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Original Article

Neuroprotective effect of Coenzyme Q10 in hippocampal injury in Balb/c mouse

Sara Rigi[1], Abolhassan Sakhaei[1], Azadeh Niknam Asl[2], Akram Alizadeh[2], Fatemeh Beigi[1], Mehdy Mehdizadeh[1], Mansooreh Soleimani[3*], Majid Katebi[4*]

Abstract

Coenzyme Q10 is a promising agent for neuroprotection in neurodegenerative diseases. Neuroprotective effects of Coenzyme Q10 demonstrated in some neurodegenerative diseases such as Parkinson, Alzimer and etc. Hippocampus is home of those diseases. We assayed Coenzyme Q10 effects on Hippocampal injury model and our hypothesis is that Coenzyme Q10 has Neuroprotective effects in some neurodegenerative diseases via hippocampus. For this purpose 24 Balb/c mouse took in 4 groups: Control (Without any treatment), Vehicle (Treated with sesame oil as Coenzyme Q10 vehicle), Hyppocampal injury model (Treated with Trimethyltin chloride neurotoxin, 2.5 mg per kg IP), and test (Treated with Coenzyme Q10 after Trimethyltin chloride injection, 10 mg per kg IP for 2 weeks). After 2 weeks brain harvested and hippocampus tissue assayed by Nissl and Tunnel staining. Hystological study showed significantly increase of normal cells and decrease of apoptotic cells in test group after Coenzyme Q10 treatment in hippocampus. This study showed Coenzyme Q10 has protective effects in hippocampus after injury and it seems that Neuroprotective effects of Coenzyme Q10 in some neurodegenerative diseases com from that.

1. Department of Anatomy, School of Medicine, Iran University of Medical Science, Tehran, Iran
2. Department of Tissue Engineering, Tehran University of Medical Science, Tehran, Iran
3. Cellular and Molecular Research Center & Department of Anatomy, School of Medicine, Tehran University of Medical Science, Tehran, Iran
4. Stem Cell Research Center& Department of Anatomy, School of Medicine, Hormozgan University of Medical Science, Bandar Abbas, Iran

* **Corresponding Author**
Mansooreh Soleimani
Cellular and Molecular Research Center & Department of Anatomy, School of Medicine, Tehran University of Medical Science, Tehran, Iran
E-mail: mansourehsoleimani@gmail.com

Majid Katebi
E-mail:majid.katebi@gmail.com

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Introduction

Coenzyme Q10 or ubiquinone abbreviated to CoQ10 is a 1, 4-benzoquinone.This vitamin-like substance is oil-soluble and present primarily in the mitochondria of most eukaryotic cells. It is a member of the electron transport chain and participates in aerobic cellular respiration, producing energy in ATP form. Ninety-five percent of the human body's energy is generated this way [1]. Therefore, heart, liver and kidney with the highest energy requirements have the highest CoQ10 concentrations [2]. It demonstrated that CoQ10 have important role in the electron transport chain (which includes the vital proton motive role of CoQ10) and a deficiency of CoQ10 in human heart disease discovered. The antioxidant role of the molecule as a free radical scavenger was widely studied by Lars Ernster. Numerous scientists around the globe started studies on this molecule since then in relation to various diseases such as cardiovascular, cancer and neural diseases. Richest source of dietary CoQ10 are meat and fish and levels over 50 mg/kg can be found in some meats. Recently many studies showed neuroprotective effects of Coenzyme Q10 in some neurodegenerative diseases such as Parkinson, Alzimer and etc [3]. In etiology and pathophysiology of those diseases hippocampus has role. For example hippocampal disruption is one of the earliest signs of Alzimer [4]. The hippocampus is often the focus of epileptic seizures: Hippocampal sclerosis is the most commonly visible type of tissue damage in temporal lobe epilepsy [5]. In schizophrenia abnormality of hippocampus reported [6]. The hippocampus is a major part of the brains of humans and other vertebrates. It belongs to the limbic system and has important roles in the consolidation of information from short-term memory to long-term memory and spatial navigation. There are two hippocampus in humans and other mammals, one in each side of the brain [7]. Because of importance of hippocampus and its role in neurodegenerative diseases, we study effects of Coenzyme Q10 in hippocampal injury mice. Our hypothesis is that almost of neuroprotective effects of Coenzyme Q10 in some neurodegenerative diseases relate to its function in hippocampus.

