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Exercise-induced oxidative stress in rats intestine

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Abstract. By activating or blocking specific molecular mechanisms, physical effort contributes directly or indirectly to regulating the functional activity of many structures, the central nervous system being followed by the cardiovascular system, digestive system, endocrine system, and finally, but having the same importance, the reproductive system. However, during physical exertion the body goes through many molecular stages that can harm and influence in the first instance the adaptive response to physical effort or can act locally on the functioning of organs directly involved in sustaining physical exercise or indirectly in post-exercise metabolic recovery. The intestine is part of the structures involved in the metabolic recovery of the body after effort and is directly involved in the phenomenon of adaptive response to physical exertion. The oxidative stress induced by physical effort can also occur in the intestine and the main mechanisms involved in this role are; the phenomenon of ischemic reperfusion and local biochemical changes. In the case of the experimental model studied, the dynamics of superoxide dismutase and catalase enzymes, as well as the tissue level of glutathione indicate the installation of the phenomenon of low-intensity oxidative stress associated with physical exertion.
Keywords: *exercise, oxidative stress, intestine, swimming.*

Introduction

Experiments aimed at studying oxidative stress in different types of physical exertion were summarized in the biochemical and molecular aspect of redox balance in striated or cardiac muscle, without taking into account the humoral or connectivity connections, that skeletal muscle has them with the organs involved in post-effort energy recovery or the set of mechanisms that contribute to the elimination or reuse of metabolic products.

An important aspect is the mechanisms involved in signaling muscle overload and the metabolism of factors and hormones synthesized progressively during physical exertion or post exertion.

A series of mechanisms that reduce the response to adaptability to physical exertion may have as a physiological basis the accumulation of hormonal metabolites or the inability of receptors to bind them specifically and implicitly to the overload of specialized structures in their metabolism. Catecholamines are synthesized in progressive amounts during exercise and post-exercise, their metabolic rate is relatively low and involves a high biofunctional and energetic effort which contributes to increasing their duration of action and thus reducing the recovery time after exercise.

The mechanism of regulation of stress hormone levels after exercise is conditioned by the ability of the liver to metabolize, while the muscular energy component is directly influenced by the glucoforming function of the liver. It is not known in detail or partially whether the two events related to liver function can compete or whether one of the biochemical pathways synthesizes precursors with an inductive effect on the other. By activating or blocking specific molecular mechanisms, physical effort contributes directly or indirectly to regulating the functional activity of many structures, the list being the central nervous system, followed by cardiovascular, digestive and finally but having the same importance reproductive system. However, during physical exertion the body goes through many molecular stages that can harm and influence in the first instance the response to adaptability to physical exertion or can act locally on the functioning of organs directly involved in supporting physical exertion or indirectly in post-exercise metabolic recovery.

No experimental study as a whole aims at the reaction of adaptability to physical effort or the communication between the organs directly involved in the support of physical effort and those directly responsible for post-exercise recovery. Such a study would clarify to some extent the functional link dictated by factors and hormones that also involve the blood vehicle in the adaptive metabolic and functional post-effort response.

