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Effect of Moderate and Severe Swimming Exercise on Hepatic Injury and Apoptosis Induced by Renal Ischemia Reperfusion in Male Albino Rats

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Keywords

- Ischemia – reperfusion
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- Malondialdehyde
- Caspase-3.

Abstract

Objective: to investigate the effects of moderate and severe exercise on hepatic injury induced by renal ischemia reperfusion (IR) in male albino rats. **Methods:** 40 male albino rats were divided into 4 groups (10 rats each): sedentary sham-operated-control, sedentary renal IR group, moderate exercise-IR group and severe exercise-IR group. In the last two groups, swimming exercise protocol performed for 6 weeks, then rats were subjected to renal IR. At the end of experiment, serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and liver levels of malondialdehyde (MDA), superoxide dismutase (SOD), reduced glutathione (GSH), catalase (CAT), caspase-3 activity and TNF-α were assessed. **Results:** renal IR caused non-significant increase in the levels of ALT and AST with significant increase in hepatic MDA and TNF-α levels, while SOD and GSH levels showed significant decrease. CAT and caspase-3 showed insignificant change in IR group compared to sham group. Moderate exercise prior to renal IR showed insignificant decrease in ALT and AST levels, significant decrease in hepatic MDA and TNF-α levels, significant increase in hepatic SOD, GSH and CAT and non-significant change in caspase-3 compared to renal IR sedentary group. On the other hand, severe exercise prior to renal IR showed significant increase in ALT and AST levels, also hepatic MDA and TNF-α levels were significantly increased, while, hepatic SOD and GSH levels significantly decreased as compared to renal IR sedentary group, CAT levels insignificantly increased as compared to renal IR sedentary group. Caspase-3 insignificantly increased as compared to renal IR sedentary group but showed significant increase when compared to sham control group. **Conclusion**s: Moderate exercise swimming ameliorates hepatic injury induced by renal IR by its antioxidant and anti-inflammatory effects. While, severe exercise deteriorates the hepatic injury induced by renal IR by increasing the oxidative stress.

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INTRODUCTION

Liver and kidney are important regulators of body homeostasis and are involved in excreting the toxic products of metabolism and exogenous drugs (1). Any injury to either the renal or liver tissue may affect the other (2).

Reactive oxygen species (ROS) and nitric oxide (NO) play an important role in mediating cell damage during ischemia reperfusion (IR) injury(3). Inflammation contributes to the pathogenesis of IR with a central role for particular cells, adhesion molecules, and cytokines (4). Neutrophils are the inflammatory cells, which produces abundantly ROS during IR injury (5). Renal IR causes tissue injury by oxygen radicals and oxidative stress caused by an imbalance between production of ROS and antioxidant capacity (6,7).

Liver injury is one of the distant-organ damages induced by renal IR. Acute renal failure associated with liver disease is a commonly encountered clinical problem of varied etiology (8). It is believed that IR injury induces inflammatory response, which elicits tissue damage in a number of organs in which reactive oxygen and nitrogen species play a key role in the pathophysiology of tissue injury (9,10). It has been demonstrated that renal IR injury might cause liver oxidative stress and increase lipid peroxidation in liver tissue (11).

Apoptosis is a physiological, highly organized and genetically programmed form of cell death which contributes to body homeostasis by removing aged and damaged cells(12). Thus, apoptosis represents a protective defense mechanism against a number of harmful factors including viral attacks and carcinogens (13). However, aberrant hepatocyte apoptosis may induce hepatic injury and disease progression via up-regulation of inflammation and fibrosis (14).

Exercise training has various effects on hepatic function (15). In rats, training modulates antioxidant enzymes in the liver, reducing oxidative damage (16). Regular physical activity reduces the risk of cardiovascular disorders, diabetes, obesity, cancer and premature death (17). However, the beneficial effects of physical activity are lost with exhaustion (18). Severe exercise training represents a physical stress that disrupts homeostasis (19), and the working skeletal muscle is clearly the organ most directly affected during physical activity (20).