Materials and methods

Animals

Balb/c mice (body weight: 18-20 gr) housed in controlled environment (humidity and temperature) on a 12/12 hours light/dark cycle with free access to standard food and water. Animals randomized to 4 groups: Control (Without any treatment), Vehicle (Treated with sesame oil as coQ10 vehicle), Hippocampus injury model (Treated with Trimethyltin chloride neurotoxin, 2.5 mg per kg IP), and test (Treated with CoQ10 after Trimethyltin injection 10 mg per kg IP for 2 weeks); 6 animals in each group. All efforts made to minimize animal suffering and to reduce the number of animals.

Hyppocampal injury modeling

Hippocampal injury model made by IP injection of Trimethyltin (TMT) in dose of 2.5 mg/kg.

Hystological studies

2 weeks after TMT injection perfused brain of animal removed from the skull and post fixed by immersion in paraformaldehyde 4% for at least two days before histological processing. One of brain hemisphere was dehydrated and embedded in paraffin. A series of 10 micrometers thick were cut by microtome and stained with crystal violate and tunnel kit.

Results

Hystological studies of hippocampus done with two techniques. Nissl staining show that in model group we have a significant decrease in normal cells in contrast with control group (P=0.05). But in test group that treated with coQ10,a significant increase in normal cells exist in contrast with model group.(P=0.01) (Figure 1 & Figure 2). Tunnel staining show a significant increase in pyknotic cells in model group in contrast with control group but in test group pyknotic cells decreased significantly. (P=0.01) (Figure 3 & Figure 4)

