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YOGA PRACTICE AS AN IMPROVEMENT FACTOR FOR BIOMARKERS OF OXIDATIVE STRESS IN INDIVIDUALS WITH CHRONIC DISEASES

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Abstract: Oxidative stress (OS) is defined as an imbalance between oxidative and antioxidant systems in favor of the former, due to the excess of free radicals (FR) or at the expense of its removal. Chronic oxidative damage to different cellular components exerts an important role in cell aging and in the pathophysiology of chronic non-transmissible diseases. The role of physical exercise in combating OS is evident, especially in moderate exercises, as an inducer of the antioxidant system. Yoga is an integrative practice capable of being incorporated as a resource in reducing risk factors and treating chronic diseases. The aim of this study was to evaluate the effects of yoga on biomarkers of OS in individuals with chronic diseases. A systematic review of the literature was carried out, using articles available in the PubMed and Cochrane. "databases, using the descriptors "yoga and oxidative stress" and as a filter was used, respectively, "Clinical Trial" and "Controlled clinical trial". Yoga is a widely accessible economic practice, and it was well tolerated by the participants of the interventions that were evaluated. The results found in the studies showed that yoga can help the control of the OS in individuals with several chronic diseases like metabolic syndrome, depression, chronic obstructive pulmonary disease (COPD), type 2 diabetes, rheumatoid arthritis, hypertension and Parkinson's disease. The Yoga benefits mainly in some OS biomarkers like malondialdehyde (MDA), superoxide dismutase (SOD), reactive oxygen species (ROS), total antioxidant capacity (TAC) and thiobarbituric acid reactive substances (TBARS). There was a diversity in the measures of OS biomarkers, also, there was an increase in the antioxidant biomarkers and a decrease in the oxidation biomarkers. In conclusion, Yoga benefits in OS are positive in most of the analyzed cases. However, there was a need for further studies regarding the relationship between Yoga and OS.
Keywords: Chronic diseases. Oxidative stress. Yoga. Superoxide dismutase. Reactive oxygen species.

INTRODUCTION

Oxidative stress (OS) is defined as an imbalance between oxidative and antioxidant systems in favor of the former, due to the excess of free radicals (FR) or at the expense of its removal. The results for this process is the formation of several reactive species that are the radicals (RL) and the non radicals. The RL are constantly produced in normal cellular metabolism, designating a physiological process and performing various significant biological functions, with mitochondria being the main source of RL through the electron transport chain OS has also been reported chronic diseases such as metabolic syndrome, depression, chronic obstructive pulmonary disease, type 2 diabetes and hypertension (BELENGUER-VAREA et al.., 2019; ATROOZ; SALIM, 2020)

Damage resulting from OS occurs through biological molecules' oxidation, notably lipids, proteins, and nucleic acids, with loss of physiological functioning, structural composition, and homeostasis due to cellular and tissue injuries. Chronic oxidative damage to different cellular components exert an essential role in cellular aging, mutation, oncogenesis, and the pathophysiology of chronic non-transmissible diseases, including cancer, atherosclerosis, diabetes, arthritis, cataracts, obesity, and neurodegenerative disorders The RLs can be endogenously, or induced by exogenous sources, such as diet, physical activity, smoking, alcohol and other factors. Similarly, antioxidant may have an endogenous or dietary origin (PELUSO et al. 2020; Jakubczyk et al. 2020)

On the other hand, as a defense mechanism to the imbalance of the oxidizing system,

the organism has developed an antioxidant protection system, which in turn, has the function of neutralizing the reactive compounds and consequently, prevent the harmful effects of OS, since all the cells of the human body are exposed and susceptible to oxidation processes The physical activity, especially moderate intensity exercise, as such yoga is a important an inducing agent of the antioxidant system and combating OS. Antioxidants are natural free radical scavenging systems, enzymatic or not. Endogenous examples are SE-glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD2) or, non-enzymatically, such as glutathione (GSH), histidine peptides, iron-bound proteins such as transferrin and ferritin, and dihydrolipoic acid. Besides these endogenous agents, there are also antioxidants obtained from the diet, such as α-tocopherol, β-carotene, ascorbic acid, and phenolic compounds. When free radicals are in excess exceeding the body's capacity to neutralize them, they become harmful and this happens in countless chronic diseases. Stimulating antioxidant agents is essential to maintain this balance. (FALKENBERG; EISING; PETERS; 2020; THIRUPATHI: PINHO; CHANG, 2020; KRUK et al 2019)