Previous studies indicate that exercise may induce structural damage to muscle cells (21), and the production of metabolic by-products, such as lactate (22), and ROS (23). The metabolic adaptations to exercise are not restricted to the working muscles, exercise also a major challenge to other organs such as cardiac muscle, stomach or brain (24). This is particularly relevant to the liver due to its central role in the maintenance of energy supply to the exercising muscle (25).

Although, there were numerous previous studies aiming to evaluate the effects of exercise on liver functions and oxidative stress in liver, but there has been no study of the effect of moderate and severe exercise on liver injury induced by renal IR. So, this study designed to investigate the effects of moderate and severe swimming exercise on hepatic injury and apoptosis induced by renal IR in male albino rats

MATERIALS AND METHODS

Animals:

This study was carried out on 40 male albino rats weighing about (200-250gm) were housed under standard laboratory conditions at room temperature (24±2°C). The rats had free access to water and food.

Experimental design:

Rats were divided into four groups (10rats each): Sedentary sham-operated-control: rats in this group were subjected to sham operation; Sedentary renal IR group; rats in this group were subjected to renal IR; Moderate exercise-IR group: rats in this group performed moderate swimming exercise for 6 weeks, then were subjected to renal IR; severe exercise-IR group: rats in this group performed severe swimming exercise for 6weeks, then they were subjected to renal IR.

Induction of renal IR injury:

According to Vaghasiya et al.,(1), the I/R to the kidneys was induced. Rats were anaesthetized with pentobarbital (40mg/kg) intraperitoneally. The abdominal region was shaved and sterilized. Rats were undergoing surgical exposure of the left and right renal pedicles via midline incision. To induce renal ischemia, both renal pedicles were occluded for 30 minutes with vascular clamps. After 30 min. of occlusion, the clamps were removed, and kidneys observed to undergo reperfusion for 24 hours. Sham-operated animals underwent identical surgical treatment, however, without occlusion of the renal pedicles.

Swimming exercise protocol:

Moderate swimming exercise protocol: the swimming exercise protocol was conducted 5 times/week for 60 min/time for 6 weeks. The rats swam individually in water tank. The tank used in this study 80 cm in length, 50 cm in width and 90cm in depth, and the swimming training was always performed in water temperature of 31±1ºC, between 10 to 12 h a.m.(26).

Severe swimming exercise protocol: The exercise regimen for severe exercise-trained rats, the same as for moderate exercise-trained rats but to augment the exercise intensity, an external load was added to the animal; the animal carried a load of 50% body weight strapped to the chest in the second week. In the third and fourth training weeks, the animals performed the same exercise carrying a load of 60% body weight, and in the last two weeks, this load increased to 70% of body weight (27).

Biochemical assays:

At the end of experiment, rats were sacrificed and blood samples were collected for biochemical assays, and livers were quickly removed and kept frozen until assayed for oxidant and antioxidant parameters.

The following parameters were determined:

Liver function assay:

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured according to the method of Rei(28) .

Estimation of lipid peroxidation and antioxidant enzymes:

Liver was removed and kept in cold conditions until assayed. The tissue was homogenized, the clear supernatant was used for assays of lipid peroxidation (MDA content) according to Esterbauer and Cheeseman(29), superoxide dismutase (SOD) according to Marklund and Marklund (30), catalase (CAT) that determined by Aebi(31) and reduced glutathione (GSH) according to Nagi et al., (32)

Estimation of caspase-3 activity and TNF-α:

Caspase-3 was measured by ELISA method according to(33), and TNF-α was determined by Endo et al., (34)

Statistical analysis:

The data were expressed as the mean ± standard deviation. Data from our study were analyzed using the unpaired student's t-test to assess significant difference between two groups. Statistical comparison between different groups was carried out by using one–way ANOVA. Significant results of analysis of variance were subjected to post hoc analysis (Tukey-Kramer multiple comparisons). P-values <0.05 were considered statistically significant. All the analyses were performed using Graph Pad Instat, 32 bit for win 95/NT (Version 3.05).

