Effect of increased endogenous glucose levels within Type 2 diabetes on cellular lipid profiles

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Introduction

- ATP binding cassette subfamily G1 (ABCG1) mediates cholesterol efflux and modulates cellular lipid homeostasis
- Type 2 diabetes (T2D) has been shown to alter cholesterol metabolism, resulting in higher cholesterol synthesis and lower cholesterol absorption
- High glucose levels associated with T2D have the ability to suppress ABCG1 expression via increased oxidative stress, inducing nuclear factor kappa B (NF-κB) activation, blocking ABCG1 transcription
- Lipid accumulation could lead to the development of atherosclerotic plaques and altered immune response

Figure 1. Lipid droplets in human adipocytes

Aims

Our aim was to examine the relationship between ABCG1 expression and lipid profiles within the increased glucose levels of subjects with Type 2 diabetes (ODM)

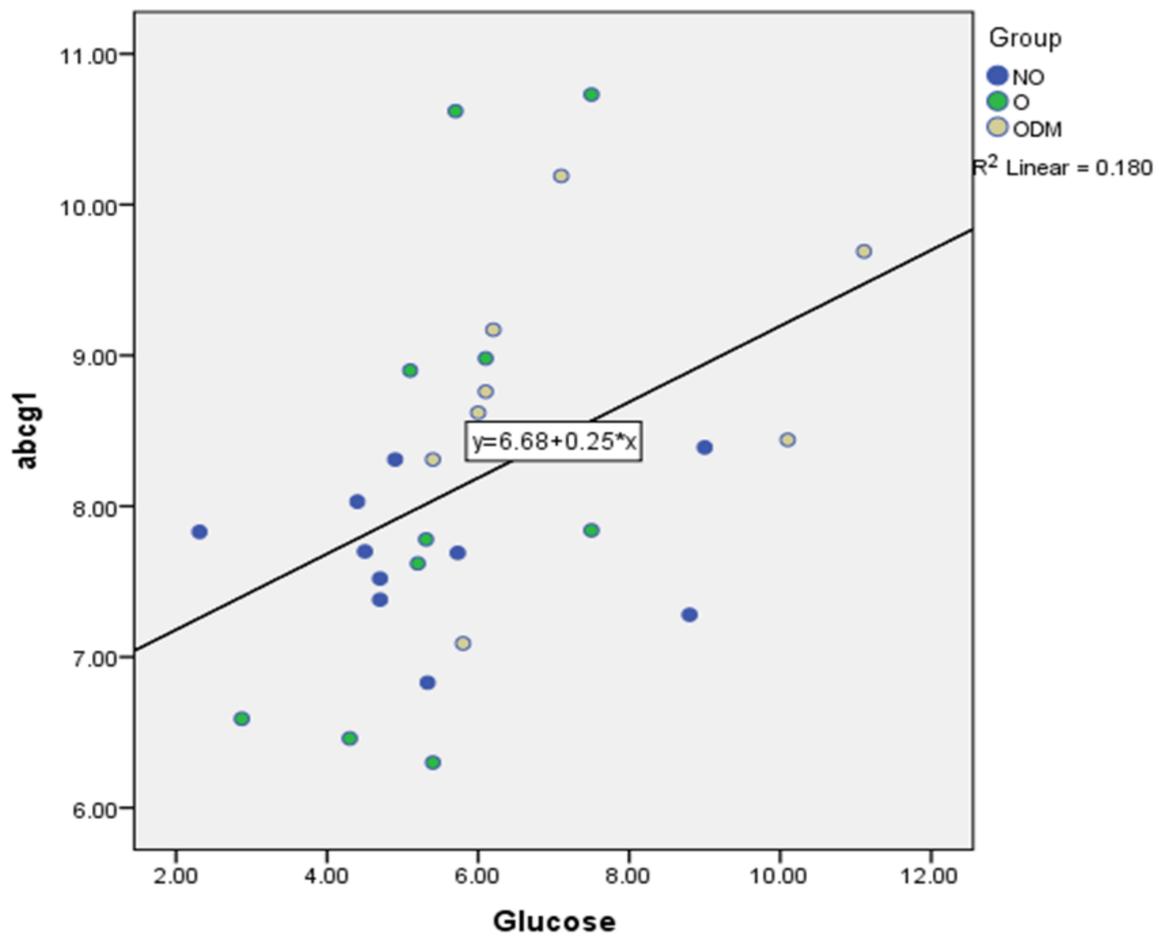
Methods

- Visceral fat and fasting blood samples were collected from 30 subjects undergoing abdominal surgery, categorised as non obese (NO, n=10), obese (O, n=10) or obese with Type 2 diabetes (ODM, n=10)
- RNA was extracted from visceral fat and used for Real-Time qPCR to determine gene expression changes of ABCG1
- Lipid profiles & plasma glucose were determined using a colorimetric assay on the Randox Daytona Plus™

