http://dx.doi.org/10.1590/1981-22562017020.160085

Oxidative damage to DNA in independent-living elderly persons and their correlations with sociodemographic, anthropometric, and functional parameters

Gilson Luis da Cunha[1]
Greice Terezinha de Oliveira[1]
Daiane Bolzan Berlese[2]
Geraldine Alves dos Santos[1]

Abstract

Objective: To evaluate the correlations between oxidative DNA damage among elderly persons aged between 60 and 79 years and sociodemographic, anthropometric and functional parameters. *Method:* The present study has a descriptive, quantitative and cross-sectional design. A group of 195 independent-living elderly persons of both genders underwent blood collection and the subsequent measurement of serum concentrations of 8-OHdG, a residue generated by the attack of reactive oxygen species to DNA. The same subjects also underwent evaluation for body mass index (BMI), body fat percentage, the Short Physical Performance Battery (SPPB), and the education level of the participants was analyzed. Statistical analysis was performed using the Spearman correlation test, adopting a 5% significance level. *Result:* Higher fat percentage and BMI are directly correlated with higher concentrations of 8-OHdG, while SPPB and education were inversely correlated with the concentration of this molecule in the sample. *Conclusion:* These results suggest factors such as lifestyle and educational level influenced oxidative DNA damage in these elderly persons and had an impact on their functional capacity.

Keywords: Elderly. Oxidative Stress. Body Mass Index. Anthropometry. Educational Status.

[1] Universidade Feevale, Programa de Pós-Graduação em Diversidade Cultural e Inclusão Social. Novo Hamburgo, RS, Brasil.

[2] Universidade Feevale. Programa de Pós-Graduação em Qualidade Ambiental, Novo Hamburgo. RS, Brasil.

Correspondence
Geraldine Alves dos Santos
E-mail: geraldinesantos@feevale.br

INTRODUCTION

The aging process is marked by a series of metabolic changes, one of which is increased susceptibility to oxidative stress, induced by the decline of mitochondrial respiratory functioning[1-3].

The Oxidative damage generated during the aging process can be evaluated through the measurement of different products. The oxidation of proteins, for example, tends to produce carbonyl and sulfhydryl residues, while malondialdehyde is a product of lipid oxidation. Oxidative DNA damage leads to the production of 8-hydroxy-2'-deoxyguanosine (8-OHdG)[4].

Assessing the levels of oxidative stress and its implications on the health of the elderly is a complex task, as different tissues, and even different cell types, present varying patterns of oxidative stress throughout the aging process[5,6]. However, 8-OHdG is produced by all the cells of the body, with varying intensity, and is continuously released into the bloodstream and excreted in the urine[7,8]. Increased levels of 8-OHdG have been found in different pathologies and chronic-degenerative diseases, including diabetes, different types of neoplasia and Alzheimer's disease[7]. In addition, an increase in the plasma and urinary concentrations of this molecule has been associated with obesity and the loss of muscle mass in the elderly[9,10].

A study by Kocael et al. found that serum levels of 8-OHdG in patients with morbid obesity declined after surgery for the implantation of a gastric band, evidencing a link between obesity and oxidative DNA damage[11].

Considering this and other evidence, the overall objective of the present study was to measure the levels of 8-OHdG found in the whole blood of elderly individuals aged between 60 and 79 years who lived independently, and to evaluate the correlation between the concentrations of this marker of oxidative damage and sociodemographic, anthropometric and functional data.

METHOD

The present study is descriptive, quantitative and cross-sectional in nature, and was carried out in 2015. The estimate of a proportion of a finite population was used to calculate the sample size, with an alpha level of 5%, a sampling error of 5% and a 50% estimate for the distribution of the study variable. By these parameters, the sample for the municipality of Ivoti was estimated at 235 elderly persons. However, this sample calculation was based on the total number of elderly people, while the present study encompassed only elderly residents in the municipality who were not institutionalized, did not present cognitive impairments, and were not physically or psychologically debilitated.

A probabilistic sample was constructed by means of the cluster sampling technique, with the 5 health centers of the municipality used as units. The total sample for Ivoti was 195 elderly persons of both genders, aged between 60 and 79 years, who lived independently in the municipality, which is located in the state of Rio Grande do Sul. Random simple sampling was performed. Elderly persons enrolled in all the health centers of the municipality of Ivoti were invited to participate in the study. The study was carried out in two stages. On their first visit to the health center, the elderly persons underwent blood collection, which was performed by a researcher in the area of Nursing. The anthropometric data and the data from the Short Physical Performance Battery Test (SPPB) were collected at a second appointment, also in the health center, by a Physical Education professional with a specialization qualification in this area. The inclusion criteria were age over 60 years, reside in the municipality of Ivoti, not be institutionalized or hospitalized, and have sufficient mental and health capabilities to possess the independence and autonomy to participate in the study. Dementia or frailty were used as exclusion criteria, and were identified by the professionals from the health center.

