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Modulation of TREM-1, Arginase and Nitric Oxide Levels under Diabetic Conditions in Macrophages.

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Abstract

Arginase is ureohydrolase enzyme that has essential actions in the body, most importantly in the urea cycle. Though, increased arginase activity has been demonstrated to contribute to vascular endothelial dysfunction (VED) in a number of disease/pathophysiological conditions, such as diabetes, aging, atherosclerosis and hypertension. Enhanced arginase activity/expression results in reduced availability of L-arginine for nitric oxide synthase (NOS) and decrease NO production. Vascular dysfunction is a common characteristic of the early vascular complications of diabetes. Inflammation has been shown to be a potent modulator of vascular dysfunction in diabetes. we have previously found that increased inflammatory mediators in diabetic conditions seem to affect arginase levels as well. we hypothesise that advanced glycated end products (AGE), which get elevated in diabetes, can stimulate expression of Triggering Receptor Expressed On Myeloid Cells (TREM-1). TREM-1 has a key role in vascular endothelial activation, inflammation and dysfunction. Also AGEs cause an increase in arginase expression and activity in macrophages. Additionally, treating macrophages with high glucose/palmitate (HG/PA); which represents a model of high fat-high sugar intake; has also resulted in upregulation of TREM-1 and arginase 2 levels in macrophages. We also looked at NO levels produced under different conditions and have seen that both AGE or HG/PA cause an increase in NO levels from macrophages. Our studies indicate that there is a cross talk between TREM-1 receptor and arginase under different diabetic conditions. Our earlier findings indicate the importance of controlling levels of arginase in diabetes to prevent vascular dysfunction. Regulating inflammatory receptors such as TREM-1 can also have a powerful impact on controlling vascular dysfunction and complications in diabetes.

Keywords: Arginase, High Glucose, TREM-1, Nitric Oxide, Macrophages

Abbreviations: NO: Nitric oxide, NO: nitric oxide synthase,TREM-1: Triggering receptor expressed on myeloid cells 1, AGE: advanced glycated end products, VED: vascular endothelial dysfunction

Funding and Conflicts of Interest

None