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ASCORBIC ACID METABOLISM IN THE ORGANISM UNDER THE LACK OF OXYGEN SUPPLY TO THE TISSUES

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Abstract

The number and ratios of the metabolites of vitamin C - ascorbic, dehydroascorbic and diketogulonic acids were studied under the action of closed space hypoxia, acute blood loss and during sleep – the conditions associated with various oxygen saturation of the organism. It was found that in case of closed space hypoxia, the level of ascorbic and diketogulonic acid decreased with a simultaneous increase in the content of dehydroascorbic acid in the heart and brain. Acute blood loss resulted in decrease in the level of all metabolites of ascorbic acid. During sleep, the level of ascorbic acid metabolites increased. The ratio of vitamin-active metabolites to vitamin-inactive form of ascorbic acid in case of closed space hypoxia and acute blood loss decreased, and during sleep – it did not change significantly.

Keywords: vitamins, metabolism, ascorbic acid, hypoxia

Introduction

The ascorbic acid metabolism in the body has been studied in sufficient details [1, 5]. However, the studies devoted to the peculiarities of the course of this process in cases of disturbed oxidation potential of tissues are very few in number [2]. Such studies are necessary as the ascorbic acid is directly or indirectly involved in a significant number of oxidation-reduction processes in the organism [3, 4, 6, 7] and, accordingly, the oxidation-reduction potential of tissues has significant effect on the metabolism of ascorbic acid [8].

Methods

The white mongrel rats weighing 320-400 g were divided into groups. Group No. 1 is control. The iron deficiency anemia was modeled in part of rats by single-time acute blood loss from tip of the tail in an amount of 7-15% of the total blood volume, or 0.5-1% of the animal body weight (group No.2) [13]. The content of ascorbic acid metabolites was determined on the fifth day after the blood loss. Group No. 3 involves the rats affected by closed space hypoxia caused by [9]. Group No. 4 is the rats in a state of sleep. The animal management and experiments were carried out in accordance with international rules [12]. The content of ascorbic acid metabolites was determined in organ homogenates by the method of Sokolovskiy, Lebedev, and Lielup, 1974 [10]. The data obtained were processed statistically according to Student's method [11].

Results

When studying the effect of closed space hypoxia (CSH) on metabolism of ascorbic acid in the tissues of white rats, it has been established that (Figure 1) that in most of the investigated organs the CSH causes a decrease in the level of ascorbic and diketogulonic acids. An exception to this is only the liver, wherein the CSH did not change the contents of diketogulonic acid. At the same time, the level of dehydroascorbic acid in the heart and, especially, in the brain increased significantly. It is important to emphasize that these patterns are most pronounced in the heart.

When using the acute blood loss as a model (Figure 2), all the studied organs demonstrated the decrease in the levels of both ascorbic acid and its metabolites. The decrease in the level of ascorbic acid in the liver by 2.24 times, and in the kidneys by 1.69 times was the most significant. In the heart and brain, the decrease in the AA level was somewhat less.

Decrease in DAA and DKGA levels was less pronounced.

