Could a sick heart be treated with additional energy substance?

The heart is a muscle organ that by means of blood pumping provides continuously changing requirements in oxygen, energetic and building material to the tissues and organs. The heart in a couple of minutes could augment the blood volume by several times that allows a man to make quite variable physical activity. To be able to perform this function the heart has the creatine kinase system within heart muscle cells that in a highly efficacious way permits to transport a huge amount of energy from the sites of energy production to the sites of energy consumption, mainly muscle contractile proteins. This system consists of enzyme creatine kinase, creatine and phosphocreatine (PCr) that acting together as an energy buffer that can near instantaneously provide high amount of energy to the heart contractile proteins.

There are acute and chronic heart disorders mainly due to insufficient blood supply when the heart does not receive enough oxygen and energy substrates. It has long been established that the components of the creatine kinase system are commonly impaired in most such conditions. In addition, the deficiency of the system is detrimental to heart functional recovery. Moreover, in patients with dilated cardiomyopathy it has been showed that ratio between the components of the creatine kinase system is a predictor of cardiovascular mortality.

For the first time we performed systematic review with the meta-analysis of all randomized clinical trials studying the clinical usage of exogenously administered PCr in patients with coronary artery disease or chronic heart failure as well as in those undergoing cardiac surgery. These clinical settings present the most common and actual alterations of myocardium energetics and work. While analysing 41 controlled trials with 5,069 patients we found that PCr used above the standard treatment can improve important clinical outcomes in acute and chronic states when the heart undergoes disturbances in the energy metabolism. In particular, PCr enhanced the heart performance in patients suffering from chronic heart failure and patients in immediate postoperative period after cardiac surgery. In acute energy deficit due to coronary artery disease and surgical stress PCr diminished the degree of heart muscle damage that was confirmed by determining of the highly sensitive biomarker. In addition, in heart surgery patients PCr reduced the number of the heart rhythm disturbances, the usage of the drugs that support cardiac work, and increased the heart recovery in the immediate post-surgical period. All these benefits of the drug could partially explain our major finding that PCr in patients with acute and chronic heart disease may reduce all-cause short-term mortality.

The findings of our meta-analysis require confirmation by a large, high-quality, blinded randomized trial. All the analysed evidence was with high risk of bias because a lot of trials were small, not blinded, and performed a long time ago. Finally, we investigated enough heterogeneous cardiac populations including patients with acute and chronic heart disorders as well as the studies in which different doses and modes of administration of PCr were used.

In the era of active search for new drugs that could influence cardiac morbidity and mortality which is considered as a number one in the world, the observed benefits of PCr, the usage of which is physiologically determined, could be an important and a timely step in the right direction. Furthermore, despite PCr is an extrinsically synthesized substance, the drug is an analogue of the human metabolite that takes part in the energy metabolism of the cells, including highly active heart muscle cells. This feature also possibly permits PCr to have a high safety profile in its use.

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Publication

Cardiac protection with phosphocreatine: a meta-analysis.
Landoni G, Zangrillo A, Lomivorotov VV, Likhvantsev V, Ma J, De Simone F, Fominskiy E
Interact Cardiovasc Thorac Surg. 2016 Oct