The effect of nateglinide stimulated insulin secretion on post challenge glucose and lipid metabolism in Type 2 diabetes

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Background and Aims: Postprandial glucose and lipid changes have been suggested as potentially modifiable risk factors for coronary heart disease in type 2 diabetes. Glucose-stimulated insulin release is not only important for glucose utilisation but also chylomicron/VLDL triglyceride lipolysis and storage in adipose tissue. Nateglinide has been shown to stimulate earlier and more rapid insulin secretion in type 2 diabetes. To determine whether a more physiological post-challenge endogenous insulin profile can improve glucose and lipid profiles.
Materials and Methods: Single doses of nateglinide 120 mg and placebo were compared in a double-blind crossover study of 20 type 2 diet-treated diabetic subjects (13 male) following a standardised 50 g fat and 50 g carbohydrate test drink. Plasma insulin, glucose, triglyceride (TG), and non-esterified fatty acid (NEFA) levels were measured fasting and post-challenge two hourly for eight hours.
Results: Mean (SD) age was 59.4 (10.7) years, BMI 32.2 (5.5) kg/m^2, and HbA1c 6.9 (1.0)%. Mild hypoglycaemia occurred in 3 subjects at 3.4 (1.0) hours after taking nateglinide. Biochemistry results are geometric mean (1 SD range) except *mean (SD) and incremental area under the curve (IAUC):

	Nateglinide	Placebo	P
IAUC insulin (pmol/L)	45655 (18725,107579)	23567 (6998,70650)	0.058
IAUC glucose (mmol/L)*	-409.1 (324.6)	-70.2 (421.6)	0.010
IAUC TG (mmol/L)	2.97 (2.80,3.15)	2.91 (2.66,3.16)	0.40
6 hour TG (mmol/L)	2.16 (1.35,3.47)	1.95 (1.11,3.40)	0.98
IAUC NEFA (μmol/L)	-130792 (-333210,394783	-51167 (-136776,57117)	0.37

Conclusion: Nateglinide reduces post-challenge glucose excursions in type 2 diabetic subjects but has no significant effect on post-challenge TG or NEFA profiles. It appears that therapies other than oral hypoglycaemic agents may be required if postprandial lipid profiles need to be improved.