The following instruments and techniques were used in data collection:

a) Socio-demographic data: identification data addressing age, sex, nationality, birthplace, profession, schooling, marital status, diseases and general health status.

b) Anthropometric evaluation: Body mass index (BMI) was calculated by the ratio between body mass (kg) and height squared (meters). Total body mass, fat percentage, and height were measured in accordance with World Health Organization standards[12] (23.5% of fat for females and 30.9% for males), and suggested by Heyward and Wagner[13] The Pan American Health Organization (PAHO)[14] recommends the following BMI classification in the elderly: BMI<23 = underweight; 23<BMI<28 = normal weight; 28<BMI<30 = overweight; BMI<30 = obesity. Abdominal obesity is defined by the WHO as a waist circumference >102 cm in men and >0.88 cm in women.

c) *Short Physical Performance Battery Test* (SPPB): this battery was created by Guralnik and the Brazilian version was adapted by Nakano[15]. It is a practical and effective instrument for the evaluation of physical performance and screening of elderly persons with a future risk of disability. The instrument evaluates the performance of the lower limbs in three aspects: muscular strength, gait and balance, as well as reflecting motor planning and the corresponding cognitive strategies. The instrument also allows the early identification of deficits not reported by the elderly or an individual providing information on their behalf. The total SPPB score is obtained by totaling the results of the balance, gait speed and lower limb strength tests and applies the following classification: 0 to 3 points: inability or poor performance; 4 to 6 points: low performance; 7 to 9 points: moderate performance and 10 to 12 points: good performance[16].

d) Detection of 8-OHdG: 8-hydroxy-2-deoxyguanosine (8-OHdG) was detected in serum samples. The KOG-HS10E (Jaica) 8-OHdG detection kit was employed. This is a competitive ELISA assay, which utilizes a monoclonal antibody which is highly specific for DNA damage, with a wavelength reading of 450 nm, and a standard curve interval ranging from 0.125 to 10 ng/ml[17].

Descriptive and inferential statistics were used to analyze the data. The following tests were used: the Chi-squared test to compare gender; the Mann Whitney test to compare age groups; the Spearman Correlation Coefficient to evaluate the relationships of the SPPB variables, abdominal waist classification, fat percentage, 8-OHdG and schooling. A level of significance of $p \leq 0.05$ was considered.

The study was approved by the Ethics Research Committee of the Universidade Feevale under nº. 6.0000.5348. The participants signed a Free and Informed Consent Form in accordance with the guidelines of National Health Council Resolution nº 466/12 of the Department of Health, which deals with research involving human beings.

RESULTS

The most prevalent age group in the sample was 60 to 64 years old (34.8%), and the majority of individuals were female (71.9%). In terms of marital status, the majority (57.4%) of the elderly persons were married or lived with a partner, while there was a significant number of widowers or individuals who were separated (31.1%). The majority (75.4%) of the sample had an incomplete primary education.

Both men and women had higher fat percentage indices than expected: 31.3% and 42.8%, respectively, while women had statistically significantly higher fat percentage indices than men (0.000). Thus, 71.8% of the elderly persons in question had a higher percentage of fat than expected, a worrying number (Table 1).

With regard to the body composition and age group components, there was only a significant difference in terms of the muscle mass and BMI classification results. The elderly persons aged between 60 and 69 years old had a greater percentage of muscle mass (p=0.046) and a higher BMI classification (p=0.018) than those aged between 70 and 79 years.

The mean SPPB score in this study was 7.25 points, with a standard deviation of 2.5. As can be seen in Table 2, the lower the age group, the higher the Balance Test (p=0.019), gait velocity test (p=0.005) and total SPPB (p=0.007) scores.

The majority (45.6%) of participants in the sample of the present study achieved a moderate SPPB classification. Table 3 shows that elderly persons aged 60 to 69 years presented greater functional capacity according to SPPB classification, although there was no significant difference between the groups in terms of gender.

Table 1. Classification of body mass index and fat percentage according to gender. Ivoti, Rio Grande do Sul, 2015.