Yoga presents variations of techniques, each with its methodological particularities, which consist of various components such as physical postures (asanas), breath control (pranayama), meditation (dhyana), the awakening of energy, alignment, flexibility, vibration, and repetition of sounds (mantras). The practice of yoga can be considered as a physical, respiratory, and mental exercise, relaxing and contracting muscles, causing, with its postures, a self-massage over the endocrine glands, expanding the breathing capacity, and exercising the cognitive part and attention, through meditation. This is an integrative and complementary practice as a non-drug therapy that can be incorporated as a resource in reducing risk factors and treatment of chronic diseases.It was included by the World Health Organization (WHO) in the set of Mind-Body Practices. Therefore, its implementation in public health services is recommended and yoga is a valuable tool to reduce illnesses increase and start physical activity (WHO, 2018; ; D'Silva et al 2020; Wu et al. 2019).

The yoga practice affects neurotransmitters and activity of the hypothalamic-pituitary-adrenal axis (HPA) and the autonomic nervous system (ANS), by reducing cognitive and somatic stimuli. This yoga action differentiates the effects of this practice concerning other physical activities. Thus, yoga presents results as efficient or even higher when compared to results from other types of physical exercises and some types of psychotherapy (KWOK et al 2019)

Thus, the gap has emerged in relation to the yoga practice's responses in the biomarkers of oxidative stress. Therefore, the objective was to review and analyze the effects of yoga on oxidative stress markers in patients with chronic diseases.

METHOD

FOCUSED QUESTION

This review was performed to answer the focused question: Can yoga promote beneficial effects for biomarkers of oxidative stress in individuals with chronic diseases?

LANGUAGE

Only studies in English were selected.

SEARCH STRATEGY

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2009).

DATABASES

The databases consulted were MEDLINE - PubMed and Cochrane in September 2020. The descriptors that were used "yoga AND oxidative stress" and the following filters, respectively, "Clinical Trial" and "Controlled clinical trial". The selected articles, in the period of the last 12 years, were investigate to with the objective of analyzing how yoga can influence the control of OS in individuals with chronic diseases.

INCLUSION AND EXCLUSION CRITERIA

For the studies eligibility, it is necessary that the research be performed in individuals with chronic diseases and that the study be the clinical trial type. The exclusion criteria used were: unavailability of the entire article on the internet, research in which oxidative stress markers were not measured and research in patients without chronic diseases

ELIGIBLE CRITERIA

The eligible criteria for this review followed the *PICO* (Population, Intervention, Comparison, and Outcomes) format for RCT. The outcomes were Data were extracted from articles that corresponded to the study's objective. The risk of bias in each article was evaluated using the Cochrane Collaboration Tool to assess the risk of bias in randomized controlled trials.Only full studies published in the consulted databases were selected.

RESULTS

The included articles were selected, independently. Then, a complete analysis of the article was carried out. In the initial search in the two databases, 37 studies were identified. Which, 14 were removed for duplicity. Between the 23 studies screened, 14 were excluded according to the inclusion and exclusion criteria. At the end, 9 clinical trials were considered eligible for qualitative synthesis, as shown in figure 1.

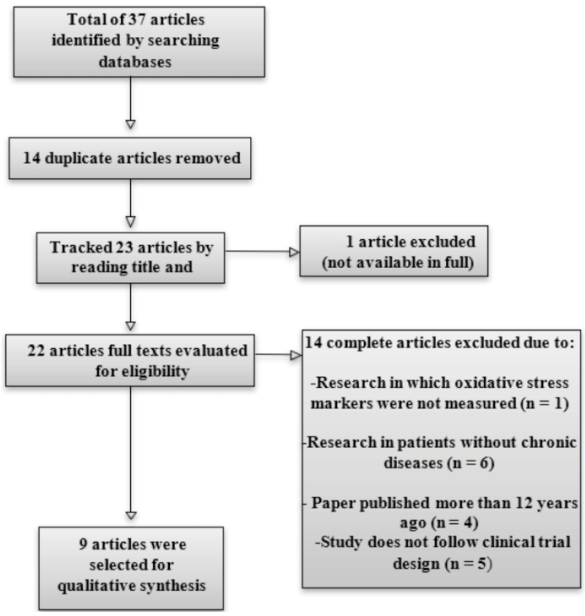

Figure 1 - *Prisma* flowchart demonstration to the article´s selection

Figure 1. Flow chart showing the study selection according to PRISMA (Moher et al, 2009).

Based on the information in each article, the risk of bias was assessed using the Cochrane Collaboration Tool to assess the risk of bias in clinical trials, as shown in Figure 2.

