Table 1 Anthropometric and metabolic parameters

Parameter	Rimonabant group						Placebo group					
	Baseline (V1)	After 6/12 rimonabant (V2)	After 3/12 metformin (V3)	V1/V2 (*P* value)	V2–V3 (*P* value)	V1–V3 (*P* value)	Baseline (V1)	After 6/12 placebo (V2)	After 3/12 metformin (V3)	V1/V2 (*P* value)	V2–V3 (*P* value)	V1–V3 (*P* value)
Weight (kg)	104.41 ± 9.72	93.68 ± 12.11	95.03 ± 11.84	<0.01	0.10	<0.01	96.51 ± 15.27	98.11 ± 15.40	97.11 ± 15.27	0.04	0.13	0.13
Body mass index (kg/m^2)	33.22 ± 2.57	29.74 ± 3.09	30.18 ± 3.11	<0.01	0.09	<0.01	31.47 ± 2.96	32.04 ± 3.45	31.70 ± 3.35	0.06	0.52	0.47
Alanine aminotransferase (U/l)	30.8 ± 8.9	20.0 ± 5.3	15.7 ± 0.4	<0.01	0.10	<0.01	34.0 ± 9.9	33.3 ± 18.1	16.8 ± 5.4	0.92	0.02	0.11
Glucose (mmol/l)	6.5 ± 0.36	5.9 ± 0.67	6.0 ± 0.79	0.02	0.35	0.13	6.2 ± 0.54	6.1 ± 0.63	5.7 ± 0.41	0.52	0.11	0.01
HOMA-IR	2.30 ± 0.76	1.68 ± 0.97	2.20 ± 1.35	0.03	0.44	0.58	2.00 ± 0.66	1.73 ± 1.02	1.40 ± 0.82	0.49	0.83	0.34

HOMA-IR is defined as: homeostasis model assessment of insulin resistance.

A. J. Dawson, D. D. Mellor, T. Sathyapalan, E. S. Kilpatrick* and S. L. Atkin
*Department of Diabetes and Endocrinology, University of Hull, Hull, UK and *Department of Clinical Biochemistry, Hull Royal Infirmary, Hull, UK*

References

1 Sjostrom L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP *et al.* Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet* 1998; **352**(9123): 167–172.
2 Fisher BL, Schauer P. Medical and surgical options in the treatment of severe obesity. *Am J Surg* 2002; **184**: 9S–16S.
3 Sathyapalan T, Cho LW, Kilpatrick ES, Coady AM, Atkin SL. Metformin maintains the weight loss and metabolic benefits following rimonabant treatment in obese women with polycystic ovary syndrome (PCOS). *Clin Endocrinol (Oxf)* 2009; **70**: 124–128.

DOI:10.1111/j.1464-5491.2010.03148.x

Endothelial dysfunctionl has vitamin D a role?

Diabet. Med. 28, 125–126 (2011)

I found the papers published in *Diabetic Medicine* on endothelial function variation with glycaemia by Buscemi *et al.* [1] and by Ceriollo *et al.* [2] of great interest because endothelial dysfunction is an important factor to allow for in aiming to reduce cardiovascular risks for patients with diabetes.

The paper published in *Diabetic Medicine* by Sugden *et al.* showed that vitamin D improved endothelial function in patients with Type 2 diabetes and low vitamin D status [3]. There are long-recognized variations in glycaemia with vitamin D status [4], and insulin resistance can be reduced by supplementation in vitamin D deficiency [5]. I wonder whether any part of the variability reported might be accounted for by differences in vitamin D status between subjects, since variations in vitamin D repletion would be likely to be present unless all tests were done at the same time of year. It would be helpful, therefore, to know whether vitamin D status could be included amongst factors to adjust for if these data are available. If vitamin D status cannot be assessed, it would be useful to know whether the associations are altered by inclusion of the date of the assessments, which could be used as a surrogate for vitamin D status.

Competing interests

Nothing to declare.