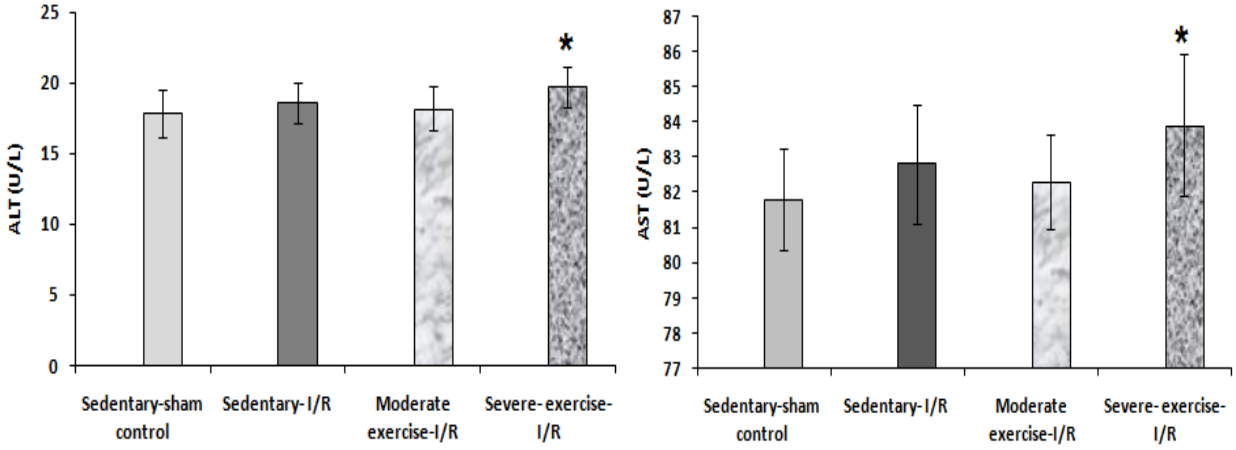

Figure (1): Effect of moderate and severe exercise on liver function after induction of renal I/R injury in rats. $^{*}P < 0.05$ vs sham-operated control group. $^{\#}P < 0.05$ vs renal I/R group. $^{\$}P < 0.05$ vs moderate exercise-I/R group.

Statistical analysis:

The data were tabulated and analyzed by SPSS (statistical package for the social science software) using statistical package version 16 on IBM compatible computer. Quantitative data were expressed as mean ± standard deviation (X± SD). The data from control and test groups were compared using an independent sample t-test. Probability value of less than 0.05 was considered as statistically significant (*P<0.05). "n" indicates the number of tested rats.

RESULTS

Effect of muscle exercise on liver function in renal IR

As shown in table fig. (1), serum levels of ALT and AST were insignificantly increased in IR group as compared to the sham-operated control group (P> 0.05). Rats underwent moderate exercise prior to renal IR were exhibited insignificant decrease in the serum levels of ALT and AST as compared renal IR group and exhibited no significant change as compared to sham-operated group. While, rats that underwent severe exercise prior to renal IR showed insignificant change in serum levels of ALT and AST as compared to renal rats in sedentary IR group, but showed significant increase when compared to the sham-operated control group.

Effect of muscle exercise on lipid peroxidation and antioxidant enzymes in renal IR

Compared with sham-operated control group, liver MDA levels were significantly increased, while

SOD and GSH levels were significantly decreased in IR group (P< 0.05). But, CAT levels insignificantly changed in IR group as compared to sham group fig. (2).

The MDA levels in liver tissue, was significantly decreased in rats that underwent moderate exercise prior to renal IR compared to rats in the sedentary IR group (P<0.05), but insignificantly changed as compared to sham-operated control group. While, rats that underwent severe exercise prior to renal IR were exhibited significant increase in the MDA levels compared to rats in the sedentary IR group, rats in sham-operated control group and rats in the moderate exercise IR group fig. (2).

