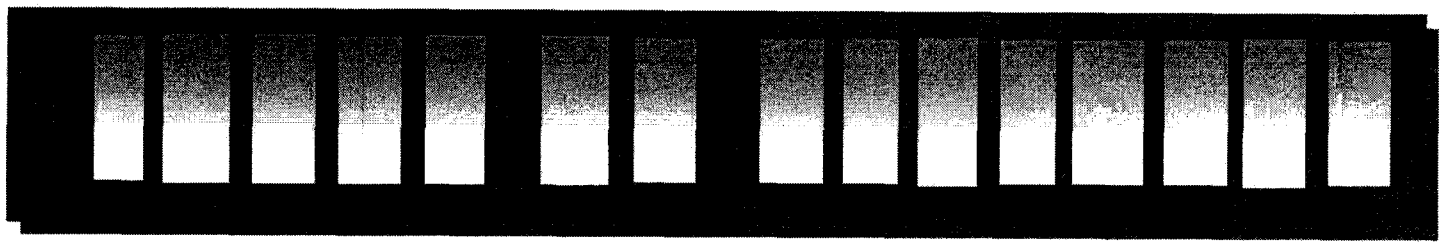
Scottish Executive Health Department Chief Scientist Office



USING THERAPEUTIC RESPONSE TO INVESTIGATE THE AETIOLOGY OF TYPE 2 DIABETES: PILOT STUDY

Researchers

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Aim

A pilot study to determine how well someone's initial response to sulphonylureas (a drug class used to treat type 2 diabetes) when prescribed in general practice predicts their subsequent response on re-challenge.

Project Outline/Methodology

Clinically there can be considerable variation in how much someone's blood glucose falls in response to treatment with oral sulphonylurea treatment. The overall hypothesis for this study is that people who respond well to sulphonylureas have a different cause for their diabetes than people who respond poorly. We therefore planned to identify people who had been treated by their GP with sulphonylurea treatment in the previous year and who had had a particularly good or poor response. Prior to this, we established a pilot study to see whether someone's initial response when treated by the GP is reproducible on careful re-challenge with sulphonylureas. In this pilot phase we recruited 20 people on the basis of their initial blood sugar response. Each participant stopped their sulphonylurea for 6 weeks, and then had a sulphonylurea, gliclazide, reintroduced according to a standardised protocol. To assess reliabilty of tablet taking, a pill container was used that logged when the container was opened. Blood was taken at each visit. In addition, each patient had an assessment to see how well their pancreas responded to injected glucose (sugar) and tolbutamide (a sulphonylurea).

Key Results

Some people responded consistently well and others consistently poorly to sulphonylureas suggesting that these people are intrinsically different in how their diabetes responds to treatment. However, for the majority the initial response to GP initiated treatment was not consistently reproduced on a careful re-challenge. This suggests that their initial response is strongly influenced by other factors at the time of the initial sulphonylurea prescription that could not be assessed, such as someone making lifestyle changes at the same time as starting the drug. When looking at the response to gliclazide during the trial, people with a greater reduction in blood sugar were more centrally obese (had a bigger waist circumference relative to their hip size) and their pancreas was more able to secrete insulin in response to sugar.

Conclusions

Initial response to GP initiated treatment cannot be used to identify people who consistently respond well or poorly to sulphonylureas and an alternative approach is required. In a carefully monitored prospective study, people with more central adiposity and greater pancreatic reserve are more able to respond to sulphonylureas.

What does this study add to the field?

No previous studies have looked to see how reproducible someone's response to diabetes medications is. This study has shown that for a given individual the response to sulphonylureas when given in general practice does not simply reflect that person's ability to respond to the drug, but is influenced by other factors.

Implications for Practice or Policy

Sulphonylurea treatments tend to be considered more for non-overweight people, yet this study suggests that a greater blood sugar reduction is seen in the more overweight, and therefore sulphonylureas should not be avoided in the overweight, although weight gain often seen with these tablets is clearly important to consider.

Where to next?

To determine what factors affect intrinsic response to diabetes drugs, a prospective study is required where people with type 2 diabetes are given diabetes treatment in a carefully controlled study to minimise other environmental factors that will alter response.

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