Letters to the Editor

Influence of mebendazole administration on metabolic control in Type 1 (insulin-dependent) diabetic patients

Dear Sir,

It has recently been suggested that in Type 1 (insulin-dependent) diabetes, mebendazole improves glycaemic control and increases C-peptide secretion [1]. We have conducted a study in 12 poorly controlled Type 1 diabetic patients (Table 1). Mebendazole (Vermox, Janssen Pharmaceuticals, Beerse, Belgium) was administered orally at a dose of 200 mg/day for 3 days, and, thereafter, at 100 mg/day throughout the 30-day study period. All patients continued their usual diet, ranging from 1500 to 2000 calories/day (carbohydrate 50%, fat 30%, protein 20%) and their usual mixtures of short- and long-acting insulin.

At the beginning of the study and at the end of the 30-day treatment period, after an overnight fast, all patients attended the outpatient clinic for measurement of glycaemic profiles, 24-h urinary glucose, total glycosylated haemoglobin (HbA_{1c}) and C-peptide levels. The results are shown in Table 1.

Although there was a trend towards a decrease in blood glucose levels at day 30, this decrease was not significant. Mean HbA_{1c} levels did not decrease and no changes in 24-h urinary glucose output were demonstrated. Fasting and post-prandial C-peptide levels did not change following the 30-day treatment period.

In a sub-group of patients ($n=5$), who demonstrated C-peptide secretion (fasting C-peptide ≥ 0.15 pmol/ml and post-prandial C-peptide ≥ 0.30 pmol/ml), similar non-significant decreases in both mean fasting and post-prandial plasma glucose levels were observed.

Although Lefebvre and Luyckx [2] demonstrated an imidazole-related increase in insulin secretion in dogs in 1971 and Kameda et al. [3] postulated that the imidazole derivative DG 5128 could stimulate glucose-induced insulin secretion in 1982, the recent report by Caprio et al. [1] was the first to outline some clinical effects of this compound in diabetes. However, our results do not confirm the findings of their preliminary study.

Yours sincerely,
L. F. Van Gaal and I. H. De Leeuw

Table 1. Results of the administration of mebendazole before and after 30 days of treatment in 12 Type 1 diabetic patients

	Before mebendazole treatment	30 days after mebendazole treatment
Age (years)	48 $\pm$ 12	
Duration of diabetes (years)	7 $\pm$ 4	
Weight (kg)	66 $\pm$ 9	66 $\pm$ 9
Daily insulin dose (U/day)	55 $\pm$ 37	53 $\pm$ 39
Fasting blood glucose (mmol/l)	12.3 $\pm$ 4.3	10.0 $\pm$ 5.8
Post-prandial glycaemia (mmol/l)	16.2 $\pm$ 3.7	13.8 $\pm$ 5.7
Mean blood glucose (mmol/l)	12.2 $\pm$ 3.2	10.4 $\pm$ 5.1
Fasting C-peptide (pmol/ml)	0.20 $\pm$ 0.18	0.23 $\pm$ 0.15
Post-prandial C-peptide (pmol/ml)	0.60 $\pm$ 0.45	0.45 $\pm$ 0.38
HbA _{1c} (%) ^a	10.7 $\pm$ 1.3	10.6 $\pm$ 2.6
24-h-urinary glucose (g/24 h)	29.3 $\pm$ 23.8	24.9 $\pm$ 24.2

Results expressed as means $\pm$ SD. ^a Normal range for HbA_{1c}: 5–7%

References

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2. Lefebvre P, Luyckx A (1971) Effets de l'imidazole et de deux de ses dérivés sur la sécrétion d'insuline du chien anesthésié. *CR Seances Acad Sci [III]* 272: 498–500
3. Kameda K, Ono S, Koyama I, Abiko Y (1982) Insulin releasing action of 2-[2-(4,5-dihydro-1H-imidazol-2-yl)-1-phenylethyl] pyridine dihydrochloride sesquihydrate (DG-5128), a new, orally effective hypoglycaemic agent. *Acta Endocrinol (Copenh)* 99: 410–415

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Physical activity and prevalence of diabetes

Dear Sir,

In a recent article in *Diabetologia*, Taylor et al. presented age-standardised prevalence of diabetes in Fiji Indians, this being very similar in rural (12.1%) and urban (12.9%) men [1, Table 1]. However, in their Table 2 where prevalence of diabetes is given, in addition, by two grades of activity level, the prevalence rates are substantially higher in rural men (27.9 and 11.1% versus 15.6 and 8.0%, respectively). I realise that the method of age adjustment is different in the two Tables but cannot see that this explains the discrepancy. I suspect the figures for rural men in Table 2 are incorrect and wonder if this affects the statistics of Table 4.