B. J. Boucher
Centre for Diabetes, Queen Mary University London,

Centre for Diabetes, Barts & The London School of Medicine & Dentistry, London, UK

References

1 Buscemi S, Re A, Batsis JA, Arnone M, Mattina A, Cerasola G *et al.* Glycaemic variability using continuous glucose monitoring and endothelial function in the metabolic syndrome and in Type 2 diabetes. *Diabet Med* 2010; **27**: 872–878.
2 Ceriello A, Esposito K, Ihnat M, Thorpe J, Giugliano D. Effect of acute hyperglycaemia, long-term glycaemic control and insulin on endothelial dysfunction and inflammation in Type 1 diabetic patients with different characteristics. *Diabet Med* 2010; **27**: 911–917.
3 Sugden JA, Davies JI, Witham MD, Morris AD, Struthers AD. Vitamin D improves endothelial function in patients with Type 2 diabetes mellitus and low vitamin D levels. *Diabet Med* 2008; **25**: 320–325.
4 Boucher BJ. Inadequate vitamin D status: does it contribute to the disorders comprising syndrome 'X'? *Br J Nutr* 1998; **79**: 315–327.
5 von Hurst PR, Stonehouse W, Coad J. Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitamin D deficient – a randomised, placebo-controlled trial. *Br J Nutr* 2010; **103**: 549–555.

DOI:10.1111/j.1464-5491.2010.03147.x

Response to Buscemi S *et al.* Glycaemic variability using continuous glucose monitoring and endothelial function in the metabolic syndrome and in Type 2 diabetes

Diabet. Med. 28, 126 (2011)

We read with interest the paper by Buscemi *et al.* regarding the role of glycemic variability in the pathogenesis of endothelial dysfunction [1]. Although a previous study [2] showed a cause–effect relation between glycaemic variability and endothelium-mediated vascular relaxation, and not a simple association as in the study of Buscemi *et al.*, the paper has the merit of extending the relevance of glucose instability to apparently health subjects (i.e. subjects without diabetes and metabolic syndrome). Moreover, compared with their previous work [3], the authors added carotid intima–media thickness evaluation to flow-mediated dilatation of the brachial artery as a surrogate cardiovascular end-point. However, the following points seem unclear and should be explained.

1 When was the flow mediated dilatation test performed? At the end of 48 h subcutaneous continuous glucose monitoring? This is of extreme relevance, as Ceriello *et al.* [2] demonstrated an immediate alteration of endothelium-mediated dilatation after the induction of glucose spikes (i.e. after only 6 h). Therefore, the alteration of flow mediated dilatation could be the effect only of the last hours of glucose fluctuations and not of the whole period of continuous glucose monitoring.
2 As an increased thickness of carotid intima–media occurs over a period of months/years, while glucose profiles have been analysed for 48 h, what can be a plausible biological explanation, above and beyond a statistical association, between this surrogate and 48 h glucose oscillations?
3 From a mathematical point of view, the mean (M) and the area under the curve (AUC) of a generic function are linked with a constant (i.e. AUC = $k \times$ M) [4], where k is, for a continuous glucose monitoring (CGMS) profile, the time of observation (48 h in the paper). Therefore, 48 h CGMS AUC and 48 h CGMS mean are linked by a constant. Considering that the time of observation was the same for all the patients enrolled (48 h), it seems strange that 'Flow mediated dilatation was exclusively and independently predicted by 48-h mean glycemia' and not by 48 h AUC. What is your explanation?

Without any doubt, we believe that the answers to these questions should better define the role of glycaemic variability in diabetic complications.

Competing interests

Nothing to declare.

F. Zaccardi, D. Pitocco, S. Caputo and G. Ghirlanda
Diabetes Care Unit, Internal Medicine, Catholic University, Rome, Italy

References

1 Buscemi S, Re A, Batsis JA, Arnone M, Mattina A, Cerasola G *et al.* Glycaemic variability using continuous glucose monitoring and endothelial function in the metabolic syndrome and in Type 2 diabetes. *Diabet Med* 2010; **27**: 872–878.
2 Ceriello A, Esposito K, Piconi L, Ihnat MA, Thorpe JE, Testa R *et al.* Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. *Diabetes* 2008; **57**: 1349–1354.
3 Buscemi S, Verga S, Basis JA, Re A, Mattina A, Arnone M *et al.* Glycemic variability using 48-hour continuous glucose monitoring and endothelial function in metabolic syndrome. *Diabetes* 2009; **58**: A107–A108.
4 Gradshteyn IS, Ryzhik IM. *Tables of Integrals, Series, and Products*, 6th edn. San Diego, CA: Academic Press, 2000: 1097–1098.