INFORMATION FOR PATIENTS WITH MATURITY-ONSET DIABETES OF THE YOUNG CAUSED BY A CHANGE IN THE HEPATIC NUCLEAR FACTOR 4 ALPHA GENE (HNF4A)

What is Hepatic Nuclear Factor 4 Alpha (HNF4A)?

HNF4A is a gene which acts as a switch which turns on and off other genes in the body. Changes in the *HNF4A* gene cause diabetes by reducing the amount of insulin that is produced by the pancreas. It allows insulin to be produced normally in early childhood but the amount of insulin produced reduces as you get older. HNF4A diabetes is one of a group of familial diabetes types called maturity onset diabetes of the young (MODY).

What can we say about diabetes caused by changes in HNF4A?

The diabetes caused by *HNF4A* tends to occur in childhood or early adulthood although some people may not be diagnosed until middle or old age. There is often an increasing need for treatment as you get older and so most affected individuals will go on to need either tablets or insulin to stop their blood glucose becoming too high. It is important to keep blood glucose controlled as (as with other types of diabetes) changes in the *HNF4A* gene can affect the small blood vessels in the eyes and the kidneys. This can be prevented if blood glucose levels are kept well controlled. Babies who inherit the *HNF4A* gene often have a high birth weight (over 4 KG) and may have low blood sugars early in life (neonatal hypoglycaemia) needing treatment. Therefore it is important to tell your doctor as soon as you are pregnant if you or your partner have HNF4A diabetes as this should alter how the pregnancy is monitored (more information about *HNF4A* and pregnancy can be found elsewhere on this website).

How is diabetes caused by HNF4A changes treated?

Individuals with HNF4A diabetes may be sensitive to the blood glucose lowering effects of a group of drugs called sulphonylureas. Sulphonylureas include drugs like Gliclazide, Glipizide, Glibenclamide and Tolbutamide, they work by stimulating the pancreas to produce insulin. Early after the diagnosis of diabetes control is often better with sulphonylurea tablet treatment than with insulin, though as diabetes progresses with time insulin may be needed. People with HNF4A diabetes who have been taking insulin from diagnosis of diabetes prior to genetic testing may be able to stop insulin and convert to sulphonylurea tablet treatment instead.

Does this result make any difference to how I should look after my diabetes?

No. One thing that our research shows is that keeping physically active and slim helps to keep the blood glucose controlled. This is no different from the advice we would give to anybody with diabetes.

Does this result mean that my diabetes is the same as my parent who had diabetes?

It is very likely that a change in the *HNF4A* gene was also present in one of your parents and would have caused them to have diabetes as well. This does not mean that your diabetes will be identical to theirs and there can be considerable variation within the family. In particular, just because a parent or other family member has had ill health resulting from their diabetes, this does not mean that you will have a similar problem, particularly if your blood glucose is well controlled.

How does this affect other family members?

Approximately half the children born to a parent with HNF4A diabetes will develop diabetes. This is due to the 50% chance of the affected gene being passed on from a parent at conception. Children and brothers and sisters of people with HNF4A diabetes have a high chance of developing diabetes if they have inherited the change in the HNF4A gene from their parent. They are also at risk of low sugars soon after birth so babies whose parents have *HNF4A* changes (whether it is the mother or father affected) should have their blood glucose tested within 24 hours of birth. Family members of a person known to have HNF4A diabetes should be aware of the symptoms of diabetes (such as thirst, passing a lot of urine or feeling very tired) and have their blood glucose measured if they are concerned that they may have it. Predictive genetic testing (to see if they have inherited the same change in the gene) is also possible – please see the section on predictive genetic testing on our website.

Further Information

Research Articles:

Clinical implications of a molecular genetic classification of monogenic beta cell diabetes. R Murphy, S Ellard, A Hattersley. Nature clinical practice endocrinology and metabolism 2008 Apr;4(4):200-213

Molecular genetics and phenotypic characteristics of MODY caused by hepatocyte nuclear factor 4alpha mutations in a large European collection. Pearson ER, Pruhova S, Tack CJ, Johansen A, Castleden HA, Lumb PJ, Wierzbicki AS, Clark PM, Lebl J, Pedersen O, Ellard S, Hansen T, Hattersley AT. Diabetologia. 2005 May;48(5):878-885

Macrosomia and hyperinsulinaemic hypoglycaemia in patients with heterozygous mutations in the HNF4A gene. Pearson ER, Boj SF, Steele AM, Barrett T, Stals K, Shield JP, Ellard S, Ferrer J, Hattersley AT. PLoS Med. 2007 Apr;4(4):e118.

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