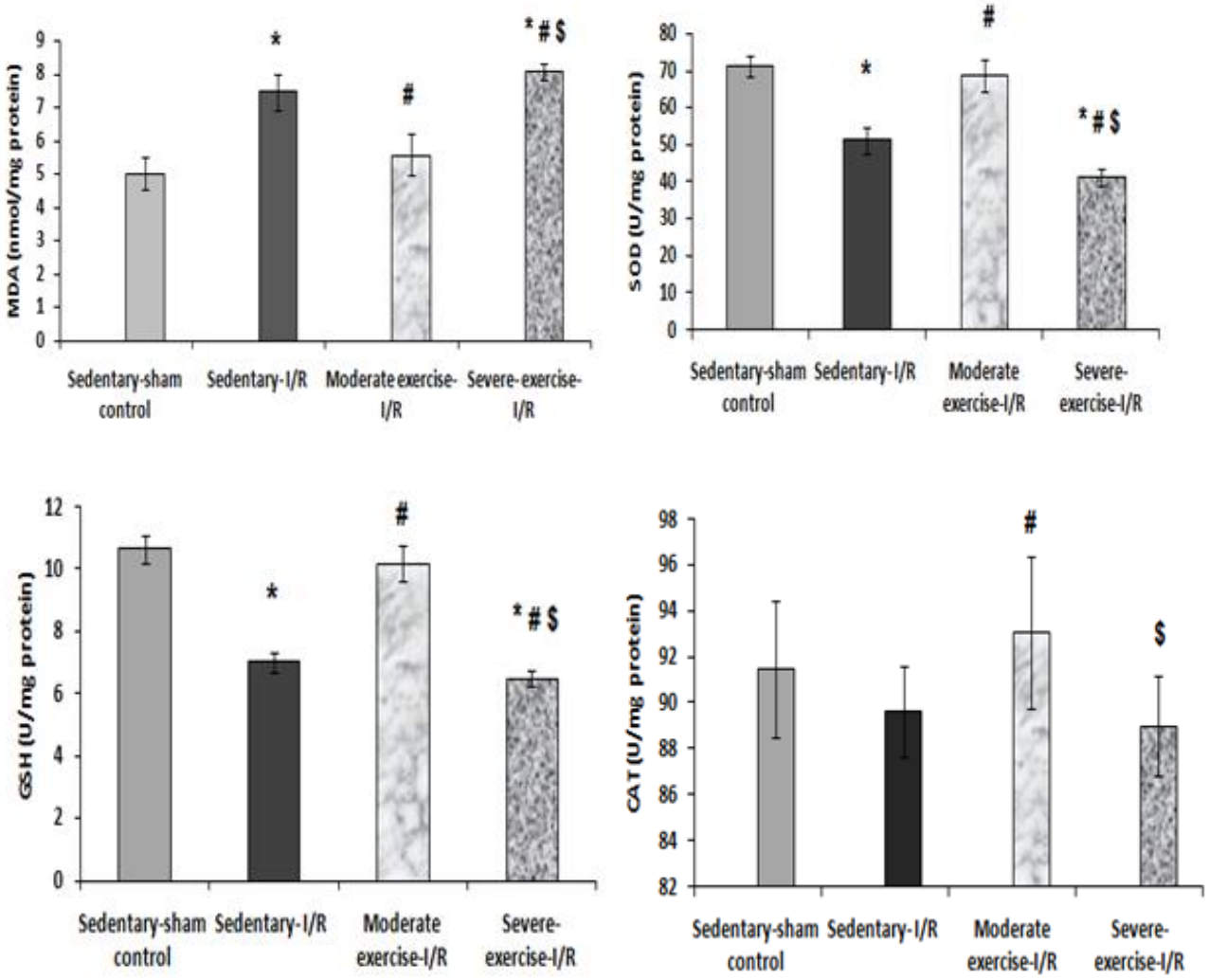

Figure (2): Effect of moderate and severe exercise on lipid peroxidation and antioxidant enzymes in the liver after induction of renal I/R injury in rats. *P < 0.05 vs sham-operated control group. #P < 0.05 vs renal I/R group. $P < 0.05 vs moderate exercise-I/R group

As regard SOD and GSH levels, both are significantly increased in rats underwent moderate exercise prior to IR as compared to the rats in the sedentary IR group, but they showed no significant difference if compared to the sham-operated control group. While, severe exercise prior to IR significantly decreased the levels of SOD and GSH as compared to rats in the sedentary IR

Table (1): Effect of moderate and severe exercise on caspase 3 activity and TNF-α in the liver after induction of renal I/R injury in rats

Parameters	Group I Sedentary-sham control (n=10)	Group II Sedentary- I/R (n=10)	Group III Moderate exercise-I/R (n=10)	Group IV Severe-exercise-I/R (n=10)
Caspase 3 activity (nmol /mg protein)	1.06±0.32	1.36±0.46	1.18±0.36	1.86±0.77[a,c]
TNF-α (pg/mg protein)	13.83±0.77	22.53±1.72[a]	15.15±1.81[b]	26.30±1.39[a,b,c]

Data are given as mean ± SD. aP < 0.05 vs sham-operated control group. bP < 0.05 vs renal I/R group. cP < 0.05 vs moderate exercise-I/R group

group, rats in sham-operated control group and rats in the moderate exercise IR group fig. (2).

