Protective Effect of CoQ10 in the Brain Temporal Cortex Neurons Following Ischemia – Reperfusion in Mice

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ABSTRACT

Aim: Previous study showed Reduce cell death in brain ischemia before and after treatment with antioxidants. The aim of this research was study of relationship between consumption of CoQ10 and neurons degeneration in brain temporal lobe following ischemia-reperfusion in mice.

Material & Methods: Experimental design includes four groups: control, ischemic, vehicle and treatment group. The mice pre-treated with CoQ10 for one week. Then, ischemia induced by common carotid artery ligation and following the reduction in inflammation in ischemic zone (one week) the mice post-treated with CoQ10 (one week). Nissl staining applied to counting necrotic cells and tunnel kit was used to quantify apoptotic cell death in temporal cortex neurons.

Results: High rate of apoptotic and necrotic cells was seen in ischemic group. Cell death was significantly lower when mice treated with CoQ10.

Conclusion: Ischemia for 15 minutes induced cell death in brain cortex. CoQ10 treated significantly reduced cell death following ischemia.

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Introduction:

Cortex is covering gray layer the brain surface. In brain, this layer is composed of nerve cells (1). Cortex is responsible for all human behavior voluntary. Human’s Cognitive behavior (cognition)al) is come from this organ (2, 3). Cortex must associate with the thalamus and thalamus is associated with specific regions of cortex. (4). Temporal cortex is damaged if subject to certain conditions such as ischemic. Ischemia is called to reduce the blood supply to the organ or area of the body. (5). Cerebral ischemia is a major cause of mortality in the world after cancer and heart attack. It also the first cause of disability over 65 years old (6). Reperfusion injury involves damage. It caused returns of blood to the tissue after an ischemic period. Reperfusion could impact on the cells and can be caused tissue necrosis and apoptosis (7). Ischemia reduces the oxygen concentration and ATP in the cells. During reperfusion, oxygen free radicals and other oxidative are formed which damage to cells with greater intensity than ischemia (8). One of the ways that can help to reduce the effects of ischemia in the brain is used of anti oxidants. CoQ10, including material that is usually associated with energy production in mitochondria. It also is known as an antioxidant (9). Coenzyme Q10 is a powerful antioxidant and may be involved maintaining normal muscle function (10). The restore barrier properties of CoQ10 enable it to be a very fat-soluble antioxidant (11). It seems that CoQ10 has the ability to stimulate the immune system. Antioxidants such as CoQ10 can neutralize the effects of harmful substances with removing them (12). The purpose of this study was investigate of the antioxidant effects of CoQ10 and its health impact on reducing the mortality rate of temporal cortex neurons after.

Material and Method

28 adult bulb-c mice, weighting 30 g ~35 g, were obtained from Iranian Razzi Institute. Mice were maintained in one colony room at temperature of 21 ± 1°C (50 ± 10% humidity) on a 12-h light/12-h dark cycle with access to water and food. The experimental protocol for animal care and handling was according to the guidelines of the National Institutes of Health.
The mice were assigned as follow (n= 7): 1- Intact group (control), 2- Ischemia control group, 3- Ischemia with vehicle group, 4- Treatment group with CoQ10.

CoQ10 were prepared as Tablets and olive oil was used as a solvent. In order to evaluate the protective effect of CoQ10 pretreatment, it was tacked one week before ischemia induction (450 mg / kg in day); Ischemia induced by clamping of common carotid artery (15 min) and after one week following reduction of inflammation on ischemic zone, CoQ10 for a week was given. Nissl staining and tunnel test performed two weeks following ischemia induction and then brains temporal cortex prepared for microscopic studies. Animals will be fasted overnight and anesthetized with ketamin (Sigma Chemical Co., Saint Louis, USA) (100mg/kg, i.P injection) and xylozine (Sigma Chemical Co., Saint Louis, USA) (10mg/kg, i.P injection). The tissue staining was performed using tunnel test and Nissl staining. The Nissl staining is commonly used for identifying the basic neuronal structure from necrotic neurons in brain. The Tunnel Apoptosis Detection Kit is one of Gen scripts newly introduced products. The kit can detect fragmented DNA in the nucleus during apoptosis.

