University of Central Lancashire
UCLan

Central Lancashire Online Knowledge (CLoK)

Title	Circadian Dysfunction of Oxydative Stress and Endogenous Antioxidants with Reference to Methylglyoxa
Type	Article
URL	https://clok.uclan.ac.uk/id/eprint/39212/
DOI	
Date	2021
Citation	Bidasee, Kishore, Singh, Ram B. and Singh, Jaipaul (2021) Circadian Dysfunction of Oxydative Stress and Endogenous Antioxidants with Reference to Methylglyoxa. World Heart Journal, 13 (1). pp. 51-53. ISSN 1556-4002
Creators	Bidasee, Kishore, Singh, Ram B. and Singh, Jaipaul

It is advisable to refer to the publisher's version if you intend to cite from the work.

For information about Research at UCLan please go to http://www.uclan.ac.uk/research/

All outputs in CLoK are protected by Intellectual Property Rights law, including Copyright law. Copyright, IPR and Moral Rights for the works on this site are retained by the individual authors and/or other copyright owners. Terms and conditions for use of this material are defined in the http://clok.uclan.ac.uk/policies/

World Heart Journal
Volume 13, Number 1

ISSN: 1556-4002
© 2021 Nova Science Publishers, Inc.

Circadian Dysfunction of Oxydative Stress and Endogenous Antioxidants with Reference to Methylglyoxal (MGO)

Kishore Bidasee[1,*], Ram B. Singh[2], and Jaipaul Singh[3]

[1]Department of Pharmacology and Experimental Neuroscience; Department of Environment and Occupational Health, University of Nebraska Medical Center, Omaha, NE, USA
[2]Medical Hospital and Research Centre, Centre of Nutrition and Heart Research, Moradabad, India
[3]School of Natural Sciences, University of Central Lancashire, Preston, PR1 2HE, England, UK

Introduction

Circadian rhythm of increased oxidative stress and deficiency of antioxidant vitamins is known to occur in the morning at 6.00 hours to 12.00 hours [1]. Apart from antioxidant and vitamin deficiency, there is also deficiency of catalase, super-oxide-dismutase (SDO) and glutathione peroxidase (GPO) due to increased requirement of antioxidant enzymes in the morning. Methylglyoxal (MGO) is a non-enzymatic metabolite in the glycolytic pathway and its concentration in blood and tissues is elevated in all the cardio-metabolic diseases, including obesity and diabetes mellitus (DM) [1, 2]. MGO is a reactive carbonyl species (RCS) and in turn it induces tissue injuries via reactive oxygen species (ROS), resulting in increased damage of target tissues, which may worsen in the morning. MGO also plays an important pathological role in the development of both cardiovascular diseases (CVDs) and diabetes via the AGEs exert irreversible effects on protein structure and function. As such, it is crucial to understand the underlying mechanism whereby MGO is inducing tissue damage. This mini-review aims to highlight the role of circadian dysfunction in the pathogenesis of diabetes mellitus and its complications.

Review and Results

There is a circadian rhythm of increased oxidative stress in the morning, due to enormous increased in cortisol and glucocorticoids, testosterone and thyroxin with decline in parasympathetic activity and anti-oxidant vitamins [1]. The circadian rhythm of MGO is not known but it is possible that MGO also increases

* Correspondence: Dr. Kishore Bidasee, PhD.
Email: kbidasee@unmc.edu

in an attempt to reset the circadian clock function (Figure 1).

In an experimental study, the harmful actions of MGO were assessed. Human aortic endothelial cells were examined for increases in intracellular ROS, which were measured with fluorescent indicator, 5-(and-6)-chloromethyl-2',7'-dichlorodihydrofluorescein diacetate acetyl ester (DCFH-DA). The addition of MGO rapidly increased the ROS in a dose-dependent manner [2]. The increment of DCF was entirely abolished by pre-treatment with superoxide anion scavenger and membrane-permeable catalase, indicating that MGO induces superoxide production. The increment was completely inhibited by 2-thenoyltrifluoroacetone or carbonyl cyanide 3-chlorophenylhydrazone and partially inhibited by N-methyl-L-arginine. These data suggest that MGO stimulates superoxide production from mitochondria and partially stimulates nitric oxide synthase (NOS) in human endothelial cells. In a healthy condition, MGO is a metabolite of glucose and it is produced at physiological level to maintain the normal homeostasis of the body. However, in conditions of elevated glucose as in DM, the level of MGO is elevated to pharmacological concentration when it can induced adverse effects in the body. Our previous study demonstrated an elevated MGO level with an increased oxidative stress in vascular smooth muscle cells (VSMCs) from spontaneously hypertensive rats [3], Figure 2.