Variables	Overall n=195 (%)	Male n=55(%)	Female n=140(%)	p
BMI Classification				
Underweight	25 (12.9)	11 (20)	14 (10)	0.006
Normal Weight	76 (38.9)	26 (47.2)	50 (35.8)	
Overweight	30 (15.4)	10 (18.2)	20 (14.2)	
Obese	64 (32.8)	08 (14.6)	56 (40)	
Fat Percentage				
Normal	55 (28.2)	4 (7.3)	7 (5)	0.536
Higher than expected	140 (71.8)	51 (92.7)	133 (95)	

BMI: Body mass index; p=Chi-squared test

Table 2. Distribution of subtests of Short Physical Performance Battery (SPPB) in relation to age group. Ivoti, Rio Grande do Sul, 2015.

	Age group (years)	N	Mean (sd)	p
Balance Test	60 to 69	127	3.02 (±1.306)	0.019
	70 to 79	68	2.56 (±1.418)	
Gait Speed Test	60 to 69	127	3.01 (±0.877)	0.005
	70 to 79	68	2.59 (±1.040)	
Chair Stand Test	60 to 69	127	1.58 (±0.996)	0.440
	70 to 79	68	1.44 (±0.761)	
Total SPPB score	60 to 69	127	7.60 (±2.473)	0.007
	70 to 79	68	6.59 (±2.475)	

p: Mann Whitney Test.

Table 3. Short Physical Performance Battery (SPPB) classification in relation to variables of gender and age group. Ivoti, Rio Grande do Sul, 2015.

	Very poor n=18(%)	Low n=53(%)	Moderate n=89 (%)	Good n=35(%)	Total n=195(%)	p
Gender						
Male	4(22.3)	11(20.7)	25(28.1)	15(42.8)	55(28.2)	0.140*
Female	14(77.7)	42(79.3)	64(71.9)	20(57.2)	140(71.8)	
Age group (years)						
60 to 69	9(50)	32(60.3)	58(65.2)	28(80)	127(65.1)	0.007**
70 to 79	9(50)	21(39.7)	31(34.8	7(20)	68(34.9)	

*p: Chi-squared test; **p: Mann Whitney Test.

Regarding the concentration of 8-OHdG, the present study recorded a mean of 6.89 ng/ml, with a standard deviation of 8.95 ng/ml. The result with the least oxidative damage was DNA, with 0.29 ng/ml. The maximum result found in the sample was 42.85 ng/ml.

Under the conditions of the present study, no differences were found between genders or the ages of the individuals for the concentrations of the oxidative DNA damage marker.

The variable 8-OHdG and the variables BMI (r=0.159, p=0.047) and fat percentage (r=0.177, p=0.027) had a positive correlation. This relationship indicates that among the individuals studied, a higher BMI and fat percentage was associated with a higher the concentration of 8-OHdG.

The 8-OHdG variable had a negative correlation with SPPB test results (r =-0.216, p=0.007) and schooling (r=-0.186; p=0.021), indicating that greater functional capacity was associated with greater concentrations of 8-OHdG.

DISCUSSION

Levels of oxidative DNA damage can vary according to endogenous factors such as age, and exogenous factors such as diet, physical activity and exposure to drugs and pollutants. In the present study, correlations were found between BMI, fat percentage, SPPB and schooling in a sample of elderly people of both genders, aged between 60 and 79 years of age, living in the municipality of Ivoti in the state of Rio Grande do Sul.

The BMI and fat percentage in the sample were directly correlated with the 8-OHdG levels found in the serum of the subjects sampled. This relationship, although it can vary due to environmental and/or genetic influences, represents an overall trend[18]. Consumption of diets rich in calories or fatty acids, obesity, overweight and a sedentary lifestyle are factors frequently associated with increased levels of oxidative stress in different populations[19]. The physiological mechanisms involved in this increase have not been fully elucidated but involve, to a greater or lesser extent, mitochondrial dysfunction and a cascade of metabolic reactions, such as exaggerated inflammatory response, which can lead to chronic and degenerative disorders often found in the elderly population, such as hypertension, diabetes, neoplasia and Alzheimer's disease[18].

In addition to population studies, experimental research also suggests that opposing associations are true: weight loss, consumption of less caloric diets, and regular physical exercise can reduce oxidative stress and the increased inflammatory response associated with it[19]. In addition, data from literature shows that rapid weight loss followed by surgeries for the introduction of gastric banding resulted in a decline in 8-OHdG concentrations excreted in the urine of patients undergoing this procedure[11].

It was decided to measure 8-OHdG from the serum, rather than the urine, of the participants of the present study, given the practicality of collection and reliability in the preservation of the sample. Such efficiency could not be guaranteed in the case of urine collection.