Moderate exercised IR group showed a significant increase in CAT activity levels as compared to the sedentary IR group and

Effect of muscle exercise on caspase-3 activity and TNF-α in renal IR:

Table (1) showed that caspase-3 was insignificantly increased in IR group as compared to sham-operated control rats (P>0.05). While, TNF-α was significantly increased in IR group in comparison with sham-operated group (P<0.05).

Table (1) showed that caspase-3 levels were insignificantly decreased in moderate exercised IR rats as compared to sedentary IR rats (P>0.05), and insignificantly changed as compared to sham-operated control group. While, in the severe exercised group, there were insignificant increase in caspase-3 levels as compared to sedentary IR group. But, the increase became significant if compared to both the sham-operated rats and to the rats in the moderate exercise IR group.

insignificant increase as compared to sham-operated group. But, in the severe exercised group, CAT activity levels were insignificantly changed compared to both the sedentary IR group and sham-operated group, and showed significant decrease if compared to the moderate exercise IR group.

TNF-α levels were significantly decreased in rats that underwent moderate exercise prior to renal IR group compared to rats in sedentary IR group (P<0.05) but, they showed no significant difference if compared to the sham-operated control group. While, rats that underwent severe exercise prior to renal IR were exhibited significant increase in the levels of TNF-α as compared to rats in the sedentary IR group, rats in sham-operated control group and rats in the moderate exercise IR group (table 1).

DISCUSSION

Renal IR injury is encountered in many clinical situations; transplantation, partial nephrectomy, sepsis, hydronephrosis, or elective urologic operations (35). At present, many studies have shown remote organ injury, including the liver, during renal IR(36).

The liver plays a role in the physiology of exercise (16). Exercise has various effects on liver function, enhancing both nutrient metabolism and antioxidant capacity (37).

The effect of exercise on health is paradoxical, because the formation of ROS induced by exercise may be detrimental for cellular functions (38). Strenuous exercise was shown to increase ROS mediated lipid peroxidation in the liver (39), skeletal muscle (40), myocardium (41), and lung tissue(42). On the other hand, exercise, while enhancing the generation of ROS, was suggested to activate the defense mechanisms that protect against detrimental effects associated with ROS (43).

The present study demonstrated that renal IR leads to damage to the liver as remote organ. Our findings suggested that moderate exercise attenuates IR-induced liver functional injury, while severe exercise deteriorates the IR-induced liver functional injury.

The present study showed that serum ALT and AST levels insignificantly increased after induction of renal IR as compared to sham control. But, we found significant higher MDA levels in the liver tissue after induction of renal IR injury as compared to sham-control, which is a major index of lipid peroxidation and oxidative stress. In the present study, renal IR leads to decreased levels of antioxidant enzymes in the liver tissue including GSH and SOD as compared to sham control, while CAT level insignificantly changed as compared to sham group. Also, the present work showed that 30 min-renal ischemia, 24 hours reperfusion was enough to significantly increase TNF-α level in the liver as compared to those levels observed in the sham-control, while caspase-3 levels were insignificantly increased as compared to sham-control.

Several mechanisms are suggested to be involved in remote organ failure, but their exact pathophysiological roles are not completely understood (9,10). Chemokines and mitochondrial products activate neutophils to amplify remote liver injury during mouse acute renal failure (44). Renal IR results in uncontrolled expression of interleukin-17A(45). IL-17A is a pro-inflammatory cytokine that causes recruiting neutrophils, activate T cells, and induces expression of other cytokines and chemokines such as TNF-α and IL-6 in liver tissue(46). It has been shown that TNF-α play an important role in early IR injury (44).