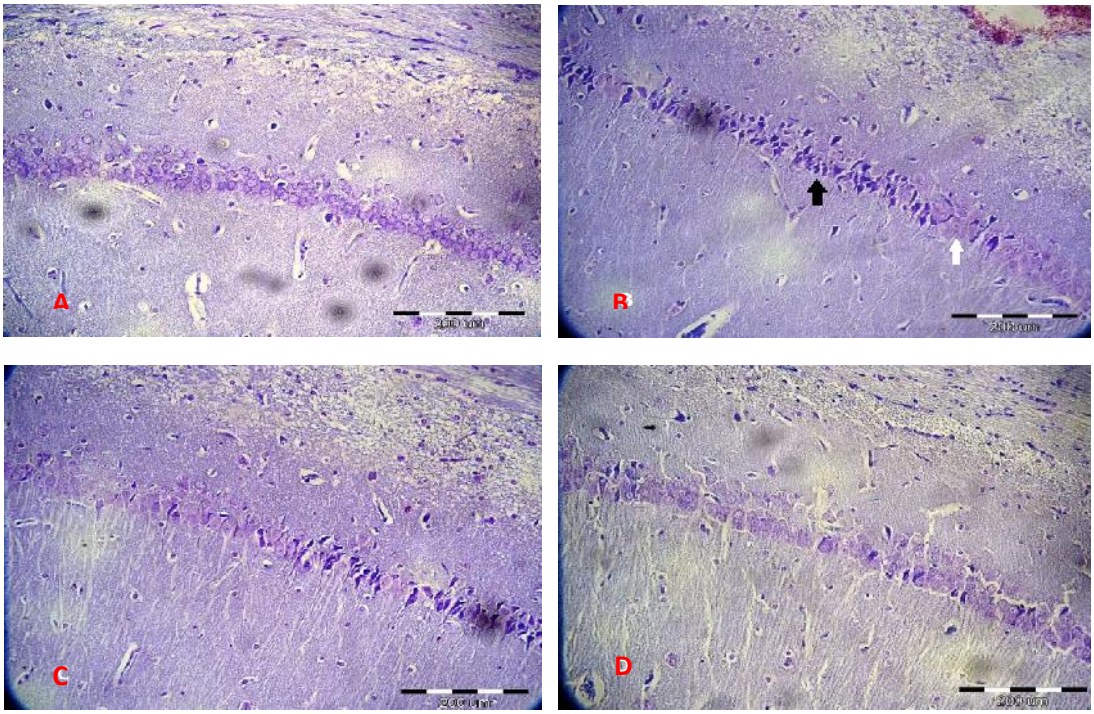

Figure 1. Nissl staining A: Control B: Model C: Vehicle D: Treatment (400X). Dark marker shows apoptotic cell and white marker shows normal cell.

Discussion

In this study we assay CoQ10 effects in Hyppocampal injury model induced by TMT. TMT make focal damage in hippocampus result in degeneration. Degeneration caused by TMT is similar to that take places in neurodegenerative diseases such as Alzheimer and other neurodegenerative diseases. Therefore this model use to study such neurodegenerative diseases. [8, 9] In neurodegeneration, normal cells in neural tissue programs to apoptosis and death so we use Nissl and Tunnel techniqs to study injury and then recovery in hippocampus. This two techniques show apoptotic cells dark in tissue. Neuroprotective effects of Coenzyme Q10 demonstrated in some neurodegenerative diseases. CoQ10 as an important co factor reduces cell death by affecting mechanisms of it. Some clinical and animal study reported that CoQ10 can slow progress of PD in early stage [10]. In our study treatment with CoQ10 started immediately after TMT injection to tracing CoQ10 effects in early stage of damage. Our findings showed effective role of CoQ10 in

prevention of cell death in hippocampus in early stage of damage but it did not mean treating with CoQ10 only in early stage is effective. This findings show that neuroprotective effects of Coenzyme Q10 in PD, Alzimer and other neurodegenerative diseases come from its protection role in hippocampus.

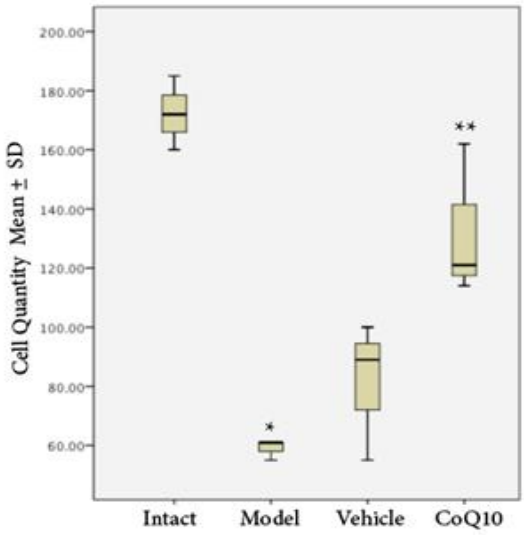

Figure 2. Cell counting of normal cells in hippocampus after Nissl staining showed a significant decrease in model group and a significant increase in test group.