Author/ year	Model	Participants (n)	Intervention group (n)	Control group (n)	Outcomes
Yadav R 2019	Randomized / Not Blinded / Intervention duration: 12 weeks	n=260 Age: 20–45 years Profile: metabolic syndrome	n=130; Yoga--based lifestyle intervention	n=130; food diet only	(+) The group submitted to the intervention showed improvement in the OS markers. TBARS (↓) 8-OHdG (↓) SOD (↑)
Gautam S 2019	Randomized / Triple-blinded / Intervention duration: 8 weeks	n=72 Age: 18-60 years Profile: Rheumatoid arthritis undergoing routine medical treatment for at least 6 months.	n=36; Yoga (Yoga-based body-mind intervention) with disease--modifying anti-rheumatic drugs	n=36; disease-modifying anti-rheumatic drugs only	(+) The intervention showed improvement in systemic OS markers, inflammation, and maintenance of cellular health. SIRT1 (↑) ROS (↓) TAC (↑) 8-OHdG (↓)
Tolahunase M 2018	Randomized / Not Blinded / Intervention duration: 12 weeks	n=58 Age: 19-50 years Profile: major depression	n=29; lifestyle intervention based on yoga and meditation, with routine drug treatment	n=29; routine drug treatment only	(+) The intervention group showed an improvement in OS. 8-OHdG (↓) ROS (↓) TAC (↑)
Cheung C 2018	Randomized / Double-blinded / Intervention duration: 12 weeks	n=20 Age: 45-75 years Profile: idiopathic Parkinson's disease	n=10; Hatha yoga and most patients used dopaminergic medication	n=10; waiting list	(0) There was no significant difference in OS markers, despite the tendency to increase antioxidants and decrease oxidants. MDA (↓)* SOD (↓)* Catalase activities (↑)* GPx(↑)* GSH (↑)*
Kaminsky D 2017	Randomized / Double-blinded / Intervention duration: 12 weeks	n=43 Age: ≥ 18 years Profile: symptomatic COPD, moderate to severe	n=22; Pranayama and COPD education	n=22; COPD education only	(-) The intervention group showed an increase in negative OS markers H2O2 (↑) 8-isoprostane (↑)
Dhameja K 2013	Not Randomized / Not Blinded / Intervention duration: 42 days	n=60 Age: 30-60 years Profile: Stage 1 and 2 Systemic Arterial Hypertension lasting up to 5 years	n = 30; Yoga practices associated with conventional therapy for hypertension	n=30; only conventional therapy for hypertension	(+) There was an improvement in the potential to combat OS with a decrease in MDA level and an increase in antioxidant capacity, in the form of FRAP and GST, in the yoga group. MDA (↓) GST (↑)* FRAP (↑)
Hegde S 2011	Not randomized / Not Blinded / Intervention duration: 3 months	n=123 Age: 40-75 years Profile: type 2 diabetes mellitus	n=60; standard care, associated with Yoga (the technique was not specified)	n=63; standard care	(+) Yoga achieved a 20% reduction in OS. MDA (↓) glutathione (↑) SOD (↔)* vitamin C (↑) vitamin E (↔)*

Agte V 2011	Not randomized / Not Blinded / Intervention duration: 2 months	n=52 Age: 30-60 years hypertension	n=26; Sudarshan Kriya Yoga in patients with hypertension	n=26; Sudarshan Kriya Yoga in healthy patients	(+) There was a significant decrease in blood pressure and MDA. MDA (↓) POX (↔) SOD (↑)* PLA2 activity (↔) Catalase activities (↑)*
Gordon L 2008	Randomized / Uni-blinded / Duration of intervention: 24 weeks	n=231 Age: 40 to 70 years Profile: type 2 diabetes mellitus	n=77; Hatha yoga	n=154, of which: 77 in conventional physical training and 77 following medical treatment	(+) Hatha yoga has preventive and protective effects in type 2 diabetes, reducing oxidative stress MDA (↓) PLA2 (↑)* POX (↔)* SOD (↑)* atividade de catalase (↑)*

↑: increase; ↓: decrease; ↔: without changes; TBARS: thiobarbituric acid reactive substances; 8-OHdG: 8-hydroxy--2'-deoxyguanosine; SOD: superoxide dismutase; ROS: reactive oxygen species; TAC: total antioxidant capacity; MDA: malondialdehyde; POX: protein oxidation; PLA2 activity: phospholipase A2; H2O2: hydrogen peroxide ; SIRT1: sirtuin 1; FRAP: ferric-reducing ability of plasma; GST: glutathione S-transferase; GPx: glutathione peroxidase; GSH: glutathione; POX: protein oxidation; *: No statistically significant value.