TNF-α is a pro-inflammatory cytokine mainly produced from macrophages and monocytes and in the liver from Kupffer cells(47). It acts locally in a paracrine fashion but also at distant sites in the manner of hormones(44). Seteser et al(48), showed that renal IR increased the hepatic levels of TNF-α. Increased oxidative stress and production of ROS in the liver that were shown in the present study are also thought to play a key role in triggering and maintaining the inflammatory response. MDA, an index of lipid peroxidation, was found to be increased in the liver after renal IR(49). In addition, hepatic glutathione, an important endogenous free radical scavenger with protective effects on the liver, was decreased(8). Administration of glutathione before renal IR decreased histological evidence of liver injury and MDA concentrations (8).

The results of the present work demonstrated that moderate exercise for 6 weeks prior to renal IR insignificantly affect serum ALT and AST levels,

but caused significant decrease in MDA in liver tissue as compared to rats in sedentary renal IR group, antioxidant enzymes like SOD, GSH and CAT were significantly increased in the liver tissue in moderate exercised-IR group compared to sedentary IR group. Also, TNF-α levels were significantly decreased in moderately-exercised IR group, while caspase-3 level insignificantly changed as compared to sedentary IR group.

In accordance to the results of the present work, Cakir et al.,(40) demonstrated that stress induced oxidative damage in the cardiac muscle, liver, stomach, and brain of sedentary rats that assessed by increased MDA levels, is ameliorated when the animals have previously swum at a moderate load for 8 weeks.

It has been hypothesized that moderate regular exercise can be beneficial by up-regulating the protective activities against oxidative stress (50). Radak et al.,(51) showed that regular exercise attenuated the increased redox status, evaluated by glutathione level that showed more than a two-fold increase in GSH in exercised rats.

The protective effect of exercise against stress-induced oxidative damage of remote organs appears to involve the maintenance of GSH stores and an inhibitory action on tissue neutrophil recruitment, alleviating neutrophil-derived oxidative injury (23)

In accordance to the results of the present work, some studies have shown that animals and humans clearly undergo significant adaptive responses to regular exercise which is permitted by reduction in oxidant production and increased antioxidant defenses (19,52). In this context, the liver plays a key role in stress-induced oxidative injury (53). For instance, liver is the major organ for de novo GSH synthesis, supplying 90% of the circulating GSH, which is one of the most important endogenous antioxidants(54) and plays an important role as a reducing agent(53) protecting the organism against hydrogen peroxide and lipid peroxides(52). Sun et al.,(53) found increased liver mitochondria GSH after 4 weeks of training exercise in rats, which was attributed to an increased antioxidant activity. Navarro et al.,(43) also reported that chronic moderate exercise increases mitochondrial SOD activity and decreased mitochondrial oxidation products in trained rat liver. In agreement to this view, Botezelli et al.,(55) have demonstrated that 8 weeks of swimming training decreased lipid peroxidation, a fact partially attributed to an improved antioxidant system with greater SOD enzyme activity.

The previous reports found no significant difference between tissue and isolated mitochondria measurements (53). Thus, no difference between GSH and MDA in tissue homogenate and isolated mitochondria have been observed following exercise training in rat(24).

Radak et al.,(56) investigated the activity of nuclear factor-kB (NF-kB) which is an important redox sensitive transcription factor that regulates various inflammatory and immune responses. The binding activity of NF-kB in nuclear extracts to deoxyoligonucleotide with the responsive element reduced with the exercise regimen suggesting that regular exercise may attenuate the inflammatory processes (57).

Additionally, it is interesting to note that proteins in cardiac muscles of rats subjected to regular swimming training for 9 weeks were more

resistant to an oxidative challenge of intraperitoneal injection of H2O2(57). Regular exercise increases antioxidant enzyme activities in rat skeletal muscles (18) and the liver (58), taken together, these results support the results of the present work that moderate exercise up-regulates protection against oxidative stress.

Concerning antioxidant effects of exercise, a substantial body of evidence suggests that regular exercise plays an important preventive and therapeutic role in oxidative stress-associated diseases including ischemic heart disease (59), type II diabetes (60), and Alzheimer disease (61).

