'I don't feel like a diabetic any more': the impact of stopping insulin in patients with maturity onset diabetes of the young following genetic testing

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ABSTRACT – Hepatocyte nuclear factor-1α (HNF-1α) maturity onset diabetes of the young (MODY) is the commonest cause of monogenic diabetes but is frequently misdiagnosed as type 1 diabetes. The availability of genetic testing in MODY has improved diagnosis. Sulphonylurea sensitivity in HNF-1α patients means that those on insulin from diagnosis can transfer to sulphonylureas and may improve glycaemic control. To gain insight into the implications for patients of stopping insulin, in-depth interviews were conducted with eight HNF-1α patients transferred to sulphonylureas after a median of 20 years on insulin. Thematic content analysis highlighted four key themes:

- **fear, anxiety and excitement regarding stopping insulin, particularly among those who had been on insulin for many years or had never omitted insulin in the past**
- **improved lifestyle and self image accompanied by feelings of relief and 'increased normality'**
- **reflections on their time on insulin, including feelings of annoyance, particularly when the need for insulin treatment had been questioned at diagnosis**
- **difficulty 'letting go' of insulin treatment – some patients found it hard to believe that they no longer required injections as this conflicted with messages previously received from healthcare professionals.**

Transferring from insulin to sulphonylureas had a positive impact on lifestyle but support was needed for patients to adjust, many having grown up with the belief they would be on insulin for life.

KEY WORDS: genetic testing, hepatocyte nuclear factor-1α (HNF-1α), maturity onset diabetes of the young (MODY), sulphonylurea sensitivity

Key Points

Maturity onset diabetes of the young (MODY) accounts for 1–2% of diabetes but is frequently misdiagnosed as Type 1 diabetes, as the significance of family history is not appreciated

Patients with NHF-1α MODY are particularly sensitive to the hypoglycaemic effect of sulphonylureas

Transferring HNF-1α MODY patients on insulin to sulphonylureas had emotional consequences for those patients who believed they would need insulin for life

Transferring from insuliin to sulphonylureas had a positive impact on lifestyle and self image but support was needed to help patients adjust

Background

Maturity onset diabetes of the young (MODY) is an unusual genetic type of diabetes affecting 20,000 people in the UK. It is characterised by a young age of onset, autosomal dominant inheritance and non-insulin dependent diabetes.[1] However, MODY is often misdiagnosed as type 1 diabetes as it presents in young, slim adults with marked hyperglycaemia[2] and the significance of the family history is not appreciated.[3] Mutations in hepatocyte nuclear factor-1α (HNF-1α) account for 65% of UK MODY[4] and these patients are particularly sensitive to the hypoglycaemic effects of sulphonylureas (Table 1).[5] Isolated cases of patients with HNF-1α MODY transferring from insulin to sulphonylureas have previously been reported.[2,7] We have recently shown no deterioration in glycaemic control in eight patients with HNF-1α MODY following transfer from long-term insulin to sulphonylureas.[8] The aim of the study was to assess the emotional impact of stopping insulin in these patients, many of whom had previously been considered to have type 1 diabetes.

Methods

Eight patients with mutations in HNF-1α who had been treated with insulin from diagnosis were transferred to a sulphonylurea. They were aged 17–48 years (median 34 years), diagnosed between the ages of 8 and 17 years (median 14 years), and had been on insulin for 4–35 years (median 20 years).

Four patients had been on insulin for more than 27 years. After obtaining written consent, open-ended in-depth interviews were conducted with each patient to gain a detailed understanding of the impact on their life of stopping insulin. Pseudonyms were used to protect the individuals' identity. The interviews were audio-taped and later transcribed. The focus of the interviews was broad, encouraging patients to express their thoughts and experiences about stopping insulin. Further details of the methods used have been published elsewhere.[9]

Results

Thematic content analysis highlighted four key areas relating to the impact of stopping insulin and transferring to a sulphonylurea:

- fear, anxiety and excitement about the prospect of stopping insulin
- improved lifestyle and self image
- reflections regarding their time on insulin
- difficulty 'letting go' of insulin treatment.

Fear, anxiety and excitement about the prospect of stopping insulin

Many patients had been assumed to have type 1 diabetes and had consequently grown up with the belief that they would survive only with insulin injections. This resulted in real feelings of panic in one patient who had been on insulin for 35 years, reflecting her beliefs regarding the need for insulin based on her former experiences:[10]

'I'd say that I panicked when I stopped insulin. I remember that being a real worry and in the night time I was thinking "Will I be all right?" and really of course I would be, but the fact this has been drummed into you for such a long time. When I think about it now the panic doesn't really make sense but it was a real feeling then.'