Table 1 – Descriptive tables of the results of the nine includedstudies

Source – prepared by the authors (2021)

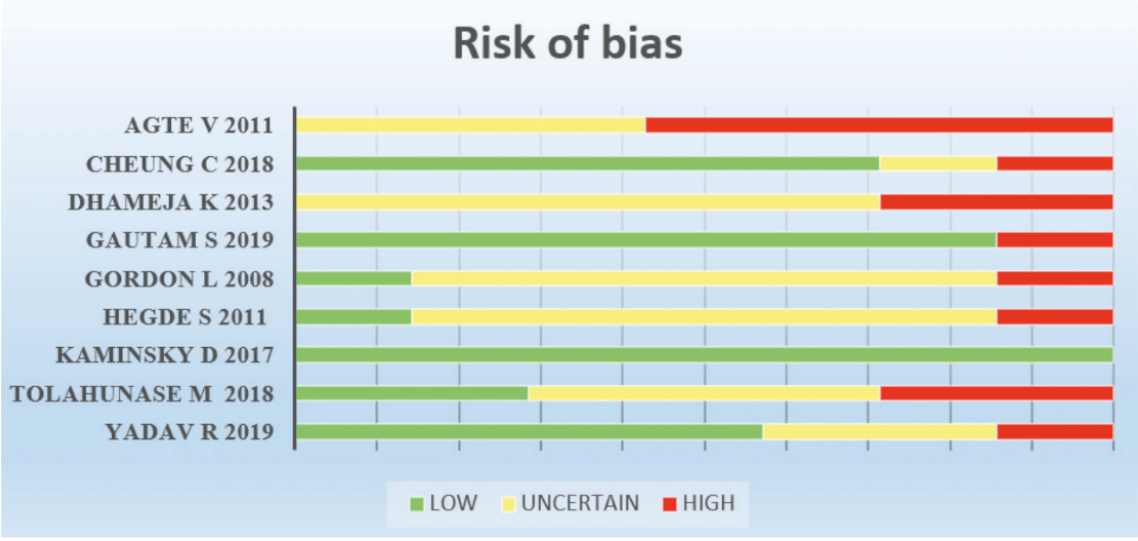

Figure 2. Illustration of the risk of bias of the included studies.

DISCUSSION

O EO é o desequilíbrio entre oxidantes ROS ou RNS e radicais livres e antioxidants e está relacionado em vários processos patológicos das doenças cronicas In view of the results of the selected article, arguments, interactions, and oppositions can be made that contributed to a better understanding of yoga practice and the impact on oxidative stress markers (PODKOWIŃSKA; DOROTA, 2020)

The OS markers in all studies were quantified and analyzed and, in their majority, yoga caused an increase in the action capacity of antioxidants and a decrease in oxidants, except in the study by Kaminsky et al. (2017) Cheung et al. (2018).

CHRONIC DISEASES AND OXIDATIVE STRESS MARKERS

It is important to note that most studies analyzed different types of markers since there is no homogeneity between the markers measured in each research, and this makes it possible to evaluate the influence of the practice of yoga on several markers.

In type 2 diabetes, hyperglycemia induces a ROS that causes OS, with the practice of yoga the MDA oxidation marker has reduced (Hegde… .. 2011; Gordon… .2008). Regarding the time of practicing yoga, the longest time for those who practiced for six months presented the increase in SOD considered positive for the pathological condition (Gordon… .2008) The practice in less time, in the time of 3 months did not show changes in the indices from SOD (Hegde… .. 2011)

In rheumatoid arthritis and depression the intervention showed improvement in systemic OS markers, inflammation, and maintenance of cellular health, and this has been demonstrated because was decrease in ROS and increased antioxidant marker TAC, besides, the marker of DNA damage decrease the 8OHdG level and longevity and health marker SIRT1 increases (Gautam 2019).