The mechanism by which moderate exercise training exerts its anti-inflammatory effects has been largely focused on the effects of reduced adiposity and reduced release of adipose tissue-derived inflammatory cytokines (62). Adipose tissue is recognized as a metabolically active tissue that plays a key role in the development of chronic low-grade inflammation (63). Adipose tissue is able to produce inflammatory cytokines such as TNF-α and IL-6 and several potent chemo-attractant cytokines (62). The accumulation of monocytes as macrophages in adipose tissue is thought to be a major source of increased systemic concentrations of inflammatory cytokines (64). With this in mind, increased physical activity that results in a negative energy balance and consequently reduces adiposity, have been typically suggested as the main mechanism by which regular exercise exerts its beneficial effects on the level of inflammatory markers(65).

The results of the present work showed that severe exercise-prior to the renal IR deteriorates the liver injury caused by renal IR manifested by significant increase in serum ALT and AST and hepatic MDA levels as compared to sedentary IR group, while, significant decrease of hepatic SOD and GSH as compared to sedentary IR group, but, CAT level insignificantly changed as compared to sedentary IR group and TNF-α in liver tissue showed significant increase as compared to sedentary IR group, while, caspase-3 insignificantly increased as compared to sedentary IR group and showed significant increase when compared to sham control group.

It is well known that exhaustion caused by exercise, especially when it occurs sporadically, leads to structural damage or inflammatory reactions within the muscles (41). This damage is due to, at least in part, to the production of ROS (66). Also, it was reported that ROS production by acute or chronic exercise may elicit different responses depending on the type of organ tissue and its levels of endogenous antioxidants (67). Severe exercise by increasing the oxygen consumption rate may result in oxidative stress in mitochondria. This results in an increased production of oxidants, which could be detrimental to the tissue (23). The liver is the organ situated at the border between the digestive and circulatory systems and their functions are not bound only by digestion (68). At level of the liver many biochemical cycles occur and they can result in free oxygen radicals (68). Physical training represents an important source of ROS development at the level of the organs directly involved in the activity and at the level of other organs because of the supplementary energetic needs and also of the oxygen consumption (69).

In agreement with the results of the present work, Liu et al.,(67) have found that acute exercise induced increases in MDA content and decrease

glutamine synthetase activity in liver. Although regular moderate exercise training is known to increase the resistance against ROS induced lipid peroxidation, and to decrease the accumulation of oxidative proteins and DNA damage (70). However, severe exercise has been shown to induce formation of ROS and nitrogen species and the related oxidative damage (18).

In support to the results of the present work, previous studies have identified elevation in blood oxidative stress markers after severe exercise (71). A number of potential pathways exist for exercise-related oxidant production (70), as increase oxygen consumption several folds with exercise (72), tissue damage resulting from exercise which may induce the activation of inflammatory cells such as neutrophils, with subsequent production of free radicals (73). Several studies indicate that strenuous exercise augments oxidative stress and that exercise-induced oxidative stress may damage biological components e.g. lipids and proteins (18). However, the intensity, duration and frequency of exercise are important in determining stress level and preventing or deteriorating stress response (71).

The results of the present work demonstrated that severe exercise prior to renal IR induced initiation of the apoptotic pathways as revealed by significant increase in the pro-inflammatory cytokine TNF-α levels and increased activity of caspase-3. Such apoptosis is probably triggered by mitochondrial permeability transition and ROS released by activated Kupffer cells (74). This leads to release of mitochondrial cytochrome c and activates caspase-9 which, in turn, activates caspase-3, the initiator of the final execution stages of nuclear apoptosis (75).

Conclusions:

Based on the current evidence demonstrating the key role of regular moderate physical activity in reducing and preventing the remote effects of renal IR and the associated oxidative stress in liver, moderate regular exercise may therefore prove effective as a non-pharmacological intervention in providing life-long protection against stress-induced oxidative injury and in preserving antioxidant capacity of the non-muscle tissues as liver.