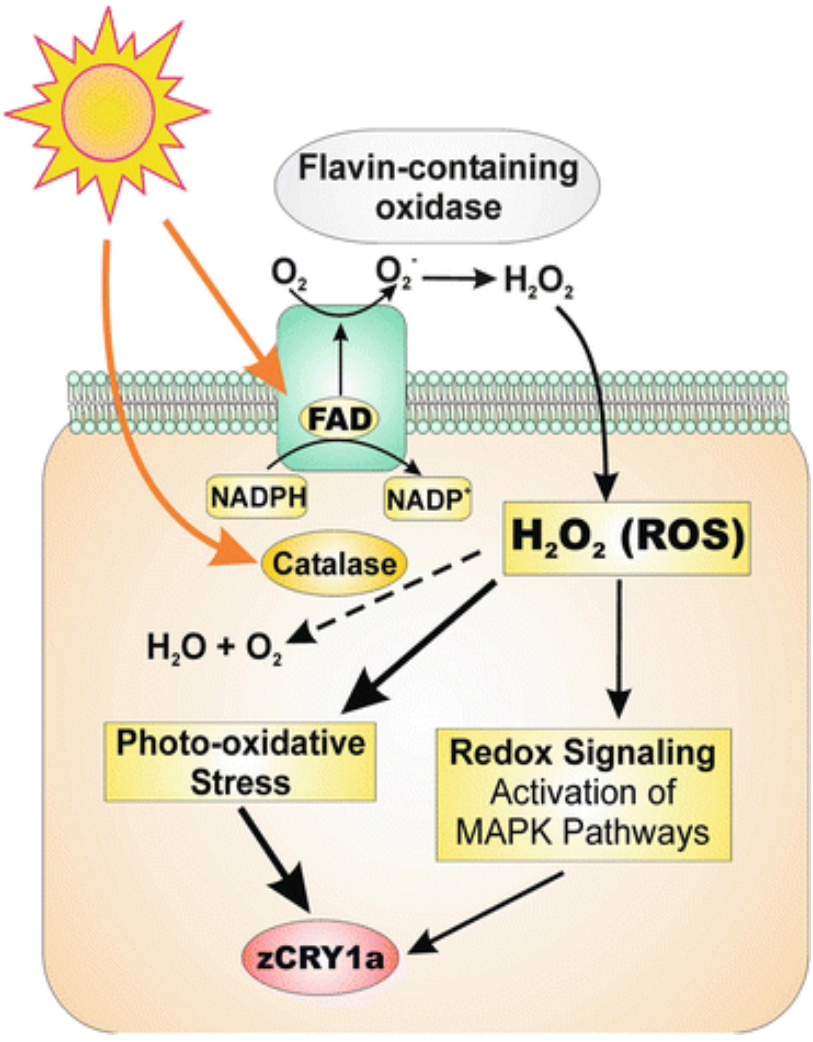

Figure 1. Increase in oxidative stress in the morning. (https://veteriankey.com/oxidative-stress-and-its-role-in-the-synchronization-of-circadian-rhythms-in-crustaceans-an-ecological-perspective/).