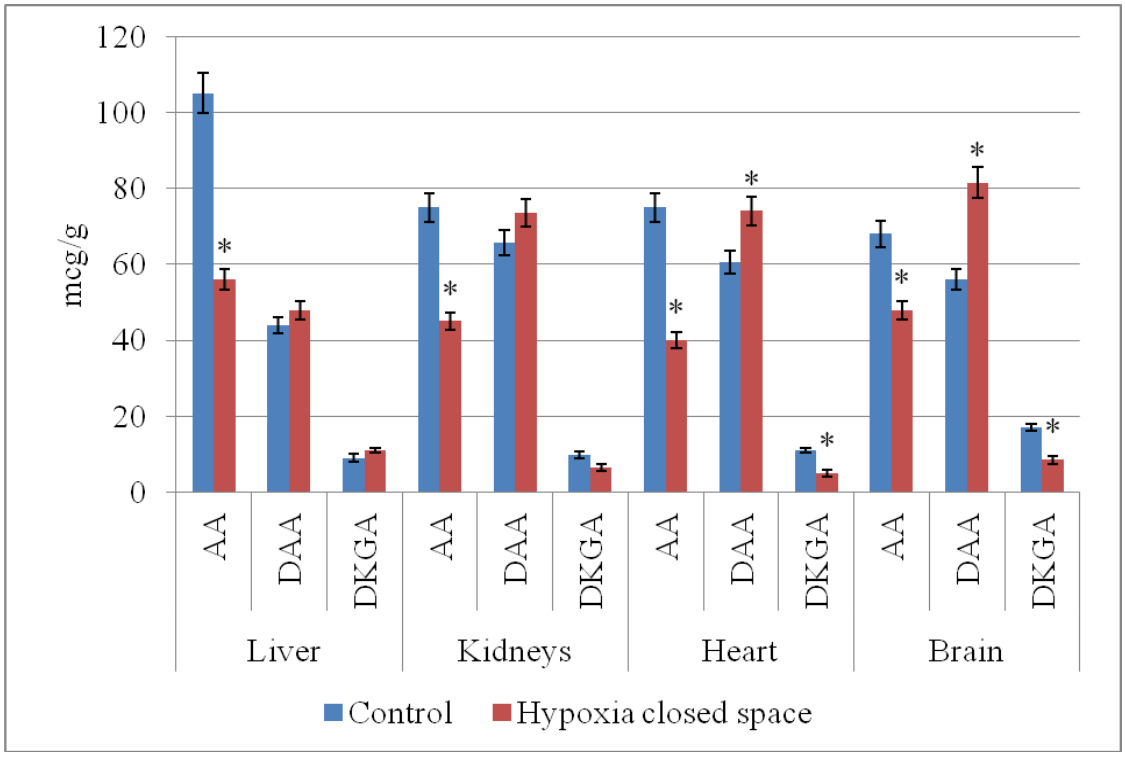

Figure.1. Contents of ascorbic (AA), dehydroascorbic (DAA) and diketogulonic (DKGA) acids in the organs of rats in case of closed space hypoxia (CSH) (μg/g), (n = 5)

Note: here and elsewhere: * - differences from the relevant control are reliable, p≤0,05.

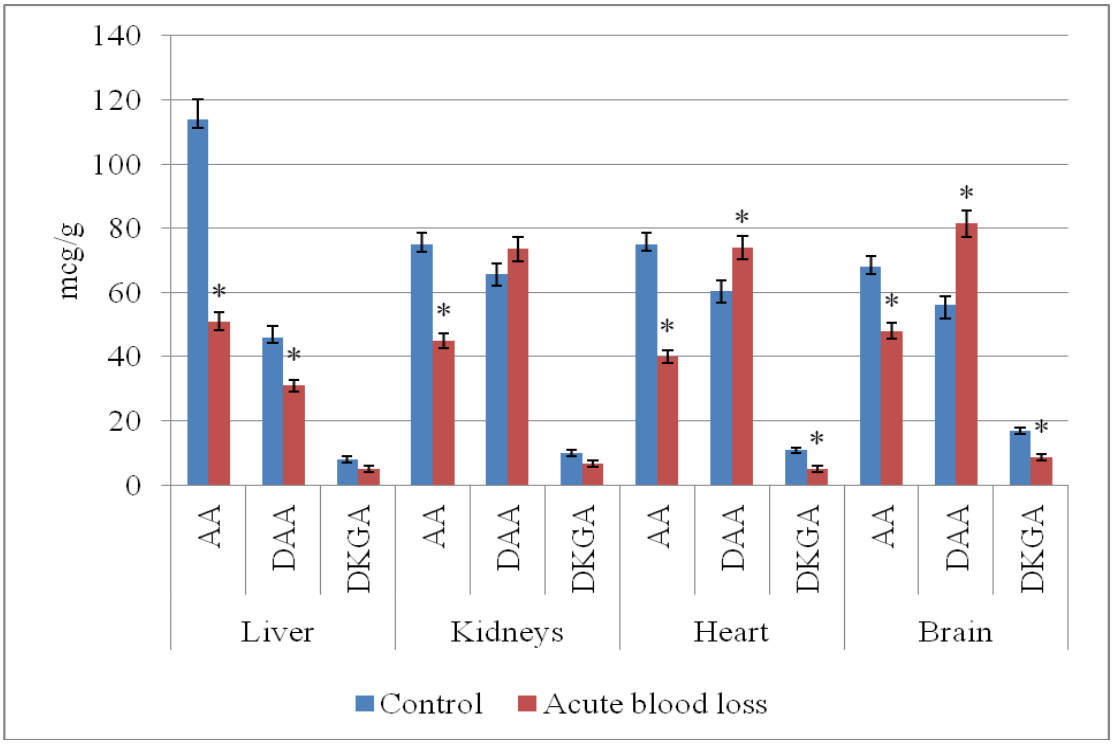

Figure 2. Contents of ascorbic (AA), dehydroascorbic (DAA) and diketogulonic (DKGA) acids in the organs of rats in case of acute blood loss (μg/g), (n = 5)

It is known that during sleep, as a result of decreased intensity of the heart performance and, correspondingly, slow blood supply to the organs, the amount of incoming oxygen is decreased. However, the demand of the body cells for oxygen is concurrently reduced. Therefore, it was necessary to study the peculiarities of the ascorbic acid metabolism during sleep, in other words, in a situation of decreased oxygen supply of tissues against the background of reduced demand for it. These data are presented in Figure 3.

