Journal of Diabetes Science and Technology
Volume 5, Issue 3, May 2011

ORIGINAL ARTICLE

Glycated Albumin Modulates Endothelial Cell Thrombogenic and Inflammatory Responses

David A. Rubenstein, Ph.D., Zahra Maria, B.Sc., and Wei Yin, Ph.D.

Abstract

Background:

It has become established that a diabetic vasculature promotes cardiovascular disease progression via changes to endothelial cells, platelets, and the interactions of these cells. It is believed that the majority of these changes are induced by the presence of advanced glycation end products (AGEs), which permanently alter various functions. Studies have shown that platelets perpetuate endothelial cell responses under these conditions. However, the role of changes in endothelial cell thrombogenicity and inflammatory responses, after subjected to AGEs, has not been characterized. Our objective was to evaluate the effects of AGEs on these functions.

Methods:

To accomplish this, albumin was chemically modified by exposure to glucose for up to 8 weeks, and endothelial cells were subjected to glycated albumin for up to 5 days in a cell culture system. A time course for changes in endothelial cell viability, density, morphology, and metabolic activity were investigated, along with the surface expression of intercellular adhesion molecule-1, thrombomodulin, tissue factor, connexin-43, and caveolin-1.

Results:

Endothelial cells exposed to irreversibly glycated albumin were less viable, proliferated slower, and had a lower metabolic activity as compared to cells exposed to nonglycated albumin. Endothelial cells that were exposed to any glycated albumin were procoagulant and proinflammatory as compared with all other conditions. There were no overall trends in the expression of connexin-43 or caveolin-1.

Conclusions:

Our data suggest that the presence of irreversible glycated albumin is deleterious to endothelial cells, makes endothelial cells more procoagulant, and promotes inflammatory responses. It is therefore possible that endothelial cell activation may precede and promote platelet activation during diabetic conditions.

J Diabetes Sci Technol 2011;5(3):703-713

Author Affiliation: School of Mechanical and Aerospace Engineering, Oklahoma State University, Stillwater, Oklahoma

Abbreviations: (AGE) advanced glycation end product, (ANOVA) analysis of variance, (BSA) bovine serum albumin, (ELISA) enzyme-linked immunosorbent assay, (HUVEC) human umbilical vein endothelial cell, (ICAM-1) intracellular adhesion molecule-1, (MTT) 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide, (PBS) phosphate-buffered saline

Keywords: advanced glycation end products, cardiovascular diseases, diabetes mellitus, endothelial cells, thrombogenicity

Corresponding Author: David A. Rubenstein, Ph.D., School of Mechanical and Aerospace Engineering, Oklahoma State University, 218 Engineering North, Stillwater, OK 74078-5016; email address david.rubenstein@okstate.edu