The association of physical effort with a number of physiological benefits indicates the molecular involvement or increase in the rate of synthesis of inducers capable of regulating or correcting mechanisms in a sleeping state or nutritionally influenced.
The nutritional path is again a desideratum of the studies aiming at the antioxidant effect of the different compounds on the structures directly involved in the support of the physical effort. The antioxidant effect induced by numerous compounds on skeletal muscle subjected to physical exertion is known and published at high speed in the last 20 years (1-4). Currently, the benefits of the associated physical effort and the concept of movement are oriented towards the pathologies known and generically integrated in the diseases of the 21st century; depression, metabolic diseases and cancer (5-8). Pathologies that no longer take into account age, sex, inclusion or exclusion criteria used in clinical trials mainly.
Another extremely important problem from a social and economic point of view is biological aging. The speed of biological aging is directly influenced by culture, socio-economic environment but also by individual biological conditions imposed socially or medically conditioned, which cannot be included in the broad categories of factors. Biological aging is a complex process that also targets socio-economic aspects, not only those related to the passage of time.
Another important direction related to physical effort and the concept of healthy lifestyle is the metabolic syndrome that leads to the declassification of metabolic pathologies that can be partially controlled by physical effort, an example is type 2 diabetes. In type 2 diabetes studies, experiments have shown that oxidative stress plays a key role in both the onset of the pathology and the evolution over time. However, the molecular biochemical mechanism by which oxidative stress is induced in the pre- or post-onset phase in type 1 or 2 diabetes is not well known.
Related to the metabolic syndrome, the intestine is the structure at the level of which transport-induced phenomena appear but also by microbiosis which inevitably lead to the installation and prolonged support of the oxidative stress state (9-11). During the physical effort, mechanisms capable of inducing an increase in the level of free radicals of oxygen are activated, and implicitly under certain conditions it is possible to reach the installation of the oxidative stress phenomenon (12-14).
The mechanism of oxidative stress is intensively studied and currently most of the molecular mechanisms by which physical effort induces the alteration of the balance between oxidants and pre-oxidants are known (15). However, physical exertion is recommended in the management of metabolic pathologies and not only. The mechanisms involved in the control of physical exertion-induced glycemia in subjects with hyperglycemia or peripheral glucose resistance syndrome are not known in detail. However, most studies cited in the literature indicate the benefits of physical exertion in the management of these pathologies (16-18).
Another class of pathologies in the field of digestion is inflammatory bowel disease, which according to some studies is based on phenomena associated with oxidative stress (19). Research topics that include bowel and physical exertion take into account to a small extent the potential sources of oxygen and nitrogen free radicals that can induce the alteration of the antioxidant response and the installation of the phenomenon of oxidative stress.
Another very important detail is the microbiosis, which has a key role in the association and intensity of oxidative stress induced by physical exertion in the intestine and glands attached to the digestive tract. The experimental study aims to explain the mechanism by which physical effort induces the change in the dynamics of oxidative stress parameters in the intestine of Wistar rats subjected to a single training, swimming, for 60 minutes.

Material and Method

Biologic material used: the animals used in our experimental model were Wistar albino rats, males. The animals were accommodated respecting the norms imposed by the legislation.
This study was conducted in compliance with the norms of ethics and methodology of experimental research on two research groups:
- control group (M) (n=6) without physical training (serving as reference for the experimental group);
- experimental group (Exp) (n=6) with one physical training session (swimming in a pool with water heated at 28 ^{o}C ± 2 ^{o}C) for 60 minutes.

The animals were sacrificed with respect to the legislation of animal protection. The samples of intestine tissues were taken immediately after slaughtering.

Analyzed parameters from the tissues were: superoxide dismutase (SOD) activity, catalase (CAT) activity, glutathione (GSH) concentration and total protein concentration (TPC).
The superoxide dismutase activity assay. This method is based on the superoxide dismutase capacity to inhibit the reduction of NBT (nitro blue tetrazolium) by the free radicals. One enzymatic unit (EU) is the enzyme amount that induces a 50% inhibition in standard conditions. Free oxygen radicals are generated through riboflavine photo-reduction (20,24).
Catalase activity was measured by the spectrophotometer method of Beers (1952), based on the descomposition of H2O2 (21,24).
Glutathione (GSH) were analyzed in the tissue, using spectrophotometric determination, previously described by Beutler 1975 (22,24).
Protein concentrations in the tissue homogenates were determined by the spectrophotometrical methods described by Lowry (23,24).
Data were processed in the program OriginPro7.5. The significance threshold was set at $p \leq 0.05$.

Results

The research results are presented in Table I.

Table I. The activity of the superoxide dismutase, catalase and reduced glutathione concentration in rat intestine tissue

Group		SOD EU/mg protein	CAT EU/mg protein	GSH mcg/mg protein
Control group (M)	X±ES	4.02±0.40	0.79±0.14	1.58±0.25
	n	5	6	6
Experimental Group (Exp)	X±ES	5.60±0.18	1.09±0.14	1.82±0.18
	n	6	6	6
	t	4.23	-	-
	p≤	0.01	NS	NS

X±ES = mean± standard error; n = the number of individual samples that represented the arithmetic mean at the end; t = the value of the "t" test taken by the student; p = the threshold of significance established on the basis of the "t" value; NS = insignificant change.