In contrast, four of the patients said that they had omitted their insulin in the past and consequently had fewer concerns about the safety of stopping insulin treatment. All patients were excited about the possibility of stopping insulin but some indicated anxiety and uncertainty about whether tablets would sufficiently control their diabetes:

'I didn't really think it would work, I'd been so long on insulin [28 years]. *I was absolutely amazed that it worked.'*

In fact, six of the eight patients showed a median reduction (IQ range) of 0.8% (–0.1–1.8) ($p = 0.26$) in glycosylated haemoglobin after transfer to sulphonylureas.[8]

Improved lifestyle and self image

The patients who stopped insulin were generally well adjusted to their injections but were amazed at the impact of stopping

Table 1. Clinical features of the different maturity onset diabetes of the young (MODY) genes (adapted from Ref 6). The eight patients interviewed for this paper have the commonest type of MODY (MODY 3) due to mutations in the hepatocyte nuclear factor-1α (HNF1α) gene.

	Glucokinase (MODY 2)	HNF-1α (MODY 3)	HNF-4α (MODY 1)	HNF-1β (MODY 5)	IPF-1 (MODY 4)	NEUROD1 (MODY 6)
Chromosomal location	7p	12q	20q	17q	13q	2q
Frequency in a large UK series (%)	15	65	5	1	<1	0
Penetrance of mutations at age 40 (%)	Diabetes: 45 Impaired fasting glycaemia: 95	>90	>80	?>80	>80	70 (2 families)
Onset of hyperglycaemia	Early childhood (from birth)	Adolescence Early adulthood	Similar to HNF-1α	Similar to HNF-1α	Early adulthood	4th decade
Severity of hyperglycaemia	Mild with minor deterioration with age	Progressive May be severe	Progressive May be severe	Progressive May be severe	Limited data	Progressive
Microvascular complications	Rare	Frequent	Frequent	Retinopathy observed	Not known	Not known
Pathophysiology	Beta-cell dysfunction	Beta-cell dysfunction	Beta-cell dysfunction	Beta-cell dysfunction	Beta-cell dysfunction	Beta-cell dysfunction
Abnormality of glucose sensing?	Yes	No	No	No	No	No
Other phenotypic features	Reduced birth weight	Low renal threshold and sensitivity to sulphonylureas	Low plasma triglycerides	Predominant renal phenotype; cysts, renal failure	Pancreatic agenesis in homozygotes	Not known

IPF-1 = insulin promoter factor 1.

insulin on their lifestyle and daily routine. After 31 years on insulin, one patient felt that a burden had been lifted and life had become easier. Patients had been taking insulin 2–4 times a day but were initially commenced on a sulphonylurea once a day. This allowed them to 'relegate' diabetes to the back of their minds for part of the day:

'I can't describe how it feels. It's as though something has been lifted off my shoulders. It's such an easier day not having to think about taking your insulin... It's just a huge relief not being on insulin. I'm more relaxed because of not having to think about it.'

'It's good because you don't have to stick a needle in yourself, so it's better. You only take a tablet in the morning. The best thing about it is that you felt like you weren't a diabetic.'

Reflections regarding their time on insulin

One patient felt angry that she had been taking insulin unnecessarily, especially as she had questioned the need for insulin because of her knowledge of other family members' experiences.

One patient on insulin for 28 years had struggled with her glycaemic control on insulin. Control had improved on tablets, causing her to wonder if she would have developed the diabetes complications she suffered if she had been treated with tablets previously:

'I do wonder in terms of complications. I mean I've had laser treatment in both eyes and I have real problems with my feet. All those years I was on insulin and my control was always less than perfect, I do wonder if it might have been different if I could have been better controlled.'

Most patients were aware that the improved understanding of HNF-1α MODY and sulphonylurea sensitivity was fairly recent and were pleased to have the opportunity to try tablets now.

Difficulty 'letting go' of insulin treatment

Patients who had been treated with insulin for many years found it hard to believe they did not require injections; several indicated difficulty in completely 'letting go' of insulin. Another patient kept insulin at home even though she had not needed to use it in the seven months she had been taking sulphonylureas:

'I've only just stopped carrying around my pen with me ... for a long time I did still carry it in my bag and ... I suppose I was just very reluctant to completely leave it.'

Medical diagnosis carries meanings of illness that can shape an individual's identity and may be difficult to relinquish.[11] Those who had accepted the need for continual insulin treatment found it hard to believe it was not required; after many years on insulin it was months before they could fully accept that tablet treatment was effective.

Conclusions

Transferring from insulin to sulphonylureas had a dramatic, positive impact on all the patients.[12] Stopping insulin was a major decision with emotional consequences, and excitement mixed with anxiety was frequently expressed. Messages previously received about the importance of insulin treatment and the length of time on insulin influenced patients' responses. In some cases the emotional adjustment to tablet treatment took months, during which process patients required support. Stopping insulin injections led to positive alterations in self perception despite taking sulphonylurea tablets. These patients are likely to need insulin again at some stage in the future due to the progressive nature of HNF-1α and they will be followed up.

These findings have implications for others who may be able to stop their insulin after many years, such as those undergoing islet cell transplantation.[13]

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