Current Research in Diabetes & Obesity Journal
ISSN: 2476-1435

Juniper Publishers
key to the Researchers

Mini Rewiew
Volume 2 Issue 1 – April 2017
DOI: 10.19080/CRDOJ.2017.2.555580

Curre Res Diabetes & Obes J

Is Telomere Shortening a Genetic Factor That Predisposes to Diabetes Mellitus 2 and Oxidative Stress, or do They Induce It? A Telomere Shortening Predisposes to T2DM

Murillo Ortiz Blanca* and Martínez Garza Sandra

High Specialty Medical Unit, Instituto Mexicano Social security, Mexico

Submission: April 03, 2017; **Published:** April 24, 2017

***Corresponding author:** Murillo Ortiz Blanca, High Specialty Medical Unit, Instituto Mexicano Social security, Mexico, Email: bomo907@hotmail.com

Abstract

Telomeres are structures at the ends of eukaryotic chromosomes and consist of tandemly repeated DNA sequences. Telomeres shorten with each cell division, and it is well known that telomere length in peripheral blood mononuclear cells (PBMCs) decreases with age. High oxidative stress can lead to accelerated telomere shortening, which causes premature cell senescence. In summary, this review shows the short Telomere Length has been identified in a limited number of population studies as a risk factor for development of T2DM. Also, it is importantly to notice the antioxidant properties of Curcumin which may play a key role in the prevention and treatment of premature aging while preserving the length of the telomeres.

Keywords: Telomere shortening; Oxidative stress; Genetic factor; Diabetes mellitus 2

Abbreviations: T2DM: Diabetes Mellitus 2; PBMCs: Cryopreserved Human Peripheral Blood Mononuclear Cells; WBCs: White Blood Cells; NO: Nitric Oxide; TBARS: Thiobarbituric Acid Reactive Substances.

Introduction

Diabetes mellitus 2 and telomere shortening

Diabetes Mellitus 2 (T2DM) is a multifactorial complex disorder which is emerging as a major cause of morbidity and mortality [1]. Telomeres are structures located at the extreme ends of chromosomes and are considered as indicators of biological age [2]. Increased telomere shortening has been demonstrated in several diseases, including diabetes type [3-6]. Telomere shortening increases with the diabetes duration, in our study, we established the potential importance of telomere dynamics in T2DM. We associated the time of disease duration closely in parallel to the progressive increased of inflammation and/or oxidative stress and both played a direct role in telomere shortening [7]. However, a study based on Chinese population found no relationship between Telomere Length and either the onset time or the Diabetes Mellitus 2 duration [8]. Genetic regulation of telomere could potentially explain telomere shortening and also an increased risk for Diabetes Mellitus 2. Zee et al. [9], analyzed 11 telomere pathway genes and their relationship to the development of Diabetes Mellitus 2. A total of eleven tSNPs within TERF1, TNKS, TEP1, ACD and TERF2 were associated with Diabetes Mellitus 2 risk [9]. These findings suggest that genetic variation within the telomere pathway gene loci examined may be a useful predictor for Diabetes Mellitus 2 risk assessment [10,11]. Paik JK, et al. [12], did not observe an association between the selected TL-related SNPs and the presence of Hypertension and Coronary Heart Disease in [12]. These findings tell us the great importance of telomere dynamics in T2DM and the need for translational research.

Discussion

Oxidative stress and Telomere Length

Endogenous factors that cause telomere shortening are aging inflammation and oxidative stress. Telomere attrition

(expressed in WBCs) can serve as a biomarker of the cumulative oxidative stress and inflammation [13,14]. The association of UCP2 gene involved in the production of reactive oxygen species and functional promoter variant in mitochondria with the telomere length implies a link between mitochondrial production of reactive oxygen species and shorter telomere length in Diabetes Mellitus 2 [15]. Oxidative stress exerts a major influence on telomere dynamics by two principal mechanisms; firstly, the GGG triples on the telomere sequence are highly sensitive to the hydroxyl radical. Masi et al. [16] demonstrated that antioxidant defenses are important to maintain telomere integrity, potentially reducing the progression of vascular ageing in patients with T2DM. Secondly in contrast to genomic DNA, telomeric DNA was reported to be deficient in the repair of single-strand breaks. Consequently telomeres appear to be especially vulnerable to the accumulation of ROS-induced DNA-strand breaks [17,18].

