Short communication

# Indicators of oxidative stress in long-lived individuals belonging to the municipality of Santa Clara

Douglas Fernández Caraballo[1*]
Manuela Herrera Martínez[1]
Danay Heredia Ruiz[1]
Sonia Chaviano Machado[1]
Emilio González Rodríguez[1]

[1]Universidad de Ciencias Médicas de Villa Clara, Cuba.

[*]Autor de correspondencia: (douglasfc@infomed.sld.cu)

## ABSTRACT

**Aim:** To determine indicators of oxidative stress in long-lived individuals.

**Methods:** 120 subjects were studied and two groups were formed: 50 individuals older than 85 years of nuclear families and 70 adults under 60 years old taken as a control group, all belonging to the municipality of Santa Clara. Indicators of antioxidant defense status included enzymatic activities superoxide dismutase (SOD) and catalase (CAT), as well as reduced glutathione (GSH) concentrations. The determinations were made with the use of spectrophotometric techniques, and the comparisons between the groups were made through the statistical program SPSS with a level of significance of 95%.

**Results:** The activity of the antioxidant enzyme SOD and GSH levels showed significant differences when comparing both study groups. In the case of the SOD enzyme, the group of long-lived individuals showed a significant reduction in their activity compared to the controls, while GSH levels also decreased in this group. The CAT enzyme activity showed no significant differences between the two study groups.

**Conclusions:** The decrease in enzymatic activity SOD accompanied by a decrease in GSH levels could be an indicator of a state of oxidative imbalance in individuals older than 85 years, which increases their susceptibility to the action of reactive oxygen species.

**Keywords:** oxidative stress; longevity; enzymatic antioxidant system.

# INTRODUCTION

Studies on oxidative stress (OS) are among the leading research in the field of medical sciences due to its wide application in the reduction of damage caused by free radicals (FRs). These FRs are produced from molecular oxygen, starting with the superoxide anion ($O_2^{\cdot -}$) and hydrogen peroxide ($H_2O_2$), and their conversion into powerful oxidants, such as hydroxyl radical ($^{\cdot}OH$) and peroxynitrite ($OONO^{\cdot -}$). When the generation of oxygen free radicals surpasses the numerous barriers of antioxidant defenses of the organism, there is an increase in the damage to the biological structures due to chemical injuries. This process is called OS and it is defined as an imbalance of antioxidant defenses with respect to the increased production of reactive species which intervene in multiple pathophysiological situations.[(1,2)]

The response to OS can play an important role in aging. The greater generation of reactive oxygen species (ROS) with age exceeds the antioxidant response and imposes a fragile state to the elderly individual, which increases the risk of infection, diseases related to age, disability and death.[(2)]

The theory of FRs in aging states that aerobic metabolism produce incidentally and uncontrollably radicals spices derived from oxygen that, once generated, promote reactions that damage macromolecules. This irreversible damage accumulates over time resulting in a gradual loss of functional capacity of the cell.[(2)]

Antioxidant molecules that constitute a defense system in living organisms act at different levels. These levels can be radical preventatives, radical elimination and repair of radical-induced damage.[3]

Numerous studies have been conducted to determine if antioxidant defenses decline with age. Among them, the analysis of the main components of these: activity or expression of antioxidant enzymes and the concentration of low molecular weight compounds with antioxidant properties.[4]

The presence of an inverse correlation between some antioxidants and the pathologies of aging indicate that very soon the determinations of antioxidant defenses will be part of the studies that evaluate the risk profile of an individual.[5]

## Aim

To determine indicators of oxidative stress to a sample of long-lived individuals belonging to the municipality of Santa Clara.

# METHODS

A basic transversal analytical research was carried out with case and control design, during the year 2018, which was developed in the Blood Chemistry Research Laboratory of the Biomedical Research Unit, belonging to the University of Medical Sciences of Villa Clara.

To study of OS parameters, enzymatic activities superoxide dismutase (SOD) and catalase (CAT) were quantified, as well as levels of reduced glutathione (GSH).

A total of 120 samples were studied, conforming two groups. The first consisted of 50 individuals older than 85 years, of them 31 women and 19 men belonging to the municipality of Santa Clara and a second group consisting of 70 individuals less than 60 years, of them 38 women and 32 men belonging to the same municipality, taken as a control group.

Once the consent of the individuals selected for the investigation was obtained and under the condition of fasting, the extraction of 5 ml of peripheral total blood was carried out, poured into glass tubes with anticoagulant and the plasma was obtained for the determinations.

Determination of SOD activity was performed by the kinetic method described by Marklund (1990), CAT by Aebi (1974) and the concentration of GSH by Beutler (1986).

The analysis of the data obtained was carried out through the statistical program SPSS version 18.0. From a database, the group statistics for each variable under study were determined and applied as a Chapiro Wills goodness of fit test, demonstrating that the data did not comply with a normal distribution ($p<0.05$). For the comparison of mean ranges, nonparametric tests were used, specifically the Mann-Whitney test for $p<0.01$ and $p<0.05$.

The research was designed taking into account the ethical aspects for human work, approved by the Center's Ethics Committee. The multidisciplinary team of researchers gave the real and objective explanations of the study to the individuals included in it, who issued their authorization in writing, respecting the principle of autonomy.

# RESULTS

The antioxidant activity of SOD enzyme and GSH levels showed significant differences between both study groups. In case of SOD activity, the long-lived group showed a statistically significant reduction ($p=0,033$) compared to controls, while GSH levels also decreased in this group ($p=0,043$). The enzymatic activity CAT did not present differences between both groups.

# DISCUSSION

The theory of OS of aging predicts that the loss of SOD activity should result in an increased sensitivity to OS, since the organism would be less able to detoxify ROS. This should, in turn, result in shortened life expectancy. This is essentially what is observed in yeast, flies and mice for both cytoplasmic SOD and mitochondrial SOD. In yeast, the elimination of sod1 has been shown to decrease clonal and replicative life and accelerate chronological aging. In flies Knockout for Sod1 life expectancy decreases. In mice, the targeted inactivation of this enzyme produces high OS and a decrease in life expectancy.[6,7]

The differences between the studies referring to SOD activity or expression prevent arriving at a definitive conclusion. The references on the behavior of the activity of this enzyme during aging are contradictory. Numerous studies have shown no changes in activity or expression with age, while other authors report a decrease or increase.[8]

These divergences in results about SOD activity determination can be caused by differences between species, conditions of the animal's habitat and by technical procedures used.

On the other hand, it has been reported that during aging the concentrations of glutathione decrease, which could indicate that the decrease of this could predispose for the development of neurodegenerative diseases typical of this age group. Different authors have shown that GSH concentrations in various tissues of murine origin decrease significantly with age; similar results have been observed in insects.[9]

Glutathione has important functions as an antioxidant, is an important part of the detoxification of xenobiotics, is a cofactor for isomerization reactions and also serves as storage and transport of cysteine. In addition, it is essential for cell proliferation and has an important role in apoptosis, since the decrease in the amount of glutathione favors the activation of caspases and the progression of apoptosis mechanisms. A very important function of glutathione is to maintain the oxide-reduction potential of the cell, since it keeps the thiol groups of the proteins in a reduced state and thus allows the generation of various cascades of intracellular signaling; an example is protein kinase C, which contains several tyrosine residues in its catalytic center, which give it sensitivity to the redox state of the cell, which can affect the signaling mediated by this enzyme.[10]

# CONCLUSIONS

The decrease in enzymatic activity SOD accompanied by a decrease in GSH levels could be an indicator of a state of oxidative imbalance in individuals older than 85 years which increases their susceptibility to the action of reactive oxygen species.

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