Republic of Iraq

Ministry of Higher Education

And Scientific Research

Al-Nahrain University

College of Medicine

The role of chemerin and apelin adipokines in the pathogenesis of insulin resistance in type2 diabetes mellitus

A Thesis

Submitted to the College of Medicine / Al-Nahrain University in partial Fulfillment of the Requirements for the Degree of Doctor of philosophy in Clinical Biochemistry

BY

Qutaiba Abdulkareem Qasim

B.Sc.Pharmacy (2004) , M.Sc. (Clinic. Biochemistry)(2010)

College of Pharmacy / University of Basra

Supervised by

Prof.Dr.Yahya Y. Fareed
Professor in clinical Biochemistry

Prof.Dr.Hashim M. Hashim
Professor in internal medicine

1437 A.H

2016 A.D

Abstract

Background : For many years, adipose tissue was considered as an inert energy storage organ that accumulates and stores triacylglycerols during energy excess and releases fatty acids in times of systemic energy need. However, over the last two decades adipose tissue had been established as highly active endocrine and metabolically important organs that modulate energy expenditure and glucose homeostasis through secretion of signaling molecules, termed adipokines like chemerin , apelin , IL-6 and TNF-α . The dysregulation of adipokines has been implicated in obesity, type 2 diabetes, and cardiovascular disease . Recently, inflammatory responses in adipose tissue have been shown as a major mechanism to induce peripheral tissue insulin resistance. In obese humans , the findings have suggested that obesity-induced insulin resistance may result, at least in part, from an imbalance in the expression of pro- and anti-inflammatory adipokines.

Objective:To evaluate the possible role of chemerin and apelin adipokines as well as inflammatory cytokines including IL-6 and TNF-α in the pathogenesis of insulin resistance in obese and non obese type 2 diabetic patients as compared to control volunteers .

Subjects and Methods: A case – control study was conducted at diabetic centre of AL-Mawana Hospital in Basra from April 2014 till March 2015

. A total of 120 subjects (61male and 59 female) aged between (23-62yr) were encountered and randomized into 4 subgroups :

25 non obese (BMI< 30 kg/m^2) control group 1 (CG1) , 25 obese (BMI≥ 30 kg/m^2) non diabetic control group 2 (CG2) subjects , 35 non obese (BMI< 30 kg/m^2) diabetic group 1 (DG1) and 35 obese (BMI ≥ 30 kg/m^2) diabetic group 2 (DG2) , Patients were collected according to the inclusion diagnostic criteria of WHO (2011); fasting serum glucose level ≥ 7 mmol/L (≥ 126 mg/dl) and glycosylated hemoglobin (HbA1c) ≥ 6.5%.

Results:Group comparison using student t-test revealed a significant ($p<0.05$) elevation of serum concentration of chemerin in obese diabetic group 2 as compared to obese control group 2 . The serum concentration of apelin-c terminus of non obese diabetic group 1 is significantly ($p<0.05$) higher as compared with non obese control group 1 , while it is significantly ($p<0.05$) lower in obese diabetic group 2 as compared to obese control group 2 . The serum concentration of IL-6 of obese and non obese diabetic patients was significantly ($p<0.05$) lower as compared with control subjects in contrast to the serum concentration of TNF-α which is significantly ($p<0.05$) higher in non obese diabetic patients in comparison to non obese control subjects . There was no significant difference in the serum concentration of FFA between control and

diabetic groups. Only apelin significantly correlated with BMI .The correlation analysis revealed a significant negative correlation between IL-6 and fasting glucose , HbA1c and HOMA-IR with significant positive correlation between IL-6 and HOMA-B% . Also there was a significant positive correlation between TNF-α and fasting glucose and HbA1c with significant negative correlation between TNF-α and HOMA-B% .

Conclusions: From the present findings , it was concluded that altered adipokines and inflammatory cytokines might represent a possible link between obesity and T2DM . It was still unclear whether altered adipokines and inflammatory cytokines were a cause or compensatory mechanism to insulin resistance in T2DM .