In parkinson's disease, yoga did not impact the OS, a fact marked by the SOD that continued to decrease, which means that the pathology continues to unbalance the markers. In metabolic syndrome the group the benefits of yoga have been demonstrated as there was decrease in TBARS and 8OHdG level suggestive of reduced oxidative stress besides having increased the level of SOD. (Yadav 2019)

Individuals with COPD evaluated and registered showed an increase in negative OS markers H2O2 and 8-isoprostane and concluded that the clinical significance of these findings is unclear and that it may be of the rapid evolution of the disease and to the high variability and small sample sizes associated with the data. (Kaminsky et al. 2017)There was an improvement in the potential to combat OS with a decrease in MDA level and an increase in antioxidants, providing balance and significantly improving hypertension

The markers analyzed by Yadav et al. (2019), Tolahunase et al. (2018), , and Gautam et al. (2019 presented statistically significant responses concerning yoga practice. While the studies by Hegde et al. (2011), Gordon et al. (2008), Dhameja et al. (2013), and Agte, Jahagirdar and Tarwadi (2011) pointed improvement in all OS markers indexes, however, only a few showed significant differences. What also happened in the study by Cheung et al. (2018), which did not show a significant difference between measurements, despite showing a tendency to increase antioxidants and decrease oxidants

YOGA

When analyzing the impact of yoga practice in the OS markers, it was observed that the articles varied a lot regarding the interventions' time and duration. In six of nine articles, the sessions had a standard

duration of 120 minutes, the exceptions were in the articles by Cheung et al. (2018) and Dhameja et al. (2013), in which the sessions lasted 60 minutes, and in the study by Agte, Jahagirdar and Tarwadi (2011), who reported only that the intervention lasted two months. Because of this, it is important to emphasize that the interventions, in some studies, took place with the guidance of instructors and professionals, while in others, the participants received training and did the practice in their own homes.

The following interventions that took 12 weeks, 3 months, 8 weeks, and 12 weeks respectively, Hegde et al. (2011); Tolahunase et al. (2018); Cheung et al. (2018) and Gautam et al. (2019), were performed in Yoga centers accompanied by instructors and other professionals. In the studies by Yadav et al. (2019) and Kaminsky et al. (2017), the interventions lasted 12 weeks, of which two were for training, while in the other ten weeks, the participants performed the activity in their own home and made records of the activities. Likewise, in the study by Gordon et al. 2018 that lasted 24 weeks, patients received training once a week and continued the treatment by performing sessions at home on other days of the week.

In the research by Kaminsky et al. (2017), which lasted 42 days, in the first 21 days, the participants received training in a clinic, and in the other 21, they performed yoga techniques at home. In all studies analyzed, participants were able to perform the techniques at home, except in the experiment by Cheung et al. (2018), that for unspecified safety reasons, the domestic practice was not prescribed. Despite the results showing positive responses about the OS markers indexes, some articles demonstrated the possibility of bias due to the time and form of application.

LIMITATIONS

Regarding the article´s origin country, the technique acceptance may have offered an influence such as those performed in India, the birthplace of yoga, which may contribute to greater acceptance and adherence by the yoga practices participants (YADAV et al., 2019; TOLAHUNASE et al., 2018; HEGDE et al., 2011; GAUTAM et al., 2019; DHAMEJA et al. 2013; AGTE; JAHAGIRDAR; TARWADI, 2011). Although, in countries where traditionally yoga is not so popular, it was observed lower adherence of the participants, as an example in the USA and Cuba (KAMINSKY et al., 2017; CHEUNG et al., 2018 GORDON et al., 2018). (colocar no inicio do topico "limitações"

Several factors may have interfered with the results and conclusions of this research. The authors report the following factors as limitations for their research: higher than expected dropout rate Yadav et al. (2019), low adherence to the activities proposed to the intervention group Dhameja et al. (2013) and Kaminsky et al. (2017) short intervention time Kaminsky et al. (2017) and Yadav et al. (2019), non-compliance with home intervention Yadav et al. (2019), small sample size, which makes it difficult to generalize the results (Dhameja et al. (2013); Tolahunase et al. (2018) and Cheung et al. (2018), only adult participants group Tolahunase et al. (2018), non-randomized study Hegde et al. (2011) and Dhameja et al. (2013), resource limitation Gordon et al. 2018; exclusion from independent yoga practice at home may have limited the therapeutic effects Cheung et al. (2018). Kaminsky et al. (2017) also reported limitations: the patient's understanding of the correct way to perform pranayama in the intervention group was not tested; non-professional yoga instructors gave difficulty in blinding; practice instructions. Agte, Jahagirdar and Tarwadi (2011) did not report

any limitations in the study. Gautam et al. (2019) refer to the need for more research to explore the possible mechanism underlying yoga's effect at the cellular level since the current evidence in this field is limited.

CONCLUSION

The benefits of Yoga in OS are positive in most evaluated clinical trials. However, there was a need for further studies regarding the relationship between Yoga and OS. Therefore, the role of yoga as an effective agent in reducing OS markers and increasing antioxidants was evident.

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