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Branched chain amino acids (BCAAs) in heart diseases (ischaemic heart disease and myocardial infarction)

Large-scale epidemiological studies have identified numerous risk factors for the development of cardiovascular disease. It has been suggested that as many as 250 factors may be associated with the development of coronary artery disease (13). The normal myocardium meets its high-energy demands by oxidation of a huge variety of substrates. Under conditions of ischemia oxygen uptake by the myocardium is insufficient to maintain normal rates of cardiac oxidative metabolism (2, 13). Heart disease appears to transform efficient cardiac metabolic cycles into less efficient pathways. Among substrates, which have received considerable interest as potential cardioprotective agents, are amino acids (11).

In physiological conditions each amino acid concentration changes defined, stable limits and depends on many factors such as sex, age, diet, intensity of physical activity or general organism status. In myocardial ischemia branched-chain amino acids (valine, isoleucine, leucine) derived from the mobilization of muscle protein may be an important alternative energy substrate for the heart. BCAAs are oxidative energy substrates for the heart and may exert anabolic effects on myocardial protein (8).

The aim of the study was to determine branched chain amino acids (BCAAs) concentrations in blood plasma of patients with ischaemic heart disease and myocardial infarction and to estimate changes that these amino acids undergo during the first five days of patients' hospitalization.

MATERIAL AND METHODS

The experiment was conducted on the blood plasma of patients in diverse age undergoing hospitalization in the Provincial Hospital in Kielce. Blood plasma was obtained during diagnostic examinations of people with ischaemic heart disease – 12 persons (5 women and 7 men, age range 42–76) and after myocardial infarction – 21 persons (7 women and 14 men, age range 40–70). As a control group blood plasma of 16 healthy individuals (7 women and 9 men, age range 28–57) was used. The materials for the experiment were collected in the moment of admission to hospital and in the first, the third and the fifth day of hospitalization.

The blood specimens were collected in heparinized tubes and centrifuged rapidly before stored at –20°C. The supernatant plasma was removed with a Pasteur pipette. Before the measurements 1 ml of each sample plasma was treated with 1 ml of 6% sulfosalicylic acid in lithium-citrate buffer pH 2.8 and centrifuged at a high speed. Branched chain amino acids analysis was performed by the automated ion-exchange chromatography (9) on an Ingos AAA 400 amino acid analyser (Czech Republic). Results were made using the t-Student test and obtained values were considered significant with $p < 0.05$.

RESULTS

Table 1 shows average content of BCAAs in blood plasma in control group and in the group of patients after myocardial infarction and standard deviations. Concentrations of those amino acids in the patients at the moment of admission to the hospital ward (day 0) were essentially statistically lower than in the control group. In the case of valine and isoleucine each amino acid decrease amounted to 15%, and in the case of leucine – 28. On the first day (day I) after occurrence of myocardial infarction the slow increase of leucine concentration and from the third day (day III) the increase of all determined amino acids were observed. On the fifth day (day V) after admission to hospital concentrations of all, valine, isoleucine, leucine turned back into the values obtained for the control group.

Table 1. Plasma BCAAs concentrations (nmol/cm^3), and a comparative analysis between the group of cardiac infarction patients and control group

	Valine		Isoleucine		Leucine	
	X	SD	X	SD	X	SD
Control	283	12	91	13	175	6
0	239*↓	12	77	5	126*↓	11
I	252*↓	4	78	3	146*↓	8
III	264	7	83	4	154	5
V	274	5	93	7	169	6

*$p < 0.05$ – statistical significance in comparison to control

BCAAs concentrations change in blood plasma of patients undergoing hospitalization because of ischaemic heart disease are shown in Table 2. At the moment of admission to hospital (day 0) valine average concentration was 10% lower than that in the control group, isoleucine concentration – 26% lower and leucine concentration – 23% lower. After five-day observation, it was stated that valine and leucine levels remained essentially statistically decreased in comparison to the control group, and only isoleucine concentration starting from the third day (day III) of hospitalization, underwent a slight increase.

Table 2. Plasma BCAAs concentrations (nmol/cm^3), and a comparative analysis between the group of myocardial ischemia patients and control group

	Valine		Isoleucine		Leucine	
	X	SD	X	SD	X	SD
Control	283	12	91	9	175	6
0	254*↓	7	67*↓	12	134*↓	12
I	248*↓	7	67*↓	7	138*↓	4
III	241*↓	6	75	8	149*↓	5
V	244*↓	5	72	7	150*↓	4

*$p < 0.05$ – statistical significance in comparison to control

DISCUSSION

In this paper BCAAs concentrations in ischaemic heart disease and myocardial infarction were compared. BCAAs, i.e. valine, isoleucine and leucine, are indispensable amino acids of special interest and are not synthesised in the body, their availability is determined by breakdown of proteins, either ingested or endogenous (7).

