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The Effects of Coenzyme Q10 (CoQ10) on Ionizing Radiation- Induced Pancreatic β-Cell Injury

ABSTRACT

Objective: This study investigated the antioxidant effect of coenzyme Q10 on ionizing radiation-induced oxidative damage in pancreatic β-cells.

Methods: Twenty-four male rats were assigned to 4 groups. Group 1 constituted the control group, Group 2 only received a single i.p. dose of coenzyme Q10, Groups 3 and 4 received a total of 4 Gy external x-ray radiation to the abdomen in a single fraction. Group 4 also received a single dose of 200 mg/kg coenzyme Q10 i.p. 30 minutes prior to x-ray irradiation.

Results: The x-ray radiation group showed decreased β-cell positivity in the islets of Langerhans compared to the control group on immunohistochemical analysis. In contrast, an increase in β-cells exhibiting insulin positivity was observed in group 4 (ionizing radiation + coenzyme Q10) compared to the irradiation group. Terminal deoxynucleotidyl transferase dUTP nick end labeling assay indicated a rise in the number of apoptotic cells in the x-ray radiation group compared to the control and coenzyme Q10-only groups (Group 2). Meanwhile, we observed a decrease in the number of terminal deoxynucleotidyl transferase dUTP nick end labeling-positive apoptotic cells in the islets of Langerhans in the ionizing radiation + coenzyme Q10 treatment group (Group 4) relative to the irradiation group.

Conclusion: This study shows that coenzyme Q10 reduces apoptosis in the rat pancreas exposed to abdominal ionizing radiation.

Keywords: Beta-cell, coenzyme Q10, pancreas, rat, x-ray irradiation

Introduction

The effect of ionizing radiation (IR) on human health has become a source of increasing concern. Numerous individuals are exposed to IR, particularly patients who undergo diagnostic and/or radiotherapy procedures for cancer.[1] In addition, nuclear and radiological accidents represent a threat to all organisms worldwide. The effects causing concern include the fact that IR induces cell death, as well as leading to mutations and cancer.[2] Ionizing radiation can result in DNA damage even at low doses, as well as damage to DNA, protein, and lipid membranes through the formation of reactive oxygen species (ROS) and free radicals.[3] Cell membrane injury is known to be capable of causing apoptosis and necrosis.[4] Ionizing radiation also leads to reduction/oxidation (redox) activation and the activation of pro-oxidant enzymes by suppressing antioxidant enzymes.[5] The early and late toxic effects of IR on specific tissues and organs pose a particularly important problem.[6,7]

Generally, animal models have been employed to study the mechanisms responsible for IR-related changes in glucose metabolism. Changes resulting in long-term impairment have been observed in the skeletal muscle metabolism, adipocytes and pancreatic function, whole-body metabolism, and insulin resistance in mice exposed to 6 Gy total-body irradiation.[3,8,9] In support of these studies, an increase in the incidence of diabetes mellitus (DM) has been observed in cohorts exposed to radiotherapy (RT) in childhood compared to individuals with no such exposure.[10-13] The pancreas is an RT-sensitive organ.[1,14] Pancreatic β-cells are susceptible to ROS because of their limited antioxidant enzyme capacity, and this renders them susceptible to apoptosis and necrosis under pro-oxidant conditions[15,16] Elevated oxidative stress leads to the development of DM by compromising the pancreatic ability to secrete insulin.[17] Since pancreatic β-cells are progenitor cells, their survival is important in terms of the preservation of the pancreatic islets.[1] The development of a protective agent may represent a promising strategy for the prevention of IR-related pancreatic β-cell damage.

