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Original Article

THE ANTI-CATARACT EFFECT OF COENZYME Q10 IN RABBITS

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ABSTRACT

Objective: cataract is the opacity of the lens which progressively impairs the light transmission to the retina and finally prevents the vision, these opacity result from the oxidative process in the eye. The study aimed to prevent opacity of the lens by using Coenzyme Q10 as eye drops.

Methods: Sodium selenite 0.01w/v injected intravitreal to the rabbit's eye to induce the disease, a group of rabbits were receive Coenzyme Q10 eye drop, and another group received distilled water, pre and post induction, cataract maturity was measured to evaluate the opacity deterioration.

Results: the group of rabbits that received distilled water after induction of cataract, the opacity occurred within 48-72 h and the mean score of opacity reached to (4±0.00), while Coenzyme Q10 treated group the degree of opacity was (1.5±0.02), and there was a highly significant difference ($p<0.01$).

Conclusion: Coenzyme q10 has an antioxidant activity when use as eye drops and this effect enable Coenzyme Q10 to prevent the opacity which is the major cause of cataract due to oxidative stress.

Keywords: Cataractogenesis, Oxidative stress, Coenzyme Q10

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INTRODUCTION

Cataract is an illness that affects the eye; it causes opacity of the lens which progressively impairs the light transmission to the retina and finally prevents the vision. Oxidative damage to lens constituents, including nucleic acids, proteins, and lipids, is considered to be a primary factor in aging-related cataract [1, 2].

Normally our bodies counteracts this oxidative damage by regular antioxidant defense pathway, however, with age, activated species of oxygen accumulate while the antioxidant defence system gradually decrease. This accumulation of oxidant products results cross-linking and aggregation of proteins with increasing in molecular weight that can scatter light. Consequently, opacification of the lens occur resulting in blocking of light transmission to the retina then blindness [3, 4].

In medicine, surgical removal of the lens considers the best therapy for treatment of the cataract. But, the cost of the cataract surgery considers the major problem for patients living in poverty countries [5]. Early diagnosis of cataract can delays the onset of the disease and reduces the option of surgery by as much as 50% [6].

Many compounds with antioxidant properties have been evaluated to prevent the cataract. N-acetylcarnosine is considered one of the powerful antioxidant which was developed as an eye drop dosage form. This compound act by delivering the L-carnosine, which act by neutralize the damage of the lens that cause by oxidative stress [7].

Coenzyme Q10 (Cq10) or Ubiquinone, which is the natural vitamin, play a vital role in the electron transport system of mitochondria and consider as the main component of oxidative phosphorylation process that produces the ATP which is the main source of energy in the cell. Besides that, it has an effect on gene expression. Current evidence indicated that Cq10 has powerful antioxidant properties [8, 10]. Hence the rational design for this research is to assess the efficacy of Cq10 eye drop in the prevention of cataract.

MATERIALS AND METHODS

Chemicals

Water soluble Cq10 was purchased from Swan Health Product, USA. Benzylkonium chloride is a gift from Sammara Drug Industry, Iraq. Sterile sodium chloride solution was utilised which made in Adwic pharmaceutical Co., Egypt. Ketamine solution also utilised which produced by Hikma Pharmaceuticals Plc, Jordan.

Animals

A group of 12 adult rabbits (Oryctologus cuniculus), aged about one year with a range of body weight of (1.5-2 kg) were purchased from the college of veterinary medicine/University of Baghdad. Animals were kept on fresh trefoil diet, water *at libitum*, room temperature (25-27 °C) and light/dark cycle of 12/12 h.

Preparation of coenzyme Q10 eye drops

Coenzyme Q10 eye drops are prepared by dissolving 300 mg of water soluble Cq10 (Swanson Health Products, USA) in sufficient amount of sterile distilled water to achieve 0.3% w/v of Cq10 solution. Benzalkonium chloride is also used as a preservative in a concentration of 0.001%. Finally, the solution was sterilised utilizing a 0.2µm pore size filters and kept in a sterile dropper to be used as an eye drop solution [10, 11].

Therapeutic groups

Therapeutic groups were 2 groups; Cq10 and distilled water (control) group. Each group included 6 rabbits. Cq10 group were administered 2 drops of Cq10 eye drop topically 3 times/day to the right eye for five days prior to induction of cataract (i.e. prophylactic use) and continued thereafter for further 21 d after the cataract being induced (i.e. therapeutic use), whereas left eyes were received the distilled water (the same volume, frequency and duration). The control group was given distilled water only.

Induction of cataract

The rabbits were anesthetized by intramuscular injection of 0.5 ml of (50 mg/ml) ketamine. Induction of disease was done by inserting the needle of (gauge 30, 12.7 mm), (4 mm behind the limbus in sclera measured by caliper) to intravitreal injection of 0.1 ml from 0.01% w/v of sodium selenite solution in right eye; it was single injection [12].

