When is Screening for Type 1 Diabetes in Children Justified?

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Abstract

Background: Screening to find individuals with high risk of developing Type 1 diabetes (T1D) is needed to recruit participants for prevention trials and studies to preserve residual beta cell function at diagnosis. Screening may also decrease the incidence of diabetic keto-acidosis (DKA) at diagnosis. However, screening may cause anxiety and decrease quality of life for patients and their relatives. The aim of this study was to get a picture of how screening followed by development of T1D can be experienced.

Material and methods: Two boys, A and B, and a girl C were identified as high risk individuals via determination of autoantibodies. They developed T1D at the age of 7, 12 and 14 years. The parents of the boys, and the now adult female, gave their views.

Results: The mother of Boy A was very anxious during years before the T1D diagnosis, and got psychiatric problems with difficulties to work long periods. Both parents emphasized that they would have preferred not to know that their son might get T1D. Already within two years blood glucose balance of Boy B deteriorated, related to his difficulties to accept his disease. The woman C told that she for 6 years after diagnosis could not accept her disease.

Conclusions: Screening for risk of getting T1D sometimes have negative consequences. Screening is justified when trials are offered, and in certain populations when other methods to prevent DKA have failed. When screening otherwise is justified needs careful evaluation.

Keywords: Type 1 diabetes; Children; Screening; Keto-acidosis; C-peptide; Psychological problems

Introduction

The cause of Type 1 diabetes is unknown. Genetic predisposition is important [1] together with environmental factors [2]. The clinical manifestation of Type 1 diabetes is preceded by a long asymptomatic period, when autoantibodies in combination with genetic factors will predict the disease [3]. The process is illustrated in Figure 1, presented 1981, and later followed by more well-known diagrams [4]. As well as celiac disease nowadays is diagnosed based on existing autoantibodies, sometimes without any clinical symptoms or signs, it has been proposed that Type 1 diabetes could be said to have different stages [5], being clinically manifest in stage IV. Screening to find individuals in stage I-III is needed to recruit participants into prevention trials, studies that are extremely important [6,7]. Screening has also shown to decrease the risk for Diabetic Keto-Acidosis (DKA) at diagnosis, in high risk individuals motivated for participation in studies [8,9]. It has also been proposed that early diagnosis of T1D might preserve residual beta cell function [10], although the evidence for this can be questioned. Thus there are many good reasons to screen to find high risk individuals, but screening has also disadvantages. Very large populations have to be screened to find high risk individuals fulfilling criteria for participation in prevention trials [11] which consumes research resources. Unless the specificity is extremely high a large number of individuals may get worried by mistake, while a low sensitivity will give a false security. Another problem is the anxiety caused by informing patients, and especially parents that their child has a high risk of developing a serious disease [12]. This is especially serious if nothing is offered to try to prevent the disaster. In this study the aim was to get a picture of how the screening process and later development of Type 1 diabetes can be experienced.

Material and Methods

Two boys, A and B, identified with high genetic HLA risk as newborns were included in the Prodia study, a pilot trial using probiotics for prevention of T1D [13]. They developed autoantibodies...
within 24 months. BoyA got the diagnosis T1D at the age of 7 years, without symptoms. He was in partial remission for two years but then with gradually increasing insulin requirement. Boy B got his diagnosis at 12 years of age when he was screened for inclusion in a prevention trial. He was metabolically stable for two years, but thereafter with less good metabolic control than average patients. A woman, C, participated as a child in ABIS (All Babies in Southeast Sweden) [14]. She got multiple autoantibodies during childhood and she and her parents were informed about her high risk when she at the age of 10 was included in a substudy of ABIS on high risk individuals [15]. She was diagnosed with T1D two years later without symptoms. Nowadays she works as influencer and gives lectures in schools. The parents of the two boys have been interviewed about their opinion and experience of getting the early information on high risk if their child to get Type 1 diabetes an its consequences, an the young woman aged 20 years has described her opinion and experience.

