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CARDIOPROTECTIVE MEDICATIONS

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Heart diseases are one of the most prevalent in the world. As a result of these diseases the state of the heart function deteriorates and can never be restored. The only known way is use of cardio protectors.

The damage to heart can be of two primary causes in case of heart disease. First one is caused due to inadequate blood supply to the myocardium, leading to ATP depletion and switch to less efficient anaerobic glycolysis as mitochondria are unable to produce ATP, this switch leads to intracellular acidosis from increase of lactic acid production and decrease of pH level in the cell. The sodium-potassium pump suffering from lack of ATP decreases its activity and then stops entirely causing an increase in calcium level within the cell. Increased calcium levels lead to swelling of the cell. Increased calcium levels in combination with decreased pH leads to mitochondrial dysfunction that releases pro-apoptotic factors ultimately leading to cell death if the blood flow to the tissue is not restored in time. The second cause is due to the so-called reperfusion injury which occurs when blood flow is restored and accounts up to 50% of final infarct size. As the perfusion is restored mitochondrial enzymes create a large amount of reactive oxygen species such as superoxide, hydrogen peroxide and hydroxyl radicals, leading to oxidative stress that damages cell structures. With the appearance if oxygen and restoration of ATP production and pH level the heightened calcium level causes a hypercontraction leading to myocyte rupture, the calcium dependent proteases (calpasins) start digestion of cellular components contributing to cellular damage. Due to previously mentioned factors (ATP depletion, ROS and high calcium) mitochondrial permeability transition pores open. The opening of these pores leads to loss of membrane potential of mitochondria, their swelling and ultimately death with release of pro-apoptotic cytokines. Reperfusion also leads to inflammation of tissue and no reflow phenomenon.

There are multiple drugs that can protect heart from this damage and such drugs are known as cardio protectors or cardioprotective drugs. Cardioprotective drugs include the following: beta blockers such as metoprolol, carvedilol, etc., ACE inhibitors such as lisinopril, etc. Cardiac glycosides such as digitoxin, digioxin, and strophantin, and black cumin (*Nigella sativa*) extract containing thymoquinone.

Beta blockers achieve their protective effect through lowering the oxygen demand of myocytes by blocking beta adrenergic receptors thus having a negative chronotropic, negative inotropic, negative dromotropic, and negative bathmotropic effects. Which allows for the slower depletion of ATP and associated consequences of ischemia occurring from a lack of oxygen (Nasoufidou A, et al. 2025).

In turn, ACE inhibitors like lisinopril reduce preload and afterload by inhibiting angiotensin I conversion into, its more potent form, angiotensin II thus decreasing systemic vascular resistance, and reducing blood volume by decreasing aldosterone secretion. It also has a direct cardioprotective effect that is achieved by preventing breakdown of bradykinin, and increasing nitric oxide (NO) production which allows to limit damage from ischemia and reperfusion injury in myocardial infarction (M Kitakaze, et al. 2000).

Administration of cardiac glycosides in low doses that cannot lead to stronger contractions show a cardioprotective effect by pre conditioning and post conditioning the heart and mimicking natural defenses decreasing the damage to the heart from ischemia and reperfusion as was shown by animal studies (Duan Q, et al. 2018).

Thymoquinone from cumin acts as an antioxidant reducing oxidative stress by neutralizing ROS. Thymoquinone also has anti-inflammatory, anti-apoptotic activities and also activates protective autophagy decreasing cell deaths from changes occurring in myocytes during ischemia and reperfusion after (Alberts A, et al. 2024).