Prospective treatment for diabetes mellitus 2

Recent studies propose that telomere shortening and abnormal telomerase activity occur in patients with diabetes mellitus 2 and targeting the telomere-telomerase system has become a prospective treatment for diabetes mellitus [19]. Dietary supplementation of antioxidants has been proposed as alternative treatment to reduce oxidative stress caused by obesity and diabetes. Different studies have shown that curcumin has antioxidant and antihyperglycemic properties in diabetes and obese animal models [20-24]. Hyperglycemia modifies oxygen consumption rate, NO synthesis and increases TBARS levels in mitochondria from the liver and kidneys of diabetic mice, whereas curcumin may has a protective role against these alteration [25-27]. Antioxidant properties of curcumin could play a key role in the prevention and treatment of chronic inflammation diseases [28]. Zhou et al. [29] demonstrated that diet ingredients significantly have an impact on inflammation and oxidative stress markers, which probably also have an effect on Telomere Length. Diabetes patients with normal plasma glucose levels had longer Telomere Length [29].

Conclusion

Telomere Length has been identified in a limited number of population studies as a risk factor for development of T2DM, antioxidant defences are important to maintain telomere integrity, Curcumin which may play a key role in the prevention and treatment of premature aging while preserving the length of the telomeres.

Acknowledgement

This work was supported by the Medical Research Council of the Mexican Social Security Institute (IMSS).

References

1. Tamura Y, Takubo K, Aida J, Araki A, Ito H (2016) Telomere attrition and diabetes mellitus. Geriatr Gerontol Int 16(Suppl 1): 66-74.
2. Aviv A, Kark JD, Susserc E (2015) Telomeres, Atherosclerosis, and Human Longevity A Causal Hypothesis Epidemiology 26(3): 295-299.
3. Willeit P, Raschenberger J, Heydon EE, Tsimikas S, Haun M, et al. (2014) Leucocyte Telomere Length and Risk of Type 2 Diabetes Mellitus: New Prospective Cohort Study and Literature-Based Meta-Analysis. PLoS One 9(11): e112483.
4. Shen Q, Zhao X, Yu L, Zhang Z, Zhou D, et al. (2012) Association of leukocyte telomere length with type 2 diabetes in mainland Chinese populations. J Clin Endocrinol Metab 97(4):1371-1374.
5. Qi Nan W, Ling Z, Bing C (2015) The influence of the telomere-telomerase system on diabetes mellitus and its vascular complications. Expert Opinion on Therapeutic Targets 19(6): 849-864.
6. Zee RY, Castonguay AJ, Barton NS, Germer S, Martin M (2010) Mean leukocyte telomere length shortening and type 2 diabetes mellitus: a case-control study. Transl Res 155(4): 166-169.
7. Murillo OB, Albarrán TF, Arenas AD, Benítez BL, Malacara HJM, et al. (2012) Telomere length and type 2 diabetes in males, a premature aging syndrome. Aging Male 15(1): 54-58.
8. Shen Q, Zhao X, Yu L, Zhang Z, Zhou D, et al. (2012) Association of leukocyte telomere length with type 2 diabetes in mainland Chinese populations. J Clin Endocrinol Metab 97(4): 1371-1374.
9. Zee RY, Ridker PM, Chasman DI (2011) Genetic variants of 11 telomere pathway gene loci and the risk of incident type 2 diabetes mellitus: the Women's Genome Health Study. Atherosclerosis 218(1): 144-146.
10. Zhou Y, Ning Z, Lee Y, Hambly BD, McLachlan CS (2016) Shortened leukocyte telomere length in type 2 diabetes mellitus: genetic polymorphisms in mitochondrial uncoupling proteins and telomeric pathways. Clin Transl Med 5(1): 8.
11. Sethi I, Bhat GR, Singh V, Kumar R, Bhanwer AJ, et al. (2016) Role of telomeres and associated maintenance genes in Type 2 Diabetes Mellitus: A review. Diabetes Res Clin Pract 122: 92-100.
12. Paik JK, Kang R, Cho Y, Shin MJ (2016) Association between Genetic Variations Affecting Mean Telomere Length and the Prevalence of Hypertension and Coronary Heart Disease in Koreans. Clin Nutr Res 5(4): 249-260.
13. Fyhrquist F, Saijonmaa O (2012) Telomere length and cardiovascular aging. Ann Med 44(suppl 1): S138-S142.
14. Babizhayev MA, Savel'yeva EL, Moskvina SN, Yegorov Y (2011) Telomere length is a biomarker of cumulative oxidative stress, biologic age, and an independent predictor of survival and therapeutic treatment requirement associated with smoking behavior. Am J Ther 18(6): e209-e226.
15. Salpea KD, Talmud PJ, Cooper JA, Maubaret CG, Stephens JW, et al. (2010) Association of telomere length with type 2 diabetes, oxidative stress and UCP2 gene variation. Atherosclerosis 209(1): 42-50.
16. Masi S, D'Aiuto F, Cooper J, Salpea K, Stephens JW, et al. (2016) Telomere length, antioxidant status and incidence of ischaemic heart disease in type 2 diabetes. Int J Cardiol 216: 159-164.
17. Sampson MJ, Winterbone MS, Hughes JC, Dozio N, Hughes DA, (2006) Monocyte telomere shortening and oxidative DNA damage in type 2 diabetes, Diabetes Care 29(2): 283-289.
18. Petersen S, Saretzki G, von Zglinicki T (1998) Preferential accumulation of single-stranded regions in telomeres of human fibroblasts. Exp Cell Res 239(1): 152-160.
19. Babizhayev MA, Vishnyakova KS, Yegorov YE (2014) Oxidative damage impact on aging and age-related diseases: drug targeting of telomere attrition and dynamic telomerase activity flirting with imidazole-containing dipeptides. Recent Pat Drug Deliv Formul 8(3): 163-192.