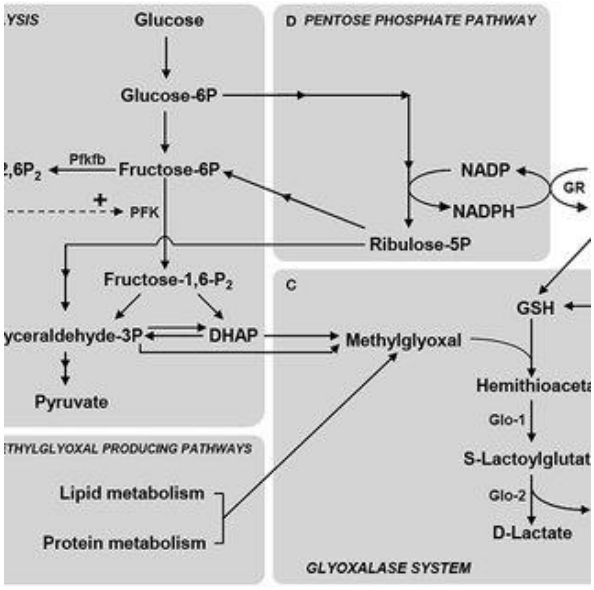

Figure 2. Oxidative stress with reference to methyl glyoxal (modified from [7]).

Whether MGO causes the generation of nitric oxide (NO) and superoxide anion (O^{2*-}), leading to peroxynitrite ($ONOO^-$) formation in VSMCs, was investigated in the present study [4, 5]. Cultured rat thoracic aortic SMCs (A-10) were treated with MGO or other different agents. Oxidized DCF, reflecting H_2O_2 and $ONOO^-$ production, was significantly increased in a concentration- and time-dependent manner after the treatment of SMCs with MGO (3-300 micro-M) for 45 min-18 h (n = 12). MG-increased oxidized DCF was effectively blocked by reduced glutathione or N-acetyl-l-cysteine, as well as L-NAME ($p < 0.05$; n = 12). Both O^{2*-} scavenger SOD and NAD-(P)H oxidase inhibitor DPI significantly ($p < 0.05$) decreased MGO-induced oxidized DCF formation. MG significantly and concentration-dependently increased NO and O^{2*-} generation in A-10 cells, which was significantly inhibited by L-NAME and SOD or DPI, respectively.

It is concluded that MGO can induce significant ($p < 0.05$) generation of NO and O^{2*-} in rat VSMCs, which in turn causes $ONOO^-$ formation [4, 5]. An elevated MGO level and the consequential ROS/RNS generation would alter cellular signaling pathways, contributing to the development of different insulin resistance states such as diabetes and hypertension [6].

Acknowledgements

The authors declare that they have no conflict of interest with this work.

References

[1] Singh RB, Niaz MA, Cornelissen G, Otsuka K,Siegelova J, Fiser B, Halberg F. Circadian rhythmicity of circulating vitamin concentrations. *Scripta Medica* (Brno) 2001; 74: 93-96.

[2] Miyazawa N, Abe M, Souma T, Tanemoto M, Abe T, Nakayama M, Ito S. Methylglyoxal augments intracellular oxidative stress in human aortic endothelial cells. *Free Radic Res* 2010; 44(1): 101-107. doi: 10.3109/10715760903321788. PMID: 19886746.

[3] Palsamy P, Bidasee KR, Ayaki M, *et al.* Methylglyoxal induces endoplasmic reticulum stress and DNA demethylation in the Keap1 promoter of human lens epithelial cells and age-related cataracts. *Free Radic Biol Med* 2014; 72: 134–148.

[4] Chang T, Wang R, Wu L. Methylglyoxal-induced nitric oxide and peroxynitrite production in vascular smooth muscle cells. *Free Radic Biol Med* 2005; 38(2): 286-293. doi: 10.1016/j.freeradbiomed.2004.10.034. PMID: 15607912.

[5] Chan CM, Huang DY, Huang YP, et al. Methylglyoxal induces cell death through endoplasmic reticulum stress-associated ROS production and mitochondrial dysfunction. *J Cell Mol Med* 2016; 20(9): 1749-1760. doi:10.1111/jcmm.12893.

[6] Singh RB, Cornelissen G, Saboo B, Mahashwari A, Otsuka K, et al. The Evolution of Biochemical Storm of Circadian Rhythm and Circadian Dysfunction in Relation to Vascular Disease and Diabetes. *Int J Open Access Clin Trials* 2016; 1(1): 5-12.

[7] Igor A, Mereille B, Pierre M. Methylglyoxal, the dark side of glycolysis. *Front Neuroscience* 2015; https://doi.org/10.3389/fnins.2015.00023.