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الملخص العربي

هدف هذا البحث : هو معرفة تأثير الممارسة المتوسطة والعنيفة لرياضة السباحة على إصابة الكبد الناتجة من نقص وإعادة التروية بالكلى فى ذكور الفئران البيضاء

طرق البحث: تم إجراء البحث على 40من ذكور الفئران البيضاء وقد تم تقسيمهم إلى أربع مجموعات تتكون كل مجموعة من 10فئران:
المجموعة الأولى: هى المجموعة الضابطة التى لاتمارس الرياضة وتم إجراء جراحة غير حقيقية لها.
المجموعة الثانية: هى المجموعة التى لا تمارس الرياضة و تم إحداث نقص وإعادة التروية بكليتيها
المجموعة الثالثة: هى المجموعة التى تمارس رياضة السباحة بشكل متوسط لمدة 6لأسابيع ثم تم إحداث نقص وإعادة التروية بكليتيها.
المجموعة الرابعة: هى المجموعة التى تمارس رياضة السباحة بشكل عنيف لمدة 6لأسابيع ثم تم إحداث نقص وإعادة التروية بكليتيها.
فى نهاية الدراسة تم ذبح الفئران وتجميع عينات الدم لقياس انزيمات الكبد وأيضا تم أخذ الكبد وطحنه لقياس المالوندهيد والسوبر أوكسيد ديسميوتيز ونشاط الجلوتاثيون المختزل والكاتالازوالكاسبيس -3 وعامل نخر الورم ألفا.

نتائج البحث: فى المجموعة التى تم اجراء لها عملية نقص وإعادة التروية بكليتيها وجد زيادة فى مستوي إنزيمات الكبد وكانت هذه الزيادة ليست ذات دلالة إحصائية بينما زادت مستويات المالوندهايد وعامل نخر الورم ألفا زيادة ذات دلالة احصائية أما مستويات نشاط السوبرأوكسيد ديسميوتيز والجلوتاثيون المختزل فقد نقصت نقصا ذا دلالة إحصائية أما الكاسبيس- 3 فلم يتغير تغيرا ذا دلالة احصائية إذا قورن بالمجموعة الضابطة.
وقد أوضحت النتائج أن ممارسة رياضة السباحة بصورة متوسطة لمدة 6 أسابيع قبل إجراء نقص وإعادة التروية بكليتيها أدت الى نقص فى مستوى إنزيمات الكبد ولكن هذا النقص لم يكن ذو دلالة إحصائية كما نقصت مستويات المالوندهايد وعامل نخر الورم ألفا وكان هذاالنقص ذو دلالة إحصائية أما مستويات السوبرأوكسيد ديسميوتيز والجلوتاثيون المختزل والكاتالاز فقد زادت زيادة ذات دلالة إحصائية أما الكاسبيس- 3 فلم يتغير تغيرا ذا دلالة إحصائية بالمقارنة بالمجموعة التى لاتمارس الرياضة وتم إحداث نقص وإعادة التروية بكليتيها.
أما بالنسبة للمجموعة التى مارست رياضة السباحة بصورة عنيفة لمدة 6 أسابيع قبل إجراء عملية نقص وإعادة التروية بكليتيها وجد زيادة فى مستوى إنزيمات الكبد وكانت هذه الزيادة ذات دلالة إحصائية كما زادت مستويات المالوندهايد وعامل نخر الورم ألفا زيادة ذات دلالة احصائية أما مستويات السوبر أوكسيد ديسميوتيز والجلوتاثيون المختزل فقد نقصت نقصا ذات دلالة إحصائية بالمقارنة بالمجموعة التى لا تمارس الرياضة و تم إحداث نقص وإعادة التروية بكليتيها. أما بالنسبة لمستوى الكاسبيس- 3 فقد زاد زيادة ذات دلالة إحصائية بالمقارنة بالمجموعة الضابطة ولكن هذه الزيادة ليست ذات دلالة إحصائية اذا قورنت بالمجموعة التى لا تمارس الرياضة وتم إحداث نقص وإعادة التروية بكليتيها

الخلاصة: إن ممارسة الرياضة بشكل متوسط أدى الى تحسين حالة اعتلال الكبد الناتجة عن نقص وإعادة التروية بالكلى وذلك عن طريق تأثيرها المضاد للأكسدة والمضاد للإلتهاب ولكن ممارسة نفس الرياضة بشكل عنيف أدى الى تدهور اعتلال الكبد عن طريق زيادة الأكسدة.