The Prevalence of Chlorpropamide Alcohol Flushing in Non-Insulin Dependent Diabetics

Dear Sir,

Leslie and Pyke have suggested that the chlorpropamide alcohol flush is a dominantly inherited trait in non-insulin dependent diabetics which is associated with a low prevalence of severe retinopathy [1, 2],

Köbberling and his colleagues have recently been unable to confirm these observations [3]. They found that the chlorpropamide alcohol flush was not specific for non-insulin dependent diabetics and they were unable to find any differences in the distribution of the chlorpropamide alcohol flush in diabetics with or without a family history of the disease.

We have performed the chlorpropamide alcohol flush test in 108 patients using 40 ml of sherry 12 h after 250 mg of chlorpropamide. The presence of a chlorpropamide alcohol flush was judged using facial temperature measurement, the feeling of a facial warmth by the patient or the appearance of a facial flush. The presence or absence of retinopathy was made following an examination through dilated pupils by an ophthalmologist who was unaware of the chlorpropamide alcohol flush status.

Table 1. The prevalence of chlorpropamide alcohol flushing in non-insulin dependent diabetics

	Chlorpropamide alcohol flush	
	Positive	Negative
No. (%)	35 (33%)	73 (67%)
Female	26 (74%)	30 (41%)
Family history	17 (49%)	30 (41%)
Years of diabetes (mean $\pm$ SEM)	6.5 $\pm$ 0.8	7.4 $\pm$ 0.7
<i>Retinopathy</i>		
Negative	19 (61%)	43 (70%)
Less than five lesions	6 (18%)	14 (22%)
More than five lesions without significant loss of visual acuity	4 (12%)	2 (3%)
More than five lesions with significant loss (more than 50%) of visual acuity	3 (8%)	3 (5%)

A chlorpropamide alcohol flush occurred in 35 (33%) of non-insulin dependent diabetics (Table 1). A positive test was obtained in 43% of the patients exhibiting a chlorpropamide alcohol flush when sherry was given alone without the previous administration of chlorpropamide. There was no difference in the prevalence of a family history of diabetes or background retinopathy in the two groups. There was however a greater percentage of patients with more than five exudates and/or haemorrhage in the chlorpropamide alcohol flush-positive patients (Table 1). Interestingly, there was an increased number of females in the chlorpropamide alcohol flush-positive group ($p < 0.025$).

In our experiment the chlorpropamide alcohol flush test, therefore, is not very specific since a sizeable proportion of chlorpropamide alcohol flush-positive patients showed a positive response to alcohol alone. The prevalence of chlorpropamide alcohol flush-positive tests was not increased in patients with a family history of diabetes nor did we find evidence that chlorpropamide alcohol flush-positive patients are protected against severe retinopathy.

Our conclusions therefore agree with Köbberling et al. [3] in that the chlorpropamide alcohol flush test is unsuitable for genetic counselling and should not be used for the prognostic labelling of non-insulin dependent diabetic patients.

References

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2. Leslie RDG, Barnett AH, Pyke DA (1979) Chlorpropamide alcohol flushing in diabetic retinopathy. *Lancet* I: 997–999
3. Köbberling J, Bengsch N, Bruggeboes B, Schwarck H, Tillil H, Weber M (1980) The chlorpropamide alcohol flush. *Diabetologia* 19: 359–363

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Delayed Menarche as an Indicator of a Prediabetic State

Dear Sir,

Bailey and Ahmed-Sorour [1] have recently demonstrated that normal ovarian endocrine function plays an important role in the long-term maintenance of glucose homeostasis. There are also reports that oestrogen increases the sensitivity of adipose tissue and skeletal muscle to the action of insulin [2]. This may explain why ovariectomy increases the incidence and severity of experimental diabetes in female animals [3].

These observations also may be relevant to certain clinical findings concerning ovarian function in diabetic women. We have found that the age of onset of menarche in 986 women in whom

diabetes appeared after the age of 20 years occurred significantly later ($p < 0.01$) than in 1952 non-diabetic subjects (14.2 ± 1.9 versus 12.8 ± 1.2 years) [4]. The number of diabetic women who had menarche at or after the age of 15 years (29%) was higher than that found in non-diabetic women (6%) (Table 1). The reason for this is difficult to define and requires further investigation. Disturbances in prolactin secretion [5–7] or the secretion of ovarian hormones [1] could provide an explanation.

Our data suggest that when menarche is delayed after the age of 15 years, there may be a predisposition for diabetes. Such patients need periodic investigation.