The increase of all BCAAs concentrations that has been observed at the moment of myocardial infarction, from the third day starts to increase, and on the fifth day reaches the level measured at healthy objects. Another situation is in case of ischaemic heart disease, where the first five days of stay in hospital do not influence essentially the BCAAs changes. Those amino acids, among others glucose, lactate, fatty acids, homocysteine, ketone bodies, are one of many substrates that undergo significantly increased intake by the heart (10). The enhanced rate of BCAAs oxidation in coronary blood is associated with the systemic inflammatory response, a host frequently induced by severe illnesses such as sepsis, trauma, burn injury (5). Several observations report that the hearts of patients with coronary artery disease extract more glutamate from arterial circulation and release more alanine into coronary venous blood than those of healthy subjects (14, 15). Under most physiological conditions BCAAs are utilized as an alternative energy source to synthesise alanine and glutamine (3). Because the needs of BCAAs for synthesis of alanine and glutamine are met mainly by increased breakdown of muscle protein, the undesirable result of activated synthesis of alanine and glutamine is muscle-protein-wasting (5). BCAAs derived from the muscle protein may be an important energy substrate for the heart. The decrease in BCAAs levels is consistent with a decrease in amino acids levels in sepsis, chronic liver disease and, probably in coronary artery disease (7, 16).

The differences between certain BCAAs depend on their metabolic activity. Leucine, of all amino acids, has a unique role in serving as a regulator of protein turnover in cardiac muscle as leucine is the only amino acid that inhibits protein degradation. Leucine is likely to be an important factor in determining the ischemia-induced fall in protein degradation (1).

The first step of BCAAs metabolism involves reversible transamination leading to the production of branched chain α-ketoacids (BCKAs) (4). BCKAs in turn are subjected to oxidative decarboxylation by α-ketoacid dehydrogenase complex (BCKDC). BCKDC catalyses an irreversible reaction that commits the individual BCKAs to their respective degradation pathways (4). The BCKAs also serve as significant sources of the intercellular amino acids used for protein synthesis in most organs, particularly the heart and the brain (12). It is possible that cellular changes seen during ischemia influence the activity of the BCKDC. Intervention in the pathway of the BCAA-BCKA cycle might be a useful method of affecting the development of negative protein balance (5). This suggests that BCAAs might serve as a preferential substrate during ischaemic heart disease. Nevertheless, the beneficial use of BCAA-enriched preparations for the human heart remains controversial.

CONCLUSIONS

1. In acute myocardial infarction and in ischaemic heart disease decrease in BCAAs (valine, isoleucine, leucine) concentrations was observed in comparison to the control group.

2. In myocardial infarction starting from the third day after its occurrence, increase in the BCAAs concentration was stated, and on the fifth day amounted to the value of the control group.

3. In patients with ischaemic heart disease till the fifth day from the moment of the hospitalization beginning the statistically important increase of valine, isoleucine, leucine concentrations did not appear.

4. Supplementation of branched chain amino acids in an ischaemic heart disease therapy may influence the improvement of patients' health, but further investigations are required.

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SUMMARY

Acute and chronic ischaemic diseases are among the main death reasons and civilized world menace. Branched chain amino acids (BCAAs): valine (Val), leucine (Leu), and isoleucine (Ile) are the main source of nitrogen to glutamine (Gln) and alanine (Ala) synthesis in muscles. In numerous cachexy-producing illnesses such as cancer, sepsis, diverse injuries and heart diseases increased consumption of BCAAs occurs. In myocardial ischemia BCAAs derived from the mobilization of muscle protein may be an important alternative energy substrate for the heart. BCAAs are oxidative energy substrates for the heart and may exert anabolic effects on myocardial protein (8). The aim of our study was to determine branched chain amino acids (BCAAs) concentrations in blood plasma of patients with chronic and acute ischeamic heart disease and to find out changes that those amino acids undergo during the first five days of patients' hospitalization.

Stężenia aminokwasów rozgałęzionych (BCAAs) w schorzeniach serca (niedokrwienna choroba serca i zawał mięśnia sercowego)

Ostra i przewlekła choroba niedokrwienna serca stanowią obecnie jedne z głównych przyczyn zgonów oraz zagrożeń cywilizowanego świata. Aminokwasy rozgałęzione: walina (Val), izoleucyna (Ile), leucyna (Leu) są głównym źródłem azotu, wykorzystywanym do syntezy glutaminy (Gln) i alaniny (Ala) w mięśniach. W wielu wyniszczających chorobach, takich jak nowotwory, posocznica oraz choroby serca, ma miejsce zwiększone zużycie tych aminokwasów. W chorobie niedokrwiennej rozgałęzione aminokwasy pochodzące z rozpadu białek mięśniowych mogą stanowić ważne alternatywne źródło energii i mogą być wykorzystane do syntezy białek własnych mięśnia sercowego. Celem badań było oznaczenie stężenia aminokwasów rozgałęzionych w osoczu krwi pacjentów z chorobą niedokrwienną serca i zawałem mięśnia sercowego oraz określenie zmian, jakim ulegają te aminokwasy podczas pierwszych pięciu dni hospitalizacji chorych.