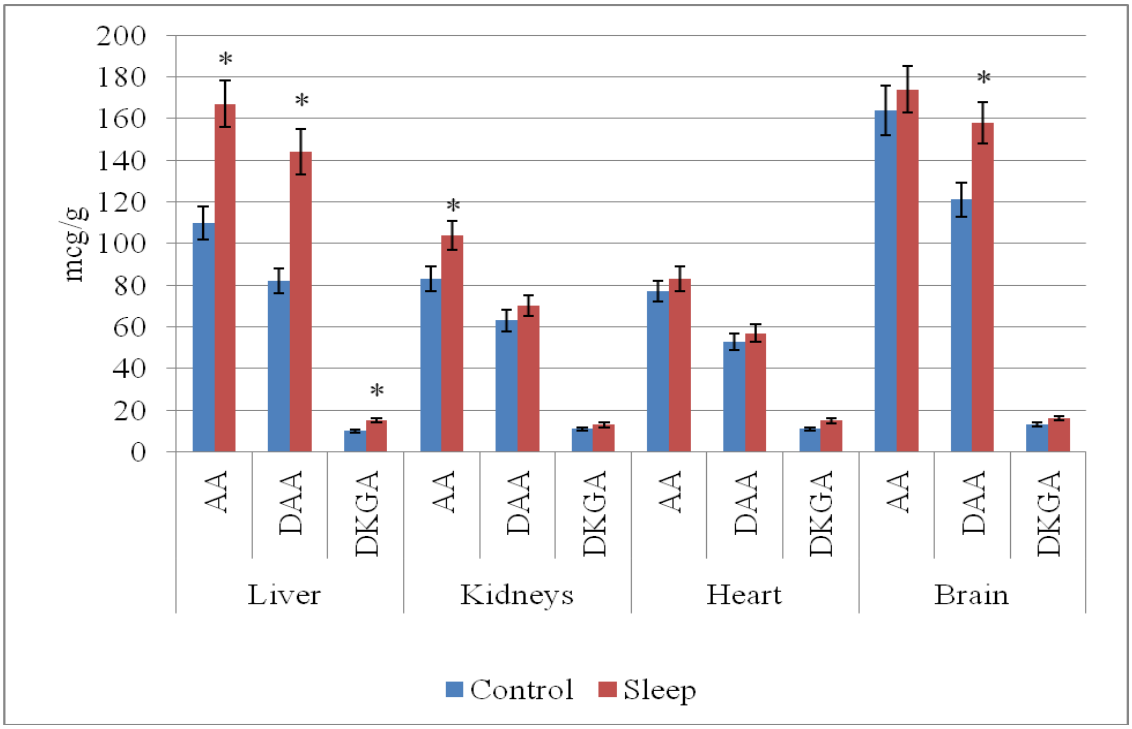

Figure 3. Contents of ascorbic (AA), dehydroascorbic (DAA) and diketogulonic (DKGA) acids in the organs of rats during sleep (μg/g), (n = 5)

As is seen from the data shown in the figure, the observed picture is precisely the opposite of picture observed in case of closed space hypoxia and acute blood loss. In particular, during sleep, the levels of both ascorbic acid and its major metabolites have increased to a greater or lesser degree. These effects were manifested to the fullest extent in the liver and in the lowest - in the heart.

In order to assess the significance of mentioned changes for the organism, we determined the total contents of ascorbic acid and its metabolites and the ratio of vitamin-active forms (AA + DAA) and vitamin-inactive form (DKGA) in the organs of rats with the use of the abovementioned three models of reduced oxygen supply to the tissues.

In case of closed space hypoxia (Table 1) it is established, that in all studied organs the sum of ascorbic acid and its main metabolites is significantly reduced. This pattern is most

pronounced in the liver (by 1.37 times), in the heart (by 1.3 times) and in the kidneys (by 1.2 times). In the brain, this parameter was virtually unchanged.

