ISSN 1948-9358 (online)

World Journal of *Diabetes*

World J Diabetes 2024 March 15; 15(3): 308-574

Published by Baishideng Publishing Group Inc

World Journal of Diabetes

Contents

Monthly Volume 15 Number 3 March 15, 2024

EDITORIAL

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

World Journal of Diabetes

Monthly Volume 15 Number 3 March 15, 2024

Contents

LETTER TO THE EDITOR

World Journal of Diabetes

Monthly Volume 15 Number 3 March 15, 2024

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Diabetes*, Jun-Ling Shi, PhD, Professor, School of Life Sciences, Northwestern Polytechnical University, Xi'an 710072, Shaanxi Province, China. sjlshi2004@nwpu.edu.cn

AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

INDEXING/ABSTRACTING

The *WJD* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJD* as 4.2; IF without journal self cites: 4.1; 5-year IF: 4.5; Journal Citation Indicator: 0.69; Ranking: 51 among 145 journals in endocrinology and metabolism; and Quartile category: Q2.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Diabetes

ISSN
ISSN 1948-9358 (online)

LAUNCH DATE
June 15, 2010

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Lu Cai, Md. Shahidul Islam, Michael Horowitz

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-9358/editorialboard.htm

PUBLICATION DATE
March 15, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Diabetes

Submit a Manuscript: https://www.f6publishing.com

World J Diabetes 2024 March 15; 15(3): 572-574

DOI: 10.4239/wjd.v15.i3.572

ISSN 1948-9358 (online)

LETTER TO THE EDITOR

Regulatory role of peroxynitrite in advanced glycation end products mediated diabetic cardiovascular complications

Asis Bala

Specialty type: Endocrinology and metabolism

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Cen LS, China; Rojas A, Chile; Swanson K, United States

Received: November 28, 2023
Peer-review started: November 28, 2023
First decision: January 15, 2024
Revised: January 15, 2024
Accepted: February 6, 2024
Article in press: February 6, 2024
Published online: March 15, 2024

Asis Bala, Pharmacology and Drug Discovery Research Laboratory, Division of Life Sciences, Institute of Advanced Study in Science and Technology, Guwahati 781035, Assam, India

Corresponding author: Asis Bala, PhD, Associate Professor, Pharmacology and Drug Discovery Research Laboratory, Division of Life Sciences, Institute of Advanced Study in Science and Technology, Vigyan Path, Guwahati 781035, Assam, India. asisbala@iasst.gov.in

Abstract

The Advanced Glycation End Products (AGE) binding with its receptor can increase reactive oxygen species (ROS) generation through specific signaling mediators. The effect of superoxide (O_2^-) and O_2^- mediated ROS and reactive nitrogen species depends on their concentration and location of formation. Nitric oxide (NO) has anti-inflammatory and anticoagulant properties and a vasodilation effect, but NO can be deactivated by reacting with O_2^-. This reaction between NO and O_2^- produces the potent oxidant $ONOO^-$. Therefore, ONOO-'s regulatory role in AGEs in diabetic cardiovascular complications must considered as a regulator of cardiovascular complications in diabetes.

Key Words: Diabetes; Cardiovascular complication; Advanced glycation end products; Reactive oxygen species; Reactive nitrogen species; Peroxynitrite

Core Tip: The binding of Advanced Glycation End Products (AGE) to its receptor triggers the activation of signaling mediators that promote the generation of reactive oxygen species (ROS). The impact of ROS on the body can be beneficial or harmful, depending on its concentration and location. In diabetic cardiovascular complications, peroxynitrite ($ONOO^-$) plays a crucial role in vascular changes. ROS, derived from NADPH oxidase, regulates host immune responses and cellular inflammation. The production of superoxide (O_2^-), hydrogen peroxide (H_2O_2), and other compounds occurs as oxygen undergoes a series of reductions. It is essential to consider the presence of $ONOO^-$ in AGEs in diabetic cardiovascular complications.