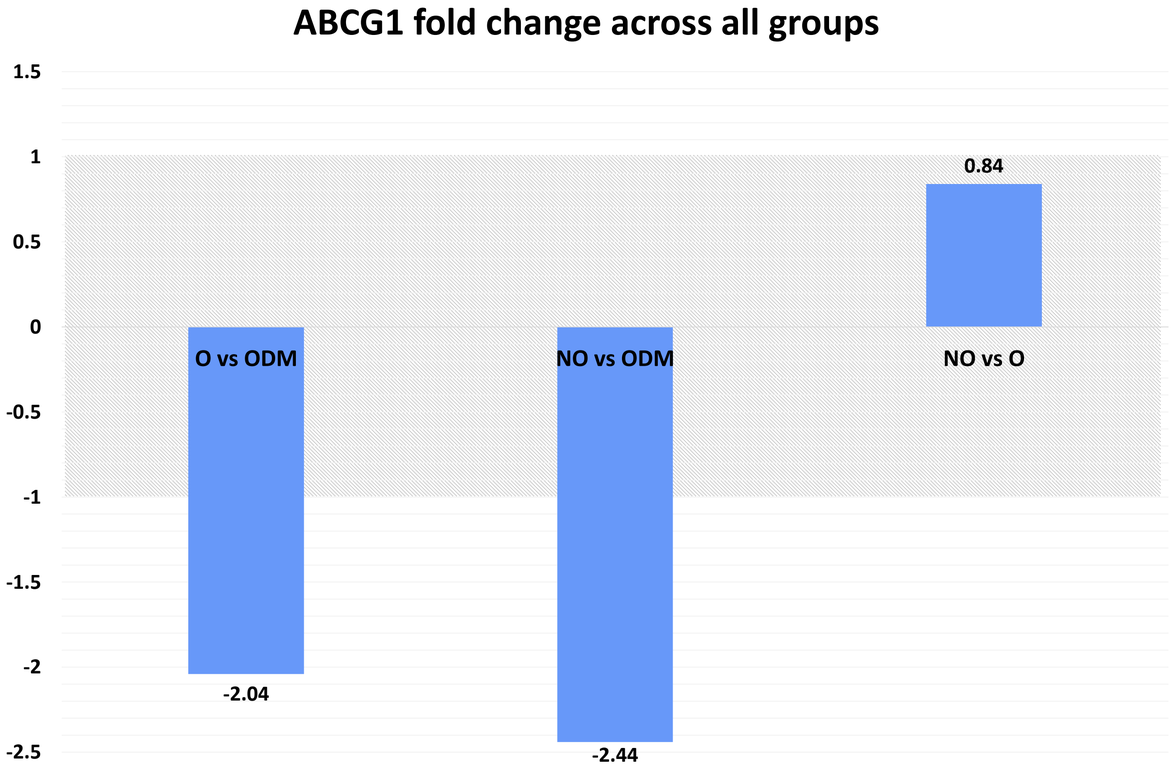
Results

	Δ NO v O	P value	ΔNO v ODM	P value	ΔO v ODM	P value
Age (Years)	-0.7	0.91	-6.3	0.25	-5.6	0.21
Mass (Kg)*	+18.5	<0.01	+59.2	<0.001	+40.7	0.10
BMI (Kg/m²)*	+8.7	<0.001	+21.2	<0.001	+12.4	<0.05
Glucose (mmol/L)*	+0.6	0.55	+1.9	<0.01	+1.3	<0.05
HbA1c (%)*	+0.1	0.51	+1.9	<0.05	+1.8	<0.05
HbA1c (mmol/mol)*	+5.5	0.47	+21.9	<0.05	+16.4	<0.05
Cholesterol (mmol/L)	+0.43	0.52	-1.3	<0.01	-1.7	<0.01
HDL (mmol/L)	+0.11	0.68	-0.4	<0.01	-0.6	<0.05
LDL (mmol/L)	+0.18	0.71	-1.2	<0.01	-1.3	<0.01

Table 1. Change in baseline characteristics and lipid profiles when compared between individual groups. Change between means shown for normally distributed data & p value determined using an independent t-test.
* Change between medians shown for not normally distributed data and Kruskal Wallis used for p value determination. Statistical significance shown for p<0.05 are highlighted in red.



Graph 2. Correlation of ABCG1 ΔCt values and fasting plasma concentrations (mmol/L). Y=6.68 + 0.25x, P<0.05, R=0.425



Graph 1. ABCG1 fold change after $2^{-\Delta\Delta Ct}$ data analysis. Shaded region indicates the range in which fold change is deemed unaltered. Bars indicated the change relative to the control group as indicated on bar title .

- Within the ODM group there was a significant decrease in plasma levels of total cholesterol, HDL and LDLs when compared to both NO and O (P; <0.01, <0.05, <0.01 respectively)
- This decrease in plasma lipids was independent of prescribed statin use
- Reduced expression of ABCG1 was observed in the ODM group compared to O and NO groups (ABCG1 = 2.0-fold and 2.4- fold decrease, respectively)
- An increase in plasma glucose correlated with the reduced expression of ABCG1 (P<0.05)

Conclusions

- Decrease in plasma lipids is hypothesised to be the result of a reduction in cholesterol export from the cell, resulting in cellular lipid retention
- Further evaluation of this pathway may provide a new therapeutic avenue for the management of obesity-related Type 2 diabetes complications

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