Assuming Table 1 to be correct, then the data for Melanesians do support the authors' view that 'activity' may be related to prevalence of diabetes. However, the Indian data are not in accord with this notion. Thus, age-adjusted prevalence is (see above) very similar in rural and urban men despite very large differences in the proportions in sedentary/light and moderate/heavy activity groups. As the urban men, 73% of whom fall into the sedentary/light category, are also, on average, fatter, what is protecting them from even more diabetes if the authors' view is correct?

Yours sincerely,
R. J. Jarrett

References

1. Taylor R, Ram P, Zimmet P, Raper LR, Ringrose R (1984) Physical activity and prevalence of diabetes in Melanesian and Indian men in Fiji. *Diabetologia* 27: 578–582

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Reply from the author

Dear Sir,

Thank you for the opportunity to reply to Professor Jarrett's astute observations on our paper entitled "Physical activity and prevalence of diabetes ..." (*Diabetologia* (1984) 27: 578-582).

The age-standardized diabetes prevalence rates presented in Table 1 of our paper are standardized onto the combined Melanesian and Indian age-structure from the 1978 Fiji Census, using the direct method. Thus these rates enable inter-ethnic comparisons, and allow estimation of the magnitude of the problem of diabetes in Fiji.

The rates of diabetes presented in Table 2 are standardized onto the age structure of each of the ethnic/geographic survey groups separately - i.e. rural Indian males, urban Indian males, rural Melanesian males and urban Melanesian males. Thus these age-standardized rates enable intra-group comparisons between the two physical activity categories *only*, since the age structures of the above mentioned subgroups vary. The data in Table 2 of our paper is correct, and a more extensive summary of the information on Fiji Melanesian and Indian males is set out below (Table 1a). Calculations using the Mantel-Haenzel method also yield similar findings for the relative risk of diabetes between the two major exercise categories for each race (Table 1b).

Neither the adjusted diabetes prevalence data from Table 1 or Table 2 of our paper affects that presented in Table 4, since the statistics in the latter table were produced directly from the raw data using the multivariate stratification method.

The thrust of our findings are that differences in diabetes prevalence between sedentary/light and moderate/heavy physical exercise categories are present in all male geo-ethnic groups in the Fiji survey, and are not removed by adjusting for possible confounding variables such as age and obesity.

Why is there no urban-rural differential in diabetes prevalence in the male Fiji Indian population despite urban-rural differences in obesity and physical activity status, and despite intragroup relationships between physical activity and diabetes prevalence? Indeed! Per-

haps there are sufficient environmental stimuli (although of different magnitude) operating in both urban and rural areas for most of the genetically predisposed to develop diabetes; or perhaps there are overriding common but unmeasured diabetogenic environmental factors (? components of diet) operating in both populations.

All of the answers are not yet clear, but our study indicates the need to include physical activity as an independent variable in future epidemiological studies of non-insulin dependent diabetes.

Yours sincerely,

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Table 1b. Relative risk for diabetes between the two major exercise categories adjusted for age and urban/rural residence in Fiji Melanesian and Indian males

	Relative risk for diabetes sedentary light : moderate/heavy	X ²	p
<i>Fijians</i>			
Adjusted for age	2.6	3.66	ns
Adjusted for age and urban/rural residence	1.9	2.00	ns
<i>Indians</i>			
Adjusted for age	2.0	5.86	<0.05
Adjusted for age and urban/rural residence	2.3	5.26	<0.05

Relative risk calculated according to the method of Mantel and Haenzel

Table 1a. Diabetes prevalence in Fiji Melanesian and Indian males by geographic and physical activity category

	Physical activity category					
	Sedentary/ light	Moderate/ heavy	Total	Sedentary/ light	Moderate/ heavy	Total
	<i>Rural Indian males</i>			<i>Rural Melanesian males</i>		
Diabetes prevalence number	8/36	19/178	27/214	1/22	3/220	4/242
%	22.2	10.7	12.6	4.5	1.4	1.7
Age-standardized diabetes prevalence %	27.9	11.1	12.6	12.8	1.5	1.7
X ² = 5.1, p < 0.05				X ² = 12.8, p < 0.01		
(Age-standardized by the direct method to the age structure of rural Indian male survey sample)				(Age-standardized by the direct method to the age structure of the rural Melanesian male survey sample)		
	<i>Urban Indian males</i>			<i>Urban Melanesian males</i>		
Diabetes prevalence Number	47/280	7/104	54/384	14/198	5/203	19/401
%	16.8	6.7	14.1	7.1	2.5	4.7
Age standardized diabetes prevalence %	15.6	8.0	14.1	5.7	3.4	4.7
X ² = 3.5, p: not significant				X ² = 1.18, p: not significant		
(Age standardized by the direct method to the age structure of the urban Indian male survey sample)				(Age-standardized by the direct method to the age structure of the urban Melanesian male survey sample)		