ORIGINAL RESEARCH

ATP-binding cassette transporter A1 (ABCA1) expression in adipose tissue and its modulation with insulin resistance in obesity

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Purpose: Adipose tissue dysfunction is at the center of metabolic dysfunctions associated with obesity. Through studies in isolated adipocytes and mouse models, ATP-binding cassette transporter A1 (ABCA1) expression in the adipose tissue has been shown to regulate high-density lipoprotein (HDL) cholesterol levels in the circulation and insulin sensitivity at both adipose tissue and whole-body levels. We aimed to explore the possible link between ABCA1 expression in the adipose tissue and metabolic derangements associated with obesity in humans.

Patients and methods: This exploratory study among individuals who were lean (body mass index [BMI]: 22.3 ± 0.34 kg/m^2, n=28) and obese (BMI: 44.48 ± 5.3 kg/m^2, n=34) compared the expression of ABCA1, adiponectin and GLUT4 (SLC2A4) in visceral and subcutaneous adipose tissue using quantitative real-time PCR and immunohistochemistry. Homeostatic model assessment for insulin resistance (HOMA-IR) and adipose tissue insulin resistance (adipo-IR) were used as insulin resistance markers.

Results: Visceral adipose tissue from individuals who were obese had significantly lower ABCA1 ($P=0.04$ for mRNA and protein) and adiponectin ($P=0.001$ for mRNA) expression compared to that from lean individuals. Subcutaneous adipose tissue did not show any significant difference in the expression. When individuals were divided into insulin-sensitive (IS) and insulin-resistant (IR) groups based on HOMA-IR, IR individuals had lower ABCA1 ($P=0.0001$ for mRNA and $P=0.009$ for protein) expression compared to IS individuals in visceral adipose tissue, but not in subcutaneous adipose tissue. The difference was significant after adjusting for age, gender and BMI. ABCA1 mRNA expression in visceral adipose tissue correlated negatively with both HOMA-IR ($r=-0.44$, $P=0.0003$) and adipo-IR ($r=-0.35$, $P=0.005$) after adjusting for age, gender and BMI. ABCA1 expression in either visceral or subcutaneous adipose tissue did not have any significant correlation with HDL cholesterol levels or mean adipocyte area.

Conclusion: Obesity and insulin resistance are associated with lower expression of ABCA1 in visceral adipose tissue in humans.

Keywords: metabolic syndrome, cholesterol, diabetes, adiponectin

Plain language summary

Obesity predisposes individuals to diabetes mellitus which presents with increase in blood sugar levels. Insulin is the hormone that prevents uncontrolled increase in blood sugar in human body. Why some individuals with obesity develop resistance to the actions of insulin and subsequently diabetes mellitus while others do not is still not known. In this study we tried to answer this question by looking at the expression of ATP binding cassette transporter A1 (ABCA1) protein in various fat depots of human body namely visceral (abdominal) and subcutaneous (beneath the skin). In this study we found that among individuals with obesity, those with insulin resistance had lower expression of ABCA1 in their visceral fat compared to individuals who were obese