Filiz Mercantepe[1]

Levent Tümkaya[2]

Tolga Mercantepe[2]

Sema Yılmaz Rakıcı[3]

[1]*Department of Endocrinology and Metabolism Disease, Recep Tayyip Erdoğan University, Faculty of Medicine, Rize, Turkey*
[2]*Department of Histology and Embryology, Recep Tayyip Erdoğan University, Faculty of Medicine, Rize, Turkey*
[3]*Department of Radiation Oncology, Recep Tayyip Erdoğan University, Faculty of Medicine, Rize, Turkey*

Corresponding author:
Filiz Mercantepe
✉ filizmercantepe@hotmail.com

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Coenzyme Q10 (CoQ10), also known as ubiquinone (2,3-dimet hoxy-5-methyl-6-multi prenyl-1,4-benzoquinone), is an antioxidant that is present in a large number of aerobic organisms.[18] It plays an important role in oxidative balance. Coenzyme Q10 produces a transmembrane electrochemical gradient by transferring electrons in the mitochondrial electron transport chain.[19] Coenzyme Q10 acts as a potent antioxidant in the inner mitochondrial membrane by directly scavenging ROS and inhibiting lipid peroxidation.[18,20] Mitochondria exert an important effect on β-cells in glucose metabolism and insulin secretion.[21] The impairment of mitochondrial function leads to cell death.[21] At the same time, mitochondria are susceptible to oxidative damage and represent a significant superoxide source in IR exposure. Studies have demonstrated the effect of CoQ10 supplementation on parameters of oxidative stress.[22-26] It is known that the effects of ROS formation play a role in the pathogenesis of DM.[27] Coenzyme Q10 supplementation increases glutathione and superoxide dismutase levels while reducing malondialdehyde (MDA) levels in diabetic patients.[25] Studies have shown that the development of DM is associated with oxidative stress and that CoQ10 produces an anti-glycemic effect by scavenging ROS.[25] Based on the hypothesis that oxidative stress caused by IR plays a role in the pathogenesis of pancreatic β-cell damage and that a decrease in oxidative stress can protect β-cells against damage, this study investigated the antioxidant effect of CoQ10 on IR-induced oxidative damage in pancreatic β-cells.

Material and Methods

Ethics

This experimental study was approved by the Recep Tayyip Erdoğan University Animal Research Ethics Committee (Approval Number. 2022/32, Approval Date 29.07.2022). The present study was done with experimental animals. There is no patient participation.

Experimental Animals

Six- to 8-week-old male Sprague–Dawley rats (n = 24, weight 300 ± 30 g) were randomly assigned to cages containing 6 animals each, which were housed in an environment with controlled room temperature, a 12-hour light-dark cycle, and unrestricted access to food and water. Rats in Group 1 (control group) only received a single 1 mL intraperitoneal (i.p.) injection of 0.9% serum saline solution. Rats in Group 2 only received a single i.p. dose of 200 mg/kg CoQ10 (Sigma-Aldrich, Germany). Group 3 (IR) and Group 4 (IR + CoQ10) received a total of 4 Gy external x-ray irradiation to the abdomen in a single fraction at 100 cm skin source distance (SSD) from the anterior field with a linear accelerator under anesthesia. Group 4 also received a single i.p. dose of 200 mg/kg bodyweight CoQ10, 30 minutes prior to x-ray irradiation. These CoQ10 doses were calculated based on the recommended doses for humans. All animals were sacrificed under 50 mg/kg ketamine HCl and 10 mg/kg xylazine HCl at the 24th hour of irradiation, and the required materials were collected.

X-Ray Irradiation Procedure

Prior to x-ray irradiation, 50 mg/kg ketamine HCl and 10 mg/kg xylazine HCl anesthesia were administered to the rats for the planning tomography scans of the parts to be irradiated (CMS Xio, Elekta, Stockholm, Sweden). After the planning tomographies, external 4 Gy x-ray radiation was applied to the abdomen in a single fraction using a linear accelerator (Elekta Synergy) at 100 cm SSD from the anterior region of the rats.

Histopathological Analysis

The rats were anesthetized, and their pancreas was removed. The obtained pancreatic tissues were trimmed to a volume