The negative correlation between SPPB and 8-OHdG levels can be interpreted as an adverse effect of weight reduction and fat percentage. With less weight, the subject becomes more agile, which is reflected in the SPPB scores. And with less weight, the individual is less subjected to the cascade of metabolic reactions related to oxidative stress. A 2014 study demonstrated that overall antioxidant capacity correlated positively with the functional performance of the upper and lower limbs among the elderly[20]. The same article suggests that low levels of hemoglobin and deficient antioxidant defenses could significantly affect functional performance, leading to the transition to a pre-frail state among elderly persons. Additionally, oxidative damage to mitochondrial DNA has been identified as one of the main factors responsible for sarcopenia and neuromuscular dysfunctions, through mechanisms such as the failure of mitophagy processes, respiratory chain defects, metabolic disorders and the pathological activation of pro-inflammatory and pro-apoptotic signals, which can contribute to the loss of muscle fibers[21].

Oxidative stress has been the subject of studies which have related it to muscular weakness, the progressive atrophy of the musculature and to the advancement of age, in a mode dependent on cellular redox status[22].

Data from literature indicates that urinary 8-OHdG levels in community-dwelling elderly persons are associated with muscle strength, and that such a finding may be clinically relevant because of the possibility of controlling oxidative DNA damage by adopting healthy lifestyles (diet, physical activity, etc.)[10].

A significant inverse correlation between schooling and 8-OHdG levels was identified in this study, suggesting that individuals with more education and/ or access to information tend to take better care of their health, avoiding harmful behaviors or lifestyles. Although literature requires reviews that directly address the issue of level of education and oxidative stress, different authors have shown a positive correlation between low levels of schooling, smoking, a sedentary lifestyle, low consumption of antioxidant foods, and high levels of oxidative stress[19,11]. Therefore, additional studies should be performed evaluating the other variables cited in research involving 8-OHdG using samples of elderly people, as studies of this population are very scarce. It is also important to consider that the present study is not representative of the population of the municipality, as only people who were not institutionalized and did not present diagnoses of dementia processes or frailty syndrome were selected.

CONCLUSION

The data of the present study presented that, among the studied population, oxidative DNA damage is positively correlated with a tendency to obesity, as indicated by the muscle mass index (BMI) and fat percentage results, and inversely correlated with schooling, probably due to the protective effect of adopting healthy lifestyles among individuals with more access to information. The negative correlation with SPPB may indicate both a secondary effect of BMI and fat percentage on the agility and muscular strength of the subjects analyzed, and to the reduced oxidative damage to the muscular tissue of such individuals, as the loss of muscle mass is often associated with increased levels of 8-OHdG.

The subjects in the present study were not evaluated for lifestyle influences, such as smoking, alcoholism, dietary patterns, quality of life and social relations. Cognitive deficit would also be an interesting factor to evaluate, as it may hamper the adoption of a healthy lifestyle, which can reduce the observed levels of 8-OHdG. The measurement of the biomolecules malondialdehyde, triglycerides, cholesterol, and glucose could help to provide a more accurate metabolic picture of the participants of this study. Therefore, subsequent evaluations of these and other parameters may help to clarify the relative contribution of environmental, cultural and physiological factors to oxidative damage in the individuals studied.

REFERENCES

1. Mikhed Y, Daiber A, Steven S. Mitochondrial oxidative stress, mitochondrial dna damage and their role in age-related vascular dysfunction. Int J Mol Sci. 2015;16(7):15918-53.
2. Dai DF, Chiao YA, Marcinek DJ, Szeto HH, Rabinovitch PS. Mitochondrial oxidative stress in aging and healthspan. Longev Healthspan [Internet]. 2014 [acesso em 4 maio 2016];3:6. Disponível em: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4013820/pdf/2046-2395-3-6.pdf
3. Onyango IG, Dennis J, Khan SM. Mitochondrial dysfunction in Alzheimer's Disease and the rationale for bioenergetics based therapies. Aging Dis. 2016;7(2):201-14.
4. Guo X, Cui H, Zhang H, Guan X, Zhang Z, Jia C, et al. Protective effect of folic acid on oxidative DNA damage: a randomized, double-blind, and placebo controlled clinical trial. Medicine [Internet]. 2015 [acesso em 4 maio 2016];94(45):1872. Disponível em: http://journals.lww.com/md-journal/pages/articleviewer.aspx?year=2015&issue=11110&article=00010&type=abstract
5. Speakman JR, Blount JD, Bronikowski AM, Buffenstein R, Isaksson C, Kirkwood TB, et al. Oxidative stress and life histories: unresolved issues and current needs. Ecol Evol. 2015;5(24):5745-57.