After the injection, the rabbits were monitored for caractogenesis which begun after one hour and when opacity progression observed [13]. Monitoring was done by slit-lamp examination to detect of cataract type [14, 15].

Ophthalmoscopic examination and opacity grading

The scoring of lens opacity from grade zero to grade 4 (by using ophthalmoscope grading criteria), was doing according to the classification of [16]. The eye examinations were daily carried out in a dark room with a direct ophthalmoscopes method to evaluate cataract maturity and the papillary response to light [17]. The retinal red reflex was visualised through the dilated pupil (installation of tropicamide 0.5% and phenylephrine 10% to obtain maximum dilatation); the opacities partially obscured the red reflex [18-20].

The obtained ophthalmoscopic scoring was found to be similar to those obtained with slit-lamp scoring for the same rabbits [21].

Statistical analysis

All data were expressed as mean (±SEM). Paired and unpaired t-tests were used accordingly for assessing the effectiveness of employed therapy between groups.

RESULTS

The type of cataract that was obtained in the present study was Posterior subcapsular (PSC) according to slit-lamp detection and according to opacity classification system, see fig. (1). In the right eyes of control group a complete opacity (mature cataract) was observed after 48 to 72 h after induction of the disease (fig. 2).

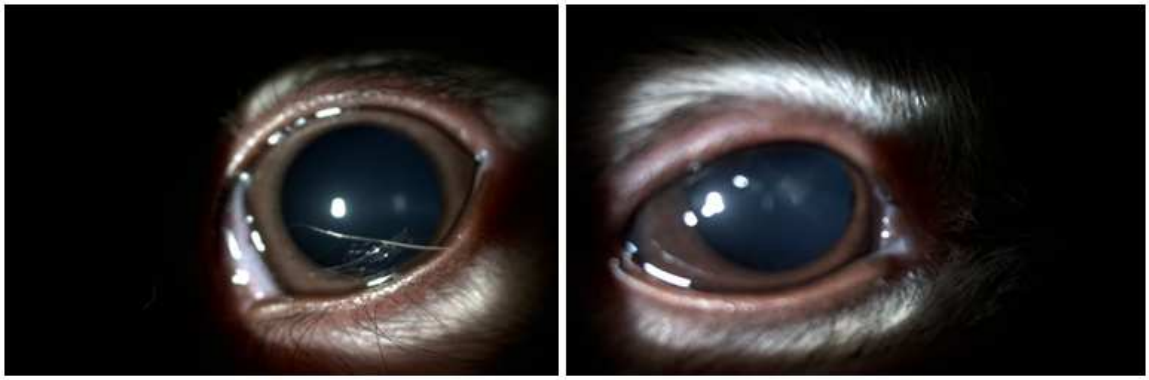

Fig. 1: Slit lamp photograph of left normal eye (A) and right cataractous eye (B) (Posterior subcapsular opacity)

Fig. 2: Mature cataract with clear opacity in the eye of control group animal

Distilled water (control) group

Prior the induction of cataract the lenses of 6 included rabbits right eye was intact and transparent pre-instillation, and post-installation of distilled water and the mean score of opacity (mean±SEM) was (0±0.00) for 5 d. After cataract being induced and installation of distilled water was continued the mean score was (2.8±1.7) at 1st day post-induction and (4±0.00) at each of 7th, 14th and 21st day of trial period, and there was a highly significant (P<0.01) difference in comparing to right eyes pre-induction (fig. 3).

All included rabbits right eye had intact light reflex after installation of distilled water for 5days. But post induction of cataract all the right eyes had no light reflex during the trial period.

Regarding light reflex, there was highly significant (p<0.01) differences post induction during the trial period.

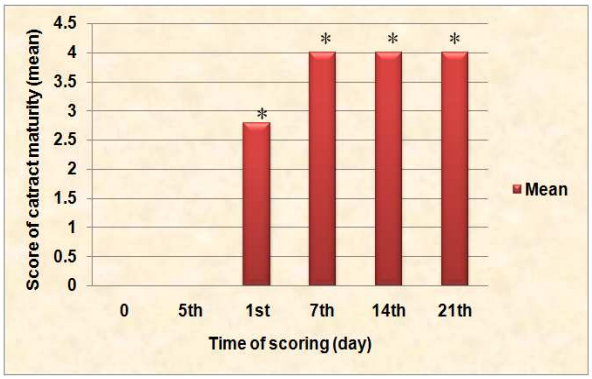

Fig. 3: Effect of distilled water on mean score of cataract maturity in eye rabbits' lenses (n=6) during pre-induction (0 and 5th day) and Post-induction period (21 d), The values are represented as (mean±SEM), SEM= standard error of mean, ** = high significant difference (p<0.01) compared to corresponding pre-induction mean score of cataract maturity

Cq10 group

Prior the induction of cataract the lenses of 6 included rabbits' right eye was intact and transparent pre and post installation of Cq10 eye drops and the mean score of opacity (mean±SEM) was (0±0.00) for 5 d. After cataract being induced and installation of Cq10 was continued the mean score was (0.1±0.03) at the 7th day, and in comparing with right eyes pre-induction there was a highly significant (P<0.01) difference, at the 14th day there was a highly significant (P<0.01) difference, the mean score was (1.5±0.05), at the 21st also there was highly significant difference (P<0.01) and the mean score was (1.5±0.02), (fig. 4).

