Chemical Physiology of Muscle Contraction

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The mechanical response of an isolated muscle to an excitant is not accompanied by any oxygen consumption increase; the additional amount of oxygen is not consumed as long as contraction and relaxation have not occurred. Thus, there are two contraction phases, an anaerobic (anoxidative) phase and an aerobic (oxidative) or recovery phase, during which the muscle resumes its previous stage. When the muscle is repeatedly excited in a nitrogen atmosphere, it strongly contracts at the beginning, but it gets quickly exhausted, since between contractions it cannot get the necessary oxygen for its recovery. Lactic acid gathers in the muscle, which becomes stiff. If it gets oxygen at the beginning of its fatigue, the lactic acid disappears and the muscle recovers its initial contraction strength. The lactic acid concentration at which complete skeletal muscle fatigue sets in (i.e. the lactic acid peak) ranges between 0.3 and 06%. In order to release the energy it needs for its contraction, the muscle does not depend on immediate oxidative processes. It continues to contract for a certain amount of time even when it is completely deprived of oxygen.

Keywords: energy metabolism, aerobic, anaerobic, contraction, chemical reaction, muscle groups

The muscle is mainly made up of proteins (18-20%) and water (75-80%). The rest is made up of different minerals and a high number of organic compounds, some of which occur only in the muscle tissue. Potassium is the main electrolyte and occurs in a concentration of about 400mg/ 100 g. Magnesium, calcium and sodium are present in much smaller amounts. The muscle contains a great variety of substances generally grouped under the name of nitrate extraction bodies, such as creatine, phosphocreatinine, alanyl-histidine and adenosine triphosphate, creatinine, purine bases, carbosin, anserine (in poultry and fish meat), etc [1].

The muscle contains between 0.5 and 1.5% glycogen, between 0.02 and 0.04% glucose and about 0.01% lactic acid. Phospholipids (1%), cholesterol (0.07-0.18%), vitamins, enzymes and a number of other organic substances are also present.

Among the muscle proteins, myosin and actin make up the contractile elements, filaments and micelles. Myosin makes up about 60% of the total proteins, and actin about 12%. Protein N, a nucleoprotein, globulin X, myogen and myoalbulin are the other proteins making up the sarcoplasm.

Myoglobulin, the muscle oxygen deposit, makes up about 1% of the red muscle.

Experimental part

Material and methods

From January 2016 to March 2017, we have investigated 5849 patients (643 children – 10.99% and 5206 adults – 89.01%) referred to the private practice office located in an urban setting, the city of Galai. Our study investigates the cases who showed symptoms indicating muscle contractions. Due to the fact that both smooth muscle contractions and the contractions of skeletal muscles cause pain, many patients referred to the services of family practice when muscle cramps, stiffness or spasms became persistent or severe.

We have avoided palpation with cold hands, as this could trigger guarding, an involuntary contraction of the abdominal muscles.

Results and discussions

Muscle contractions were found in 7 cases of hypothermia, when shivering occurred, in order to generate heat.

As a sign of miscarriage in pregnancy, uterine muscle contractions were expressed as pelvic cramping in 17 patients aged between 27 and 39 years. Only 2 teenage patients complained of dysmenorrhea, which is caused by the lack of oxygen supply to the uterus, following the uterine muscle contractions. In 6 preadolescent boys, the growing process was the cause of pain, and not the failure to relax and prolonged muscle contractions.

There were 2 patients with anaphylactic syndrome and 5 patients with asthma, who showed dyspnea, caused by the narrowing of the airways induced by smooth muscle contractions.

Smooth muscle contractions can also cause biliary colics, as an attempt of the body to clear a gallstone from a cystic duct or from a common bile duct. 643 patients showed vomiting and abdominal pain associated with gastritis, cholecystitis and pancreatitis. Sometimes, the pain was caused by vomiting, following the forceful contractions of abdominal muscles.

A number of 32 patients were required to make a tetanus toxoid vaccine, after getting injured from falling and using rusty nails. Tetanus manifests itself through severe muscle contractions. Spasms occur not only in the masseter muscles, but also in the muscles of the back, arms, diaphragm and lower extremities.