Results

The mother of Boy A was very anxious for years before the T1D diagnosis, and got psychiatric problems with difficulties to work certain periods. Both parents expressed clearly that they would have preferred not to know for years that their son had high risk of getting T1D. Boy B was initially metabolically stable but when his blood glucose balance deteriorated he has had difficulties to accept his disease as he has never felt that the treatment saved him from disease symptoms. The woman C tells that she for long time could not at all accept her disease. She had felt completely healthy at diagnosis, could omit insulin doses and blood glucose still rarely passed > 8 mmol/l. Therefore she also felt different from other diabetic children who were suspicious on her "so called diabetes". It took 6 years for her to finally accept her disease and the hateful treatment.

Discussion

These three cases illustrate how early information about high risk of getting T1D can lead to quite negative consequences. The possible benefits of diagnosis during stage III, with multiple autoantibodies and gradual glucose intolerance but without symptoms, should be weighed against the negative psychological consequences of knowing the risk sometimes for many years. People not knowing so much about T1D do not seem to worry when participating in a prospective trial like ABIS [14]. In ABIS, a general population without any genetic predisposition to get T1D, we did not actively inform about laboratory results unless asked for according to the decision of the Research Ethics Review Board. The parents were told that they could get information and ask for their child’s risk, but less than one promille ever did. But studies where participants have been actively informed show that parents of high risk children get worried, and even more so in families with T1D members, probably as they know the disease and its negative consequences. Their anxiety lasts for years, and this burden, as well as the burden of getting the diabetes diagnosis a long time before clinical manifestation of symptoms, sometimes making it difficult for the child to accept the disease, has to be weighed against the value of screening.

It is expected that diagnosis in stage III, with multiple autoantibodies and abnormal glucose intolerance but no clinical symptoms or signs, means better beta cell function and beta cell preservation. However, diagnosis during this stage does not necessarily mean better beta cell function at a certain age than if the child had got the diagnosis later when stage IV starts, with clinical symptoms (Figure 2). Age-matched controls who get clinical disease (stage IV) at the same age as individuals diagnosed during stage III, just with abnormal OGTT, can be expected to have lower C-peptide because of a more pronounced disease process. Diagnosis in early stage III, means that the patient will get a heavy treatment with insulin, glucose monitoring, restrictions in life style, sometimes for years, when he/she otherwise would have lived as “healthy” with good quality of life. Thus the girl C in this study might have had years being “healthy”, without T1D, as she for several years could omit insulin without getting high blood glucose, and we do not know whether her C-peptide at 18 years of age was better because of diagnosis at 12 years of age, than if she had been diagnosed at age 15 with clinical symptoms. It is valuable to avoid severe keto-acidosis (DKA) at onset, but there are other possibilities to decrease incidence of DKA with information campaigns [16] without creating the negative consequences of screening. Furthermore DKA at diagnosis is far from completely avoided by screening [8], as there may even be a risk that screening gives a false security, while rapid progression may cause serious disease also in these individuals. Early screening is necessary and valuable to find participants for secondary prevention trials and then justified. The same may be true when there are safe, efficacious interventions to preserve beta cell function at diagnosis. Some parents may also want to get a sibling tested for autoantibodies, when there already is T1D in the family. No autoantibodies will then be calming, while autoantibodies just confirm what the parents already feared, without increasing their anxiety. This study has limitations: Three cases cannot be generalized to all others in the same position. Most probably there are many who do not worry very much about the high risk, and who may be grateful for the screening also after T1D diagnosis, as their child avoided serious symptoms and DKA at diagnosis. However, the two boys are not selected but are the only two cases of children in the Prodia study who developed T1D. The girls is one of few cases in the ABIS study where information was given before diagnosis.

Conclusions

Screening for risk of getting T1D sometimes have negative consequences. Screening is justified as part of research when trials are offered, and in certain populations when other methods to prevent
DKA have failed. When screening otherwise is justified needs careful evaluation.

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References