FOOD REGIMES AND OXIDATIVE STRESS: A STATISTICAL ANALYSIS BASED ON PERMUTATION SOLUTION.

Angela Alibrandi¹, Agata Zirilli¹, Campennì Alfredo², Cannavò Salvatore³, Ruggeri Rosaria Maddalena³

¹ Department of Economics, Unit of Statistical and Mathematical Sciences - University of Messina

² Department of Biomedical, Dental and Morphological and Functional Imaging Sciences- University of Messina ³Department of Human Pathology of Adults and Developmental Age "G. Barresi" - University of Messina

INTRODUCTION

Oxidative stress is a dangerous process that occurs when excess free radicals accumulate in tissues and cells; it represents a consequence of the lack of balance between oxidant and antioxidant agents [1].

Free radicals are normally products of cellular metabolism and are essential elements in numerous enzymatic and metabolic processes, when at low levels. Under normal physiological conditions there is "redox homeostasis", i.e. a balance between the production and removal of free radicals.

Conversely, when there is an excess of free radicals, due to their overproduction or inadequate removal, oxidation of macromolecules (proteins, lipids and DNA) occurs. In this way the structure undergoes an alteration that inhibits normal functions. These oxidative changes cause cell injury, which results in inflammation and tissue damage [2, 3], determining a condition of oxidative stress (OS) [2-5].

The modern lifestyle, associated with unhealthy eating habits, sedentary lifestyle, psychological stress, high exposure to chemical substances (such as environmental pollutants, smoke, etc...) can favor the onset of an OS condition, which in turn can lead to a greater chronic disease risk in industrialized societies [3, 6]. In particular, changes in eating habits constitute one of the main causes of pathologies, also linked to the increase in OS.

PURPOSE

In this background the main purpose of this paper is to analyze the possible relation between dietary regimes and oxidative stress parameters. More specifically, we evaluated possible differences between subjects with a variegate diet (omnivorous) and subjects with a diet mainly based on the consumption of foods of vegetable nature (semivegetarians), with reference to some oxidative stress markers, measured on plasma samples: SOD, GR, GPx, TRxR, AGEs and AOPPs.

METHODS

Certainly in nature the subject omnivores are more numerous than the semi-vegetarians; a statistical comparison based on parametric assumptions does not guarantee valid results due to the absence of the balancing condition. As a methodologically valid solution to this research condition, we decided to apply the Non Parametric Combination (NPC) methodology, based on permutation tests [7]. It allows to perform statistical comparison when the sample sizes are unbalanced, it is free from distributional assumptions e, also, allows to perform stratified analyses.

By means of NPC test, all comparisons between omnivorous (139 subjects) vs (semi)vegetarians (61 subjects) were performed stratifying for gender (male vs female), age class (\leq 40 vs > 40 years), BMI class (normal weight vs overweight), TSH (low vs high), FT4 (low vs high), diagnosis of Hashimoto's Thyroiditis (yes or no) and physical activity (sedentary vs active lifestyle).

Both for THS and FT4 we merged the observations that fall within the first two quartiles (indicating them as Low) and those that fall within the last two quartiles (indicating them as High). More specifically, quartile boundaries for TSH were < 1.40, 1.41–1.98, 1.99–2.80 and >2.81 mU/l; quartile boundaries for FT4 were <14.46, 14.47–15.8, 15.9–17.1 and >17.32 pm/L.

RESULTS

By means of NPC test, we have been able to identify statistically significant differences especially with reference to two oxidative stress parameters: GPx and TRxR. In particular, they are significantly higher in vegetarians compared to omnivorous in female subjects (p=0.016 and p=0.001 respectively), in subjects with an age \leq 40 years (p=0.026 and p=0.005 respectively) and also with age > 40 years (p=0.030 and p=0.012, respectively), in subjects with normal weight (p=0.006 and p=0.001 respectively), in subjects with low TSH levels (p=0.044 and p=0.005, respectively) and high TSH levels (p=0.047 and p=0.028, respectively), subjects with low FT4 levels (p=0.012 and p=0.019, respectively), in subjects not affected by Hashimoto's thyroiditis (p=0.036 and p=0.003, respectively) and, with reference to physical activity, in sedentary subjects (p=0.041 and p=0.018, respectively) and in active lifestyle subjects (p=0.043 and p=0.003 respectively). We also found that AGEs were significantly lower in (semi)vegetarians over 40 years old (p=0.042). In addition, semi-vegetarians show significantly higher AOPPs values than omnivores within the strata of subjects with normal weight (p=0.047) and low FT4 levels (p=0.031).

CONCLUSION

Our paper, based on the application of the multivariate and multistrata NPC methodology, allowed to identify some interesting relationships between oxidative stress parameters and dietary habits. More specifically, oxidative stress parameters were compared between omnivores and semi-vegetarians, stratifying for some confounders, considered relevant for the purposes of the analysis.

The obtained results show that, among all examined parameters, GPx and TRxR play a particular role into discriminating omnivores and semi-vegetarians. As a further result, we found that AGEs are significantly lower in (semi)vegetarians than in omnivores, and in particular, in the over 40-year-old stratum. It is known that high values of AGEs have negative effects as they favor the development of certain pathologies affecting the metabolic system, for which the semi-vegetarian diet, in subjects over 40 years old, would seem to have a protective effect.

Finally, semi-vegetarians of normal weight and with low FT4 levels show higher AOPP values than omnivores; therefore, the protein products of late oxidation would seem to characterize those who have a diet based on the use of products of a vegetable nature, without problems related to obesity or to the load of the endocrinological system (FT4 low levels). Therefore, we can say that changing eating habits, mostly preferring foods of plant origin, can be a useful strategy to counteract oxidative stress.

BIBLIOGRAPHY

- 1. Valko M., Leibfritz D., Moncol J. et al., Free radicals and antioxidants in normal physiological functions and human disease. Int J Biochem Cell Biol. 2007, 39, pp. 44–84, <u>doi: 10.1016/j.biocel.2006.07.001</u>
- McCord JM. Human disease, free radicals, and the oxidant/antioxidant balance. Clin Biochem. 1993 Oct;26(5) pp. 351-7. doi: 10.1016/0009-9120(93)90111-i.
- 3. Ruggeri RM., Campenni A., Giuffrida, G. et al., Oxidative stress as a key feature of autoimmune thyroiditis: an update. Minerva Endocrinol 2020; 45(4) pp.326-43 doi: 10.23736/S0391-1977.20.03268-X.
- Steinbrenner H., Speckmann B., Klotz LO, Selenoproteins: antioxidant selenoenzymes and beyond. Arch Biochem Biophys. 2016 Apr 1; 595:pp. 113-119. doi: 10.1016/j.abb.2015.06.024.
- 5. Sies H., Oxidative stress: a concept in redox biology and medicine. Redox Biol. 2015; 4. pp.180-183. doi: 10.1016/j.redox.2015.01.002.
- Sharifi-Rad M., Anil Kumar NV., Zucca P. et al., Lifestyle, Oxidative Stress, and Antioxidants: Back and Forth in the Pathophysiology of Chronic Diseases. Front Physiol. 2020 Jul 2;11:694. <u>doi: 10.3389/fphys.2020.00694</u>.
- 7. Pesarin F, Permutation Tests for Complex Data: Theory, Applications and Software, 2010, Wiley