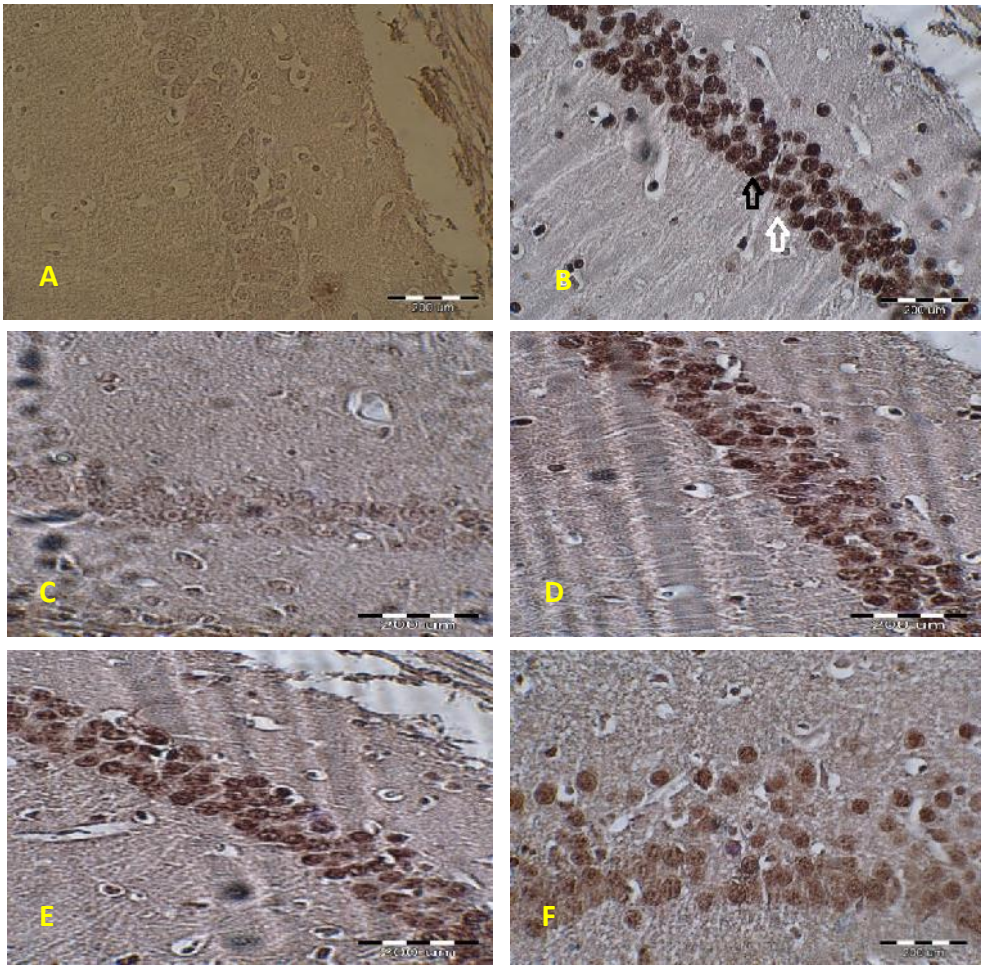

Figure 2. Tunnel staining A: Negative for Tunnel staining, B: Positive for Tunnel staining, C: Control, D: Model, E: Vehicle, F: Treatment (400X). In this technique apoptotic cells stain dark. Dark marker shows apoptotic cell and white marker shows normal cell.

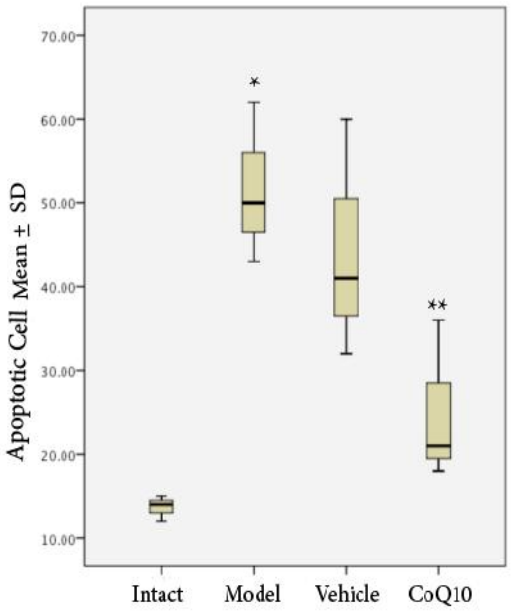

Table 4. Cell counting of apoptotic cells in Tunnel staining showed a significant increase in model group and a significant decrease in test group.

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