67 patients with headache could have had pain caused by muscle contraction, due to the overuse of the masseter muscle or to the prolonged contraction of the extraocular muscles. However, since the exact etiology of headaches could not be established, the goal of our intervention was to provide pain relief.

There was 1 pediatric patient aged 2 who had seizures that might indicate epilepsy. The seizures caused by disturbances in the motor cortex lead to muscle contractions.

Work accidents occurred in 11 male patients. The excessive muscle contractions were caused by the body's effort to secure the area of injury and to reduce further tissue damage.

There were no cases of muscle contractions caused by lightning or electrocution. Electrical injuries caused by alternating current and not direct current, as in lightning, could be especially dangerous, due to the locking on phenomenon, the tetanic muscle contractions that prevent the victim from releasing the electrical source. There were also no children with movement disorders such as spastic

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displegia, where leg spasticity makes walking difficult, or dystonia, with repetitive muscle contractions.

The diagnosis of disorders that prevent the delivery of glucose or fatty acids and impair the production of energy for muscle contraction requires further laboratory tests. That is why, we could not identify such cases during the physical examination and history taking.

It is well known that a muscle may contract in anaerobic conditions; lactic acid and CO_2 is formed in a muscle which is contracted in a nitrogen atmosphere.

Despite these observations, it has been believed that a muscle gets its energy from the oxidative processes. Otherwise, how could CO_2 have been generated? It has been assumed (Hermann, Pflüger) that the muscle substance itself has oxygen stored in certain giant molecules called *inogen* by Hermann. Thus, *intramollecular* oxygen was thought to be the oxygen deposit which the muscle resorts to during its anaerobic contraction. Also, lactic acid was believed to originate in the decomposition of this hypothetical molecule.

This theory was ruled out by Fletcher's and Hopkins' well-known experiments conducted in 1907. These researchers showed that the CO_2 occurring during anaerobic contraction was not the result of oxidation, but it preceded it, being released by the action of lactic acid on the sodium bicarbonate in the muscle fluids. They showed that the oxidative process occurred after the contraction had ended, when the lactic acid disappeared and CO_2 was formed. They wrongly assumed that the disappearing lactic acid was completely oxidized in CO_2 and water [2].

The fact that glycogen was the precursor of the lactic acid was proven by the fact that the amount of lactic acid produced in the tired muscle in a nitrogen atmosphere was proportional to the amount of disappearing glycogen. Meyerhoff later found that carbohydrates were the substances burnt during the recovery phase of an isolated muscle.

Oxygen is needed for muscle recuperation, i.e. for the recovery of its energy reserves. The muscle may be compared to an engine; when it contracts it makes an oxygen debt, which it pays when the contract is over.

Research conducted on the enzymatic systems in the aqueous muscle extracts and brewer's yeast juice during alcoholic fermentation has provided data on the anaerobic chemical processes.

One of the first stages in releasing the energy required for muscle contraction is the coming apart of the glycogen stored in the muscle fibers. Glycogen fixes the orthophosphoric acid components (H_3PO_4) and is neutralized in glucose 1-phosphate molecules (Cori ester). This reaction is catalyzed by phosphorylase [3].

Glycogen molecule neutralization occurs successively at the level of the bonds 1-4 (C-O-C) between the glucose units. In the separation process, the H atom of the phosphoric acid is bound to the carbon atom 4, whereas the carbon atom 1 of the neighboring glucose molecule fixes the–O-PO_3H_2 group.

Phosphoric acid fixation and glycogen neutralization in glucose-phosphate units were accurately called by Parnas *phosphorolysis*, since the process obviously resembles hydrolysis in which water (H.OH) is fixed instead of phosphoric acid, the H and OH atoms being bound to the neighboring groups of larger molecules (proteins, disaccharides, polysaccharides, etc.) when they are changed.

The glucose 1-phosphate formed further to the phosphorolysis reaction undergoes an intramolecular transfer of its phosphate group to carbon 6, thus turning into glucose 6- phosphate (Robinson ester). This reaction is catalyzed by phosphoglucomutase. Under the action of *phosphohexose isomerase*, glucose 6-phosphate produces fructose 6-phosphate (Neuberg ester), which receives a phosphate group from adenosine triphosphate (ATP) to form fructose-1, 6-diphosphate and adenosine diphosphate (ADP) [4].