Citation: Bala A. Regulatory role of peroxynitrite in advanced glycation end products mediated diabetic cardiovascular complications. *World J Diabetes* 2024; 15(3): 572-574
URL: https://www.wjgnet.com/1948-9358/full/v15/i3/572.htm
DOI: https://dx.doi.org/10.4239/wjd.v15.i3.572

TO THE EDITOR

I am writing to express my appreciation for the article published by Bansal *et al*[1] in the *World Journal of Diabetes* in 2023, titled "Advanced glycation end products: Key mediator and therapeutic target of cardiovascular complications in diabetes". The article provides a clear explanation of the role of Advanced Glycation End Products (AGE) in cardiovascular complications.

I want to draw attention to the role of superoxide (O_2^-) in connection to AGE, reactive oxygen species (ROS), and reactive nitrogen species (RNS) mediated immune inflammation. The article comprehensively outlined the impact of AGE on diabetic cardiovascular disease, encompassing both cellular and extracellular pathological effects. These effects include extracellular matrix oxidation, glycation of low-density lipoprotein, and the triggering of inflammatory signaling cascades, such as NADPH oxidase, NRF-2, NFκB, JAK, and STAT pathways. On the contrary, the article partially emphasized the significant role of Nitric oxide (NO) and NO synthase (NOS) in regulating AGE formation.

As mentioned in the article, AGE binding with its receptor increases ROS generation through stimulation of specific signaling mediators such as ERK, phospholipase A2, phosphoinositide 3-kinase activation, activation of NADPH oxidase, inducible NOS, PKC, and p38 MAPK[2]. However, the beneficial or detrimental role of O_2^- and O_2^- -mediated ROS or RNS is determined by its concentration and the places where it is formed[3]. Studies have shown that O_2^- immediately interacts with NO to produce the highly toxic peroxynitrite ($ONOO^-$), which plays a crucial role in vascular changes in diabetic cardiovascular complications[4,5].

The damage to vascular endothelial cells is a leading cause of diabetic vascular complications, which can be combated using endothelial progenitor cells (EPCs)[6]. The activation of various pathways such as xanthine and NAD(P)H oxidases, uncoupled NOS, cyclooxygenase, glucose autoxidation, the mitochondrial respiratory chain, polyol, and AGEs is triggered by hyperglycemia[4,7]. These pathways lead to the production of superoxide anion (O_2^-)[4,5]. The generation of superoxide due to hyperglycemia can also increase NO generation by enhancing the expression of NOSs by activating NF-κB[8]. However, O_2^- can quench NO, reducing the efficacy of the endothelium-derived vasodilator system[4]. Moreover, superoxide dismutase can convert superoxide to hydrogen peroxide (H_2O_2), which can react further with NO to form $ONOO^-$[9]. $ONOO^-$ can cause damage to cells by initiating lipid peroxidation, inactivating enzymes and proteins *via* oxidation and nitration, and activating matrix metalloproteinases[10]. Additionally, $ONOO^-$ can decrease the membrane potential by acting on mitochondria, triggering the release of proapoptotic factors such as cytochrome c and apoptosis-inducing factor[4,9,10]. These factors can mediate caspase-dependent and -independent apoptotic death pathways, which may contribute to the progression of diabetic cardiovascular complications[4]. Therefore, $ONOO^-$ is considered one of the critical modulators of diabetic cardiovascular complications since high glucose levels can impair EPC function and reduce NO production.

Furthermore, NADPH oxidase-derived ROS have become critical regulators of host immune responses and cellular inflammation[11,12]. Activation of phospholipase A2 in human neutrophils and other inflammatory cells by polyunsaturated fatty acids stimulates O_2^- production, triggering innate immune reactions. Increased O_2^- production may also activate the arachidonic acid pathways[5]. Oxygen undergoes a series of univalent reductions, sequentially producing O_2^-, H_2O_2, *etc*. NO always shows its anti-inflammatory, anticoagulant properties and vasodilation effect. Still, it can be inactivated by reaction with O_2^-, producing the potent oxidant $ONOO^-$[11-13]. Therefore, the regulatory role of $ONOO^-$ in AGEs in diabetic cardiovascular complications also needs to be considered.

FOOTNOTES

Author contributions: Bala A solely planned and wrote the manuscript.

Conflict-of-interest statement: No conflict of interest to declare.

Country/Territory of origin: India

ORCID number: Asis Bala 0000-0002-2148-2331.

S-Editor: Lin C
L-Editor: A

P-Editor: Chen YX

REFERENCES

1 **Bansal S**, Burman A, Tripathi AK. Advanced glycation end products: Key mediator and therapeutic target of cardiovascular complications in diabetes. *World J Diabetes* 2023; **14**: 1146-1162 [PMID: 37664478 DOI: 10.4239/wjd.v14.i8.1146]

2 **Begum R**, Thota S, Abdulkadir A, Kaur G, Bagam P, Batra S. NADPH oxidase family proteins: signaling dynamics to disease management. *Cell Mol Immunol* 2022; **19**: 660-686 [PMID: 35585127 DOI: 10.1038/s41423-022-00858-1]

3 **Di Meo S**, Reed TT, Venditti P, Victor VM. Role of ROS and RNS Sources in Physiological and Pathological Conditions. *Oxid Med Cell Longev* 2016; **2016**: 1245049 [PMID: 27478531 DOI: 10.1155/2016/1245049]

4 **Pacher P**, Szabó C. Role of peroxynitrite in the pathogenesis of cardiovascular complications of diabetes. *Curr Opin Pharmacol* 2006; **6**: 136-141 [PMID: 16483848 DOI: 10.1016/j.coph.2006.01.001]

5 **Changkakoti L**, Das JM, Borah R, Rajabalaya R, David SR, Balaraman AK, Pramanik S, Haldar PK, Bala A. Protein Kinase C (PKC)-mediated TGF-β Regulation in Diabetic Neuropathy: Emphasis on Neuro-inflammation and Allodynia. *Endocr Metab Immune Disord Drug Targets* 2023 [PMID: 37937564 DOI: 10.2174/0118715303262824231024104849]

6 **Benítez-Camacho J**, Ballesteros A, Beltrán-Camacho L, Rojas-Torres M, Rosal-Vela A, Jimenez-Palomares M, Sanchez-Gomar I, Durán-Ruiz MC. Endothelial progenitor cells as biomarkers of diabetes-related cardiovascular complications. *Stem Cell Res Ther* 2023; **14**: 324 [PMID: 37950274 DOI: 10.1186/s13287-023-03537-8]

7 **Tangvarasittichai S**. Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World J Diabetes* 2015; **6**: 456-480 [PMID: 25897356 DOI: 10.4239/wjd.v6.i3.456]

8 **González P**, Lozano P, Ros G, Solano F. Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections. *Int J Mol Sci* 2023; **24** [PMID: 37298303 DOI: 10.3390/ijms24119352]

9 **Wang Y**, Branicky R, Noë A, Hekimi S. Superoxide dismutases: Dual roles in controlling ROS damage and regulating ROS signaling. *J Cell Biol* 2018; **217**: 1915-1928 [PMID: 29669742 DOI: 10.1083/jcb.201708007]

10 **Szabó C**, Módis K. Pathophysiological roles of peroxynitrite in circulatory shock. *Shock* 2010; **34** Suppl 1: 4-14 [PMID: 20523270 DOI: 10.1097/SHK.0b013e3181e7e9ba]

11 **Bala A**. Importance of protein kinase C (PKC) in phosphorylation of AMP-activated protein kinase (AMPK) in endocrine control. *Endocrine* 2023 [PMID: 37864651 DOI: 10.1007/s12020-023-03576-4]

12 **Bala A**, Haldar PK, Kar B, Naskar S, Mazumder UK. Carbon tetrachloride: a hepatotoxin causes oxidative stress in murine peritoneal macrophage and peripheral blood lymphocyte cells. *Immunopharmacol Immunotoxicol* 2012; **34**: 157-162 [PMID: 21721906 DOI: 10.3109/08923973.2011.590498]

13 **Bala A**, Matsabisa MG, Haldar PK, Biswas S, Mukherjee AK. Superoxide (O2-): A Biological Prodigy for Developing and Curing Disease. In: Jana K. The Role of Reactive Oxygen Species in Health and Disease. Nova science publisher: Hauppauge, 2024 [DOI: 10.52305/TRSI2511]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com