**Statistical Analysis:** Data were statistically analyzed by SPSS software (version16). All data were expressed as Standard error of the mean (SEM). One way ANOVA, followed by Tukey post hoc test, was used for each group at different time points. In all analyses, the null hypothesis was rejected at the level of 0.05.

**Results:**

In this study we used the nissl staining to count the necrotic cell and used the tunnel kit to detect the apoptotic cell in the temporal cortex. The pictures in bellow show the result of these methods.

**Figure 1:** the nissl staining result in 4 groups. (400x) In this staining method, the necrotic cells indicated with dark and compact nucleus. The intact group without necrotic cell (1). The ischemic group with a lot of necrotic cells (2). The vehicle group with less necrotic cell rather ischemic group (3). The treatment group with infrequent necrotic cell (4).

**Diagram 1:** cell counting results in 4 groups. Ischemic group compared with the intact group (control) represents significant difference (P<0.001) *. Treatment groups compared with ischemic group represents significant difference (P<0.001) **. Cresyl violet staining showed the situation of healthy and necrotic cells in tissue sections. The Animals treated with CoQ10 had less death cells and had more cell density compared to the vehicle and ischemia groups.
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Figure 2: tunnel test result in 4 groups. (400x).
The intact group without apoptotic cell(1) and the ischemic group with a lot of apoptotic cell(gray cells)(2)and vehicle group with some apoptotic cell(3) and the treatment group with the less than other group is indicated (4).

Figure 4: Comparison of the tunnel test in 4 groups. Ischemic group compared with the intact group represents significant difference. (P<0.0001) **. Treatment group represents significant difference compared with Ischemic group. (P<0.0001) ***. Tunnel test that use for detect the apoptotic cell, showed increase of this cells in ischemic group and decrease of this cells in the treatment groups. Although in the vehicle groups the apoptotic cell was less than ischemic group but the treatment group has better position.

Discussion:

Abnormal structure of the small vessels is considered as risk factors for cerebrovascular events (13, 14). In addition to high intake of saturated fat causes accumulation in the vessel wall. It increases the extent of ischemic area (15). The purpose of this study was investigate of the antioxidant effects of CoQ10 and its health impact on reducing the mortality rate of brain cortex neurons after induction of ischemia-reperfusion. Ischemia - reperfusion reduces the oxygen level inside the cell. If sells don’t be access to enough oxygen, disrupts the cell's normal metabolism and the cell dies. After Reperfusion a lot of free radicals build up around cells and invade to sell membrane and subsequent cell begins to death (16, 17). In these conditions, cells affected by this material are necrosis immediately or starts a series of reactions in cell that ultimately cause programmed cell death or apoptosis. Cells have the ability to resist if the damage is not lethal to them. In this case, cells increase the restorative processes and returns to normal their function rapidly (18, 19). In this study, following the review of the treatment group was observed in this area decreased cell death which due to antioxidant effects of CoQ10 and synergistic effects with olive oil probably. By taking CoQ10, increases the cell resistance from several ways. CoQ10 can increase the energy level of the cell cycle involved in energy production in mitochondria .and it has antioxidant property in body. CoQ10 Puts at the disposal cell conditions and sufficient time for repair (20). CoQ10 prevent from the reaction of free radicals to the lipid membranes of adjacent cells. It reduces the extent of damage cells in the brain temporal cortex following ischemia- reperfusion. CoQ10 reduces complications after ischemic and these facts are consistent with tests performed in the treatment group. The result of this intracellular activity is inhibition process of apoptosis and cell death that subsequent reduction of ischemic complications.
Conclusion:

Temporal cortex region is vulnerable against ischemia-reperfusion. CoQ10 intake after brain ischemia can reduce the mortality of temporal cortex neurons and protect the neurons from the harmful agents. CoQ10 reduces consequent adverse effects of ischemia significantly.

Reference: