are relieved when the results are available. This is often the case in any study particularly with children at high risk for developing a disease. However, several studies have shown that participation in studies and contact with study specialists could help the parents to cope with their fears. In the population-based Finnish DIPP (Type 1 Diabetes Prediction and Prevention) Study, it was shown that parental stress was not increased by notification of antibody positivity or by participation in an interventional double-blinded, placebo-controlled trial. Although the authors postulated that the ethnic homogeneity and the good education level of the study population may have positively influenced the results, parental anxiety has not been significantly increased in other screening programmes for type 1 diabetes risk such as those conducted in the USA (PANDA study) or in Germany (BABYDIAB study).

On the other side we know that participants of screening programmes for type 1 diabetes can obviously profit from their active study participation. The analysis of the results from the American DAISY study showed that children who took part in the screening programme and developed type 1 diabetes suffered significantly less frequently from diabetic ketoacidosis, a potentially life-threatening acute complication of the disease, at the onset of diabetes that those from the general population. Moreover, these kids had significantly lower HbA1c values at diagnosis and needed less insulin up to 6 months later when compared to children outside of the screening programme. In other words, if diabetes can be detected early, the management of hyperglycaemia and the start of insulin treatment are easier. Early insulin treatment benefits the preservation of residual beta-cell function.

In addition to the regular study visits, the invitation to participate in a TRIGR-family meeting organized by the study staff is a highlight in a child's calendar. Kids like the activities organized by the TRIGR staff and parents enjoy the possibility to come together with other TRIGR families and exchange their experiences. TRIGR study coordinators, nurses and physicians are competing in getting new ideas how to surprise the growing kids and answer their curious questions like the examples above.

As a member of the big TRIGR family I am looking forward to continuing this special trial together with all of you. I know how important it is that more than 80% of the randomized TRIGR babies will remain in the study up to the age of 10 years. Taken into consideration the encouraging results from the 10-year-follow-up of the pilot TRIGR study, I am confident that in 5 years from now I will be proud not only to have been an active member of the TRIGR study, but also to have contributed to answer one

of the most important and unsolved questions in the history of medicine: is there an easy way to prevent type 1 diabetes in those children who are genetically at risk?

Professor Olga Kordonouri

Sources:

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Barker JM, Goehrig SH, Barriga K, Hoffman M, Slover R, Eisenbarth GS, Norris JM,
Klingensmith GJ, Rewers M; DAISY study. Clinical characteristics of children diagnosed with type 1 diabetes through intensive screening and follow-up. Diabetes Care 2004;27:1399-1404.

The Estonian Story

It was in January 1991 at one pediatric meeting in Helsinki, Prof. Hans K. Åkerblom asked if our Estonian research team would like to participate in a childhood diabetes prevention study. I was afraid that we could not possibly meet the demands of the study protocol. At that time, Estonia was seeking independence from the Soviet Union. Many Estonian families were without telephones at home, cars and lacked experience of taking part in research projects. There were some more serious obstacles, like no computers in hospitals and it was strongly forbidden to send any biological material (blood samples etc) to abroad. Childhood diabetes was, however, an increasing disease in Estonia at that time, although the incidence was three times less than in Finland. So our decision was – let`s try to overcome all difficulties and obstacles. We started to prepare for Estonia's participation in the study. After the first pilot study in Finland in 1992-1994, we were involved in the second pilot study in 1995-1999 together with Finland and Sweden. In 2002, Estonia began participation in the international TRIGR Study.

Estonian TRIGR team

After Estonia's independence from the Soviet Union in the autumn of 1991 everything developed very rapidly. Everyone was enthusiastic to start in a new and excited way to join an international research team. Families with type 1 diabetes were eager and thankful to participate in the study. Formula consignment was kept in a customs warehouse until our team managed to collect all the necessary permits from several authorities to deliver the formula parcels to the hospitals. From 2002 on, everything worked well. We were very proud that our first TRIGR child, born in the Tallinn maternity hospital on May 8, 2002 was the second baby enrolled in the TRIGR study. Our families actively participate in the TRIGR Study. They come to the study center for their annual visit and blood draw. The children like the small gifts given to them after the visit. The TRIGR team and families are like one big family. Every year, a meeting is organized in some nice place where families and study team members gather to discuss study matters but also other problems. The children have fun from playing together. TRIGR doctors are always ready to consult if there is a child who has some health issues. We are happy to see TRIGR children growing. We also keep in contact with the children who unfortunately have got diabetes during these years.

TRIGR is an excellent study, hopefully giving families useful information and advice. TRIGR international teams are friendly and work well together, no matter where in the world. An excellent example of the collaboration between teams and families is one Estonian boy, now 9-year-old, lived for two years in Belgium and for one year in USA. During that time his TRIGR visits were completed in the Rotterdam study centre and a USA study centre. I would like to thank and congratulate teams and families in all countries for taking part in this important study.

Anne Ormisson MD, PhD
Assoc. Prof. Emeritus
TRIGR Estonian National Investigator

Vitamin D intake during early pregnancy and type 1 diabetes risk in the offspring

Vitamin D deficiency during the fetal period or infancy is one of the implicated environmental risk factors for type 1 diabetes that may contribute to the increasing disease incidence. In the Finnish Maternity Cohort Study[1] no difference was observed in vitamin D intake during early pregnancy between mothers whose children later on developed type 1 diabetes (case mothers, n= 343), and mothers of non-diabetic healthy children (control mothers n=343). Mean 25(OH)D levels in case mothers (43.9 nmol/l) and control mothers (43.7 nmol/l) were not different. Among all mothers, as many as 481 (70.1%) were vitamin D deficient or insufficient. In this study vitamin D intake was assessed only during early pregnancy. However, supplementary vitamin D intake has been shown to be more frequent in later pregnancy. In Finland, all pregnant and lactating women are recommended to take daily 10 ug vitamin D from supplements. The recommended circulating concentration of 25(OH) vitamin D is 50-75 nmol/l.

More studies are needed to evaluate whether vitamin D deficiency during pregnancy is associated with type 1 diabetes risk in the child. A recent Norwegian study[2] reported an association between lower vitamin D concentrations in pregnant women and higher risk of type 1 diabetes in the offspring. However, in Norway cod liver oil which also comprises high concentrations of n-3 fatty acids is an important source of vitamin D.

Mila Hyytinen, European Study Monitor

References:

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2. *Sørensen I et al. Maternal serum levels of 25-hydroxy – vitamin D during pregnancy and risk of type 1 diabetes in the offspring. Diabetes 2012;61 (1): 175-178.*

Kid's corner

My name is Alissa. I am 6 years old. I live in Cootamundra, Canberra, New South Wales, Australia.

I like ice-cream, chocolate and lollies. My favourite toy is my big and small pigs. I like school and playing soccer. I like to eat meat. I like to play with animals. I like fruit and vegetables. I love swimming in summer. I love going to Nan and Pop's farm and my Uncle and Auntie's farm. My mum has Diabetes. Dad likes going to the beach. I like music and dancing. I also like watching TV. I made the front cover to the TRIGR Calendar this year! Hope you like it.