Table 1: Effect of Cq10 (0.3%) eye drops on prevention of cataract maturity in right eyes of rabbits (n=6) compared with distilled water

Groups	Score of cataract maturity (mean±SEM)					
	Pre-induction of cataract (Day)		Post-induction of cataract (Day)			
	0	5	1st	7th	14th	21st
Distilled Water	0±0.00	0±0.00	2.8±1.7	4±0.00	4±0.00	4±0.00
Cq10	0±0.00 N °	0±0.00N °	0.4±0.0	0.1±0.03 **	1.5±0.05**	1.5±0.02**

Value are represented as mean±SEM, 0 = Baseline (Pre-treatment), SEM=standard error No (normal eye), ** = highly significant difference (P ≤ 0.01), Cq10= Coenzyme Q10.

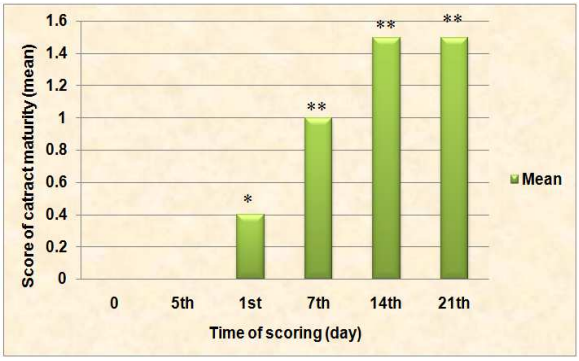

Fig. 4: Effect of Cq10 on mean score of cataract maturity in eye rabbits' lenses (n=6) during pre-induction (0 and 5th day) and Post-induction period (21 d), Values are represented as (mean±SEM), * = Significant difference (0.01≤ p<0.05) compared to corresponding pre-induction mean score of cataract maturity, ** = high significant difference (p<0.01) compared to corresponding pre-induction mean score of cataract maturity

The Cq10 (0.3%) eye drop was more efficient in cataract prevention effect than distilled water during the trial period, (table 1).

All included rabbits right eye had intact light reflex after installation of Cq10 for 5days. Post-induction of cataract also all right eyes had light reflex until the 7thday, but there was no response at day 14th and 21st post induction.

Regarding light reflex, there was a significant difference (0.01 ≤ p<0.05) during the trial period. However there was significant (0.01≤ p<0.05) difference regarding comparison results of light reflex, of Cq10 with those of distilled water post induction.

DISCUSSION

Selenite-induced cataract has received considerable attention and was worked upon as a model system for oxidative stress-induced cataract [22]. Selenite causes increasing lipid peroxidation and oxidation of sulfhydryl groups and damage of membranes of lens fibres. This mechanism resembles age-related cataract [23]. These processes lead to protein aggregation and result in a decrease the water soluble proteins followed by opacification of the lens [24, 25]. Chung *et al.* 2001, Chung *et al.* (2002) suggest that nitric oxide had an important role in the development of selenite-induced cataracts [26]. Many researchers have been demonstrating the effectiveness of high doses of antioxidant supplements (vitamins C and E) in attenuating (but not preventing) the oxidative stress-induced cataractogenesis [27, 28]. Cq10 is a synthesis in the human body and involved in the cell function. It has a powerful antioxidant effect. An *in vitro* study has been observed the efficacy of Cq10 in prevention the effects of light-induced oxidative stress and apoptosis in human lens epithelial cells in a cell culture model [29]. Coenzyme q10 has an antioxidant activity against oxygen species which responsible for the oxidative stress, and when Cq10 used topically as eye drop, it was able to prevent the oxidative stress in the eye, so the expected mechanism to reduce opacity, is the antioxidant activity of Cq10 that prevent aggregation of lens proteins and enhancing to dissociation of cross-links between aggregated proteins to the normal state, and prevents progression of the opacity [30].

CONCLUSION

Coenzyme Q10 has an antioxidant activity when uses as eye drops and this effect enable Coenzyme Q10 to prevent the opacity of the lens which is the major cause of cataract due to oxidative stress.

CONFLICT OF INTERESTS

Declared none

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