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MODULATION OF MYOCARDIAL COLLAGEN REMODELING BY MILK THISTLE AND SAFFLOWER EXTRACTS AFTER CARBON MONOXIDE EXPOSURE

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Abstract

Carbon monoxide exposure causes tissue hypoxia and may lead to structural remodeling of the myocardium. One of the important manifestations of chronic myocardial injury is excessive collagen accumulation and development of interstitial fibrosis. The aim of this study was to evaluate collagen remodeling in the myocardium of white outbred rats after carbon monoxide exposure and to assess the corrective effect of milk thistle and safflower extracts. The study was performed on 6- and 18-month-old white outbred rats. Collagen fibers were detected using Van Gieson staining and assessed by digital morphometry.

Keywords: carbon monoxide, myocardium, collagen remodeling, fibrosis, Van Gieson staining, milk thistle, safflower, phytocorrection.

Introduction

Carbon monoxide poisoning remains an important toxicological problem due to its ability to cause systemic tissue hypoxia. Carbon monoxide binds to hemoglobin and reduces oxygen transport, which leads to impaired tissue respiration and damage to organs with high oxygen demand [1,2]. The myocardium is particularly vulnerable to hypoxic injury because cardiac muscle depends on continuous oxygen supply for contractile function.

Myocardial injury under carbon monoxide exposure is associated with several mechanisms, including tissue hypoxia, microcirculatory disorders, oxidative stress and mitochondrial dysfunction [3,4]. These changes can lead not only to cardiomyocyte damage, but also to stromal remodeling. One of the main structural outcomes of prolonged or severe myocardial injury is increased collagen deposition in the interstitial tissue.

Collagen remodeling plays an important role in the progression of myocardial dysfunction. Excessive accumulation of collagen fibers increases myocardial stiffness, impairs capillary-tissue exchange and disrupts normal architecture of cardiac muscle [5]. Therefore, quantitative assessment of collagen fibers is an important criterion for evaluating the severity of myocardial remodeling.

Van Gieson staining is widely used for histochemical detection of collagen fibers. In combination with digital morphometry, this method allows objective evaluation of the relative area of collagen structures in myocardial tissue.

Plant-derived compounds with antioxidant and membrane-stabilizing properties may reduce tissue damage caused by hypoxia and oxidative stress. Milk thistle contains silymarin, which is

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known for its antioxidant and cytoprotective effects [6]. Safflower also contains biologically active compounds that may improve microcirculation and reduce inflammatory and oxidative changes in tissues [7]. However, the effect of combined milk thistle and safflower extracts on myocardial collagen remodeling after carbon monoxide exposure remains insufficiently studied.

Aim of the study

The aim of the study was to evaluate collagen remodeling in the myocardium of 6- and 18-month-old white outbred rats after carbon monoxide exposure and to assess the effectiveness of correction with milk thistle and safflower extracts.

Materials and methods

The experimental study was carried out on white outbred rats weighing 150–170 g. The animals were kept under standard vivarium conditions. Myocardial tissue of 6- and 18-month-old rats was examined.

The animals were divided into the following groups: control group, carbon monoxide exposure group, carbon monoxide exposure with simultaneous correction, and carbon monoxide exposure with post-exposure correction. Milk thistle and safflower extracts were used as corrective agents.

After completion of the experiment, heart tissue samples were collected and fixed in 10% neutral buffered formalin. The material was processed by standard histological technique, embedded in paraffin and sectioned. To evaluate collagen fibers, histological sections were stained by the Van Gieson method.

Results

In 6-month-old control rats, collagen fibers were present in small amounts. They were mainly located between cardiomyocytes and around blood vessels. The structure of the myocardium remained compact and organized. According to morphometric analysis, collagen fibers occupied 5.2–6.8% of the myocardial tissue area.

In 18-month-old control animals, the collagen fiber area was higher and reached 14.3–16.7%. This increase reflected age-related stromal remodeling of the myocardium. Collagen fibers were distributed mostly in interstitial and perivascular areas, without formation of large fibrotic fields.

After carbon monoxide exposure, collagen accumulation increased in both age groups. In 6-month-old rats, the collagen fiber area increased to 11.5–17.2%. Collagen fibers were more clearly detected between cardiomyocytes and around vessels. In some areas, interstitial thickening was observed.

In 18-month-old rats exposed to carbon monoxide, fibrotic changes were more pronounced. The relative area of collagen fibers increased to 24.6–32.8%. Collagen bundles became denser and were distributed between cardiomyocytes and in perivascular zones. These changes indicated marked interstitial fibrosis and more severe myocardial remodeling in older animals.

Simultaneous correction with milk thistle and safflower extracts reduced collagen accumulation. In 6-month-old rats, the collagen fiber area decreased to 8.6–11.4%. In 18-month-old rats, this parameter was 14.8–19.6%. Although the values did not completely return to the control level, they were clearly lower than in the carbon monoxide group without correction.

Post-exposure correction also reduced the amount of collagen fibers, but the effect was weaker. In 6-month-old rats, collagen fibers occupied 10.8–14.6% of myocardial tissue. In 18-month-old rats, the collagen fiber area remained at 18.6–24.9%. These values were lower than in the untreated carbon monoxide group but higher than in animals receiving simultaneous correction.

Table 1.

Collagen fiber area in the myocardium of white outbred rats after carbon monoxide exposure and correction

Group	6 months	18 months
Control	5.2–6.8%	14.3–16.7%
Carbon monoxide exposure	11.5–17.2%	24.6–32.8%
CO + simultaneous correction	8.6–11.4%	14.8–19.6%
CO + post-exposure correction	10.8–14.6%	18.6–24.9%

Conclusion

1. Carbon monoxide exposure causes increased collagen accumulation in the myocardium of white outbred rats, indicating the development of interstitial fibrosis.
2. Fibrotic changes are more pronounced in 18-month-old rats, which reflects age-related reduction of myocardial adaptive capacity.
3. Simultaneous correction with milk thistle and safflower extracts reduces collagen fiber accumulation more effectively than correction performed after carbon monoxide exposure.
4. Post-exposure correction has a partial protective effect, but it does not restore collagen values to the control level.
5. Early use of milk thistle and safflower extracts may limit myocardial collagen remodeling under carbon monoxide-induced hypoxic injury.

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