How to cite this article: Murillo O B, Martínez G S. Is Telomere Shortening a Genetic Factor That Predisposes to Diabetes Mellitus 2 and Oxidative Stress, or do They Induce It? A Telomere Shortening Predisposes to T2DM. Curre Res Diabetes & Obes J 2017; 2(1): 555580. DOI: 10.19080/CRDOJ.2017.2.555580.

20. Sharma S, Kulkarni SK, Agrewala JN, Chopra K (2006) Curcuminattenuates thermal hyperalgesia in a diabetic mouse model of neuropathic pain. Eur J Pharmacol 536(3): 256-261.

21. Sharma R, Euden S, Platton S, Cooke D, Shafaya A, et al. (2004) Phase I clinical trial of oral curcumin: biomarkers of systemic activity and compliance. Clin Cancer Res 10(20): 6847-6854.

22. Suryanarayan P, Satyanarayana A, Balakrishna N, Kumar PU, Reddy GB (2007) Effect of turmeric and curcumin on oxidative stress and antioxidant enzymes in streptozotocin-induced diabetic rat. Med Sci Monit 13(12): 286-292.

23. Seo KI, Choi MS, Jung UJ, Kim HJ, Yeo J, et al. (2008) Effect of curcumin supplementation on blood glucose, plasma insulin, and glucose homeostasis related enzyme activities in diabetic db/db mice. Mol. Mol Nutr Food Res 52(9): 995-1004.

24. Ejaz A, Wu D, Kwan P, Meydani (2009) Curcumin Inhibits adipogenesis in 3T3-L1 adipocytes and angiogenesis and obesity in C57/BL mice. J Nutr 139(5): 919-925.

25. Soto UMG, López S, Pérez VV, Saavedra MA, González HGA, (2014) Curcumin restores mitochondrial functions and decreases lipid peroxidation in liver and kidneys of diabetic db/db mice. Biol Res 22(47): 74.

26. Martínez MA, Soto UMG, Franco RE, Zúñiga TI, Campos CA, et al. (2013) Curcumin decreases oxidative stress in mitochondria isolated from liver and kidneys of high-fat diet-induced obese mice. J Asian Nat Prod Res 15(8): 905-915.

27. He Y, Yue Y, Zheng X, Zhang K, Chen S, (2015) Curcumin, inflammation, and chronic diseases: how are they linked? Molecules 20(5): 9183-213.

28. Von Ziglinicki T, (2000) Role oxidative stress in telomere lenght regulation and replicative senescence. Ann N Y Acad Sci 908: 99-110.

29. Zhou M, Zhu L, Cui X, Feng L, Zhao X, et al. (2016) Influence of diet on leukocyte telomere length, markers of inflammation and oxidative stress in individuals with varied glucose tolerance: a Chinese population study. Nutr J 15: 39.

DOI: 10.19080/CRDOJ.2017.2.555580

How to cite this article: Murillo O B, Martínez G S. Is Telomere Shortening a Genetic Factor That Predisposes to Diabetes Mellitus 2 and Oxidative Stress, or do They Induce It? A Telomere Shortening Predisposes to T2DM. Curre Res Diabetes & Obes J 2017; 2(1): 555580. DOI: 10.19080/CRDOJ.2017.2.555580.