Discussion and conclusion

Physical exertion is increasingly becoming a key tool in the treatment but especially in the prevention of many medical conditions, including rheumatoid arthritis, diabetes, cancer, depression and digestive diseases, pathologies considered as diseases of the century.
The oxidative stress induced by physical effort remains an area of real interest for research but also for the clinical community. Oxidative stress is characterized by increased levels of free radicals of oxygen and nitrogen and their ability to reduce or inactivate the ability of the antioxidant cell defense system, which in turn consists of an enzymatic component that includes enzymes such as superoxide dismutase, catalase, peroxidase and other primary or secondary enzymes with antioxidant role, and from the non-enzymatic component consisting of constituents with antioxidant role such as vitamin A, C, E, reduced glutathione or some phytocomponents (25,26).
An example of an extremely studied phytocomponent and whose antioxidant effect is the subject of many studies is resveratrol. Recent experimental studies have shown that at physiological concentrations, free oxygen radicals are involved in redox signaling and cell survival by activating or inhibiting the synthesis of key enzymes or proteins in the process of apoptosis (27). However, above the reference limit, oxygen free radicals induce changes or damage to DNA, proteins and lipids that irreversibly lead to the onset of the apoptosis process.
The pancreas is a structure with a cellular community capable of mixed endocrine and exocrine synthesis. In the first phase, we cannot associate in any way the direct involvement of the pancreas in the physical effort. However, the pancreas is part of the structures involved in the metabolic recovery of the body after exertion and is directly involved in the phenomenon of adaptive response to physical exertion.

The oxidative stress induced by the physical effort can also appear at the level of the pancreas and the main mechanisms involved in this role are the phenomenon of ischemic reperfusion and on the insular and acinar synthesis. Post ischemic reperfusion is a phenomenon that occurs in the abdominopelvic organs during intense physical exertion, when blood flow is sent to structures directly involved in supporting physical exertion such as skeletal muscles and when physical exertion decreases in intensity or vascular compensatory phenomena occur. A large volume of blood enters the temporarily deprived organelles of blood flow and as a result the synthesis of oxygen and nitrogen free radicals increases on a background of stress dictated by the decrease of the partial pressure of oxygen or by the gradual increase, phenomena encountered in reperfusion and post reperfusion.

Another potential cause of the installation of the phenomenon of oxidative stress in the pancreas is the endocrine oversynthesis as an adaptive compensatory response to physical effort. In both cases, the phenomenon of oxidative stress can be installed, which is characterized by the modification of the activity of antioxidant enzymes with induced synthesis, but also of compounds with non-enzymatic antioxidant effect.

The intestine is part of the category of organs involved in restoring the body post effort as well as the pancreas, in the case of the intestine the mechanisms involved in the installation of oxidative stress are more complicated because it involves the activity of microbiosis that plays a well established role in the equation.. The phenomenon of post ischemic reperfusion is much more important in the small intestine compared to the pancreas or other abdomino-pelvic structure because it induces the functional alteration of trans membranous transport, changes the biological dynamics of the intestinal microbiota and the enterohepatic circuit.

The literature is poor in experimental models to indicate the potential correlations between physical effort, oxidative stress, microbiota balance and its role as an immune signal. However, there are studies that show that physical effort has statistically significantly improved the biological condition of individuals with inflammatory bowel disease, but the mechanism involved remains unknown in detail (28).

Due to the potential connections and involvement in post-exercise body recovery, we chose to compare and explain the potential mechanisms involved in the installation of the phenomenon of oxidative stress induced by physical effort in the small intestine and pancreas. In the case of the experimental model, a dynamics of the biochemical parameters taken into account can be observed, which indicates the installation of the phenomenon of low-intensity oxidative stress. The dynamics of biochemical parameters explain the ability of the intestinal antioxidant system to react specifically and reduce the level of oxygen free radicals to the safety limit against the installation of oxidative stress in the intestine. We cannot omit the possibility that the experimental model has a high intensity, time and type of physical effort not to synthesize through the specific sites a high concentration of oxygen free radicals. The mechanism by which physical effort induces oxidative stress in the intestine and glands attached to the digestive tract remains an open research topic.

The experimental study provides practical evidence that the small intestine is a potential target for the phenomenon of oxidative stress induced by physical exertion. Due to the limitation, the links between physical exertion, microbiosis and oxidative stress have not been identified. Therefore, the study is an important pillar for future research to assess physical effort on bowel function.

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