Table 1

Sum of ascorbic acid and its metabolites (AA+DAA +DKGA) (μg/g) and ratio of vitamin-active forms (AA + DAA) to vitamin-inactive form (DKGA) in case of closed space hypoxia (CSH) (n=5)

Organ	Index	Control	CSH
Liver	Sum	158±7,9	115±5,75*
	(AA+DAA) / DKGA	16,56	9,455
Kidneys	Sum	150,6±7,53	125±6,25*
	(AA+DAA) / DKGA	14,37	18,23
Heart	Sum	146,6±7,33	119±5,95*
	(AA+DAA) / DKGA	12,33	22,8
Brain	Sum	141±7,05	138±6,9
	(AA+DAA) / DKGA	7,294	15,24
Here and elsewhere: * - differences from the relevant control are reliable, $p \leq 0,05$.			

The ratio of vitamin-active forms (AA + DAA) and vitamin-inactive form (DKGA) in the liver and kidneys decreased, but in the heart and brain it did not change.

In case of acute blood loss (Table 2), a similar pattern was observed generally, but it was even more pronounced than in case of closed space hypoxia.

Table 2

Sum of ascorbic acid and its metabolites (AA+DAA +DKGA) (μg/g) and ratio of vitamin-active forms (AA + DAA) to vitamin-inactive form (DKGA) in case of acute blood loss (n=5)

Organ	Index	Control	Acute blood loss
Liver	Sum	168,0±7,1	87,0±3,9*
	(AA+DAA) / DKGA	20,0	16,4
Kidneys	Sum	164,0±10,7	111,0±5,1*
	(AA+DAA) / DKGA	15,4	7,5
Heart	Sum	159,0±12,4	127,9±9,6
	(AA+DAA) / DKGA	5,1	4,9
Brain	Sum	155,0±14,0	118,8±11,0*
	(AA+DAA) / DKGA	6,7	7,0

The opposite picture was established with the use of sleep model (Table 3). In this

state, the sum of ascorbic acid and its major metabolites was higher than in the control. This pattern was especially pronounced in the liver. At the same time, the ratio of vitamin-active metabolites to vitamin-inactive form practically was virtually unchanged.

Table 3

Sum of ascorbic acid and its metabolites (AA+DAA +DKGA) (μg/g) and ratio of vitamin-active forms (AA + DAA) to vitamin-inactive form (DKGA) during sleep (n=5)

Organ	Index	Control	Sleep
Liver	Sum	202,0±12,0	326,0±21,0*
	(AA+DAA) / DKGA	19,2	20,7
Kidneys	Sum	157,0±12,0	187,0±14,0
	(AA+DAA) / DKGA	13,3	13,4
Heart	Sum	141,0±10,0	155,0±9,0
	(AA+DAA) / DKGA	11,8	9,3
Brain	Sum	298,0±21,0	348,0±22,0
	(AA+DAA) / DKGA	21,9	20,8

Discussion

The ascorbic acid is directly and indirectly involved in many oxidation reduction processes in the body due to its ability to transfer from oxidized form to reduced one and vice versa. Therefore, the dependence of metabolic transformations of this vitamin on the oxygen supply to the tissues is an important indicator.

Our work demonstrates that decreased oxygen supply to the tissues both in case of closed space hypoxia and acute blood loss results in decrease in the level of reduced metabolites (AA and DKGA) and increase in the level of oxidized metabolite (DAA) of the ascorbic acid. This phenomenon probably should be considered the manifestation of a “defense reaction”, which reduces to the storage of an oxidized form in case of oxygen deficiency.

While using the sleep model, the contents of ascorbic acid, DAA and DKGA increased to different extents, despite the reduced oxygen supply to the tissues. This effect may be associated with a decrease in the intensity of ascorbic acid catabolism during sleep, in parallel with its continuing synthesis. This concept is indirectly confirmed by the fact that during sleep the ratio of ascorbic acid metabolites is virtually unchanged along with an increase in the sum of ascorbic acid and its metabolites.

The ratio of vitamin-active forms of AA to vitamin-inactive form decreased both in

case of CSH and acute blood loss, which indicates increased catabolism of this vitamin. This is also indicated by a decrease in the content of the sum of AA metabolites in all studied organs in cases of CSH and acute blood loss.

Conclusions

1. The decreased level of ascorbic and diketogulonic acid with simultaneous increased content of dehydroascorbic acid in the heart and brain has been observed in case of closed space hypoxia.

2. The acute blood loss results in decrease in the level of both ascorbic acid and its metabolites.

3. Increase in the level of both ascorbic acid and its metabolites due to a significantly decreased intensity of its catabolism with its continuing synthesis in the body has been observed during sleep.

4. The ratio of vitamin-active metabolites to vitamin-inactive diketogulonic acid in case of closed space hypoxia and acute blood loss is reduced, and during sleep it is virtually unchanged.

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