6. Szczesny B, Brunyánszki A, Ahmad A, Oláh G, Porter C, Toliver-Kinsky T, et al. Time-dependent and organ-specific changes in mitochondrial function, mitochondrial DNA integrity, oxidative stress and mononuclear cell infiltration in a mouse model of burn injury. PLoS One [Internet]. 2015 [acesso em 4 maio 2016];10(12):1-26. Disponível em: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4668069/pdf/pone.0143730.pdf

7. Yadav UC, Rani V, Deep G, Singh RK, Palle K. Oxidative stress in metabolic disorders: pathogenesis, prevention, and therapeutics. Oxid Med Cell Longev [Internet]. 2016 [acesso em 4 maio 2016]. Disponível em: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4753342/pdf/OMCL2016-9137629.pdf

8. Kobayashi S, Myoren T, Oda S, Inari M, Ishiguchi H, Murakami W, et al. Urinary 8-hydroxy-2'-deoxyguanosine as a novel biomarker of inflammatory activity in patients with cardiac sarcoidosis. Int J Cardiol. 2015;190:319-28.

9. Al-Aubaidy HA, Jelinek HF. Oxidative DNA damage and obesity in type 2 diabetes mellitus. Eur J Endocrinol. 2011;164(6):899-904.

10. Muzembo BA, Nagano Y, Eitoku M, Ngatu NR, Matsui T, Bhatti SA, et al. A cross-sectional assessment of oxidative DNA damage and muscle strength among elderly people living in the community. Environ Health Prev Med. 2014;19(1):21-9.

11. Kocael A, Erman H, Zengin K, Kocael PC, Korkmaz GG, Gelisgen R, et al. The effects on oxidative DNA damage of laparoscopic gastric band applications in morbidly obese patients. Can J Surg. 2014;57(3):183-7.

12. World Health Organization. Obesity: prevention and managing the global epidemic. Report of a WHO consultation. Geneva: WHO; 2000.

13. Heyward VH, Wagner DR. Applied body composition assessment. Ilinois: Human Kinetics; 2004.

14. Lebrão ML, Duarte YAO, organizadores. SABE – Saúde, Bem-Estar e Envelhecimento. O projeto SABE no Município de São Paulo: uma abordagem inicial [Internet]. Brasília, DF: Organização Pan-Americana da Saúde; 2003 [acesso em 4 maio 2016]. Disponível em: http://www.paho.org/bra/

15. Nakano MM. Versão brasileira da Short Physical Performance Battery – SPPB: adaptação cultural e Estudo da confiabilidade [dissertação]. Campinas: Universidade Estadual de Campinas; 2007.

16. Silva TO, Freitas RS, Monteiro MR, Borges SM. Avaliação da capacidade física e quedas em idosos ativos e sedentários da comunidade. Rev Bras Clin Med. 2010;8(5):392-8.

17. Shi GX, Liu CZ, Wang LP, Guan LP, Li SQ. Biomarkers of oxidative stress in vascular dementia patients. Can J Neurol Sci. 2012;39(1):65-8.

18. Cadet J. Oxidative degradation pathways of cellular DNA: product formation and mechanistic insights. Free Radic Biol Med [Internet]. 2014 [acesso em 4 maio 2016];75(Suppl 1):1-2. Disponível em: http://www.sciencedirect.com/science/article/pii/S0891584914010995

19. Black CN, Bot M, Scheffer PG, Penninx BW. Sociodemographic and lifestyle determinants of plasma oxidative stress markers 8-OHdG and F2-Isoprostanes and associations with metabolic syndrome. Oxid Med Cell Longev [Internet]. 2016 [acesso em 4 maio 2016]. Disponível em: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4781979/pdf/OMCL2016-7530820.pdf

20. Caballero B, Rubio-González A, Potes Y, Martínez-Reig M, Sánchez-Jurado PM, Romero L, et al. Associations of the antioxidant capacity and hemoglobin levels with functional physical performance of the upper and lower bodylimbs. Age (Dordr). 2014;36(2):851-67.

21. Rygiel KA, Picard M, Turnbull DM. The ageing neuromuscular system and sarcopenia: a mitochondrial perspective. J Physiol. 2016;594(16):4499-512.

22. Powers SK, Morton AB, Ahn B, Smuder AJ. Redox Control of skeletal muscle atrophy. Free Radic Biol Med [Internet]. 2016 [acesso em 4 maio 2016];98(2016):208-17. Disponível em: http://www.sciencedirect.com/science/article/pii/S0891584916000721

Received: May 23, 2016
Reviewed: October 17, 2016
Accepted: March 09, 2017