Under the action of aldolase, fructose-1, 6-diphosphate splits in the triose phosphates *dihydroxyacetone phosphate* and 3-phosphoglyceraldehyde (Fisher-Baer ester).

3-*phosphoglyceraldehyde* reacts with the inorganic phosphate and is turned into 1,3-diphosphoglyceric acid in the presence of glyceraldehyde-3-phosphate dehydrogenase and DPN (diphosphopyridine nucleotide or coenzyme 1).

DPN accepts H_2 and reduces to $DPNH_2$. As soon as dihydroxyacetone phosphate is formed, it is turned into 3-phosphoglyceraldehyde (called the reactive form of sugars), which is quickly removed in the presence of glyceraldehyde-3-phosphate dehydrogenase. The reaction is this diverted to the right.

1,3-diphosphoglyceric acid undergoes a dephosphorylation process and forms 3-phosphoglyceric acid, and the phosphate group released turns ADP into ATP. By the intramolecular transfer of the phosphate group, the 3-phosphateglyceric acid turns into 2-phosphoglyceric acid, the reaction being catalyzed by phosphoglycerate mutase. 2-phosphoglyceric acid is turned by dehydration into *phosphoenolpyruvic* acid under the action of *enolase*.

Phosphoenolpyruvic acid reacts with ADP, and pyruvic acid and APT are thus produced. This reaction is catalyzed by a transphosphorylase in the presence of magnesium and potassium ions [5].

In the absence of oxygen, pyruvic acid is reduced to lactic acid by the reduced coenzyme ($DPNH_2$) in the presence of lactate dehydrogenase enzyme, the coenzyme resuming its oxidized form (DPN).

In *aerobic* conditions, the reduced coenzyme is not oxidized by pyruvic acid, but by molecular oxygen under the combined action of a specific flavoprotein and of the cytochrome system. Thus, due to an adequate amount of oxygen, lactic acid is not formed, whereas 1/5 of the lactic acid formed in anaerobic conditions is oxidized in carbon dioxide and water, passing through pyruvic acid, whereas the rest is resynthesized in glycogen. In intact animals, the synthesis occurs in the liver. Lactic acid oxidation in pyruvic acid is done under the action of lactate dehydrogenase in the presence of DPN. Pyruvic acid is oxidized in the presence of oxygen and follows a series of stages called the tricarboxylic acid cycle [6].

Oxaloacetic acid and acetyl coenzyme A combine to form citric acid. Citric acid loses a water molecule and is turned into cis-aconitic acid; it then regains a water molecule to produce isocitric acid, which is oxidized in oxalosuccinic acid. The latest is decarboxylate, being turned into α-ketoglutaric acid, which is oxidized into acid succinic acid, carbon dioxide and water.

Succinic acid is oxidized in oxaloacetic acid, after passing through the fumaric and malic acid stages. The cycle repeats itself after oxaloacetic acid regeneration. An acetylic group derived from pyruvic acid is oxidized during each cycle; therefore, while an oxaloacetic acid molecule is recovered, each pyruvic acid molecule makes up two water molecules and three carbon dioxide molecules. Thus, a single oxaloacetic acid molecule may be used repeatedly in acetyl group oxidation in carbon dioxide and water; therefore, it acts as a catalyst.

The energy supplied for performing a thing by the anaerobic formation of lactic acid from glycogen is only a small part of the energy resulting from lactic acid oxidation. The energy released for each molecule-gram of lactic acid formed amounts to about 29 000 calories, whereas the oxidation of an equal amount of lactic acid into carbon dioxide and water releases about 325000 calories.

Transfer of the chemical energy accumulated in ATP to the muscle fibers and its turning into mechanical energy

When adenosine triphosphate is split, the energy of one of its pyrophosphoric bonds is turned in the muscle fibers into mechanical energy needed for muscular work performance. After ATP splitting, the Atp deposits are restored by its re-synthesizing from ADP and phosphate derived from phosphocreatine, as well as from glycolysis. Thus, the ATP/ADP system serves as transmission belt used to carry the energy of the phosphatic bonds in phosphocreatine and glycolytic processes to the muscles [7].

Adenosine triphosphatase (ATP-ase) catalyzes terminal phosphatic group splitting in the nucleotide molecule and, consequently, ADP formation. After Enghelhardt's findings, according to which myosin, the main muscle protein, that had long been recognized as the contractile element, has ATP-asic activity, chemical reactions have been seen as closely connected with mechanical effects, i.e. closely connected with the real muscle contraction. In reference to muscles, energy transformation may be compared, up to a certain point, to what happens in a spark-ignition engine; in the muscles, ATP, which is the immediate source of energy needed for movement, is the explosive mixture, whereas myosin is the piston (Enghel-hardt); yet, the analogy ends here, since in the muscular machine myosin, i.e. "the piston", is the ignition system (ATP-asic activity of myosin). The muscle may be much more accurately compared to an imaginary heat engine, in which the piston itself is heated to a temperature at which it manages to ignite the gaseous mixture; then, the combustion products act on the piston and produce movement by changes in their physical properties. Nonetheless, the muscle is not a heat engine; its drive force does not depend on the pressure of the heated molecules, but on the energy released by the inter- and intra-molecular transfer of the chemical groups [8].

Myosin is formed as small needle-shaped crystals; after repeated crystallizations, no ATP-ase activity loss is detected, but rather its increase. Myosin and ATP-ase were considered identical, although there is no evidence to support this assumption.

If not anything else, they are very closely related.

- Unprocessed myosin preparations contain many other enzymes, which may be completely removed by successive precipitations.

- Myosin and ATP-ase thermolability is very similar, the protein being distorted and the enzymatic activity being abolished at the same temperature, which is relatively very low.

- Electrophoretic research has showed that myosin is highly homogeneous, and the large fraction which migrates rapidly and makes up over 90% of the preparation protein has double ATP-asic activity, as compared to the smaller fraction which migrates slowly and has low protein content.

- A muscular aqueous extract (deprived of myosin) only has poor ATP-asic activity.

Myosin only splits a phosphatic group from adenosine triphosphate. ADP is not attacked. In this respect, it is highly specific. Calcium ions activate ATP-ase, whereas magnesium, copper and silver inhibit it; enzyme activity is not influenced by cyanide [9].

ATP neutralization by ATP-ase is the immediate fundamental chemical process which occurs in muscle contraction. In the muscle relaxation state, the polypeptidic chains of myosin are partially folded, the folding becoming more complete during muscle contraction. Thus, the micelle polypeptide chains, laid out in approximately parallel bunches, become shorter or longer just like the accordion bellows.

Effects of chemical changes and energetic transformations related to muscle contraction

The sequence of chemical changes leading to the release of energy required for muscle contraction will be represented by observing the order of their occurrence in the body.

The first reaction is the splitting of the terminal phosphatic group of ATP. This reaction is catalyzed by ATP-ase. ADP is formed. Simultaneously, the phosphate released is involved in glycogen phosphorylation, the adenylic acid acting as a coenzyme, in an unknown way. ATP is re-synthesized by the phosphate released by phosphocreatine (Lohmann reaction). Glycogen turning into lactic acid supplies the energy necessary for phosphocreatine re-synthesizing and then, as the contraction unfolds, for ATP re-synthesizing, which stores energy as phosphatic bonds. These reactions may also occur in the absence of oxygen [10].

In the presence of oxygen, about 1/5 of the lactic acid formed is oxidized; it supplies the energy necessary for the re-synthesizing in glycogen of the remaining 4/5. If the oxygen intake is adequate, lactic acid formation is reduced or null. In the absence of oxygen, lactic acid accumulation first slows down and then discontinues glycogen splitting into lactic acid and, consequently, phosphocreatine and ATP re-synthesizing is prevented.

Conclusions

Most muscle contractions cause pain that is usually not ignored by the patients registered to family practice. Digestive disorders, the risk of pregnancy loss and work accidents were the most common reasons for referral to the family practice office that involved muscle contractions. That is why family doctors should achieve a better understanding of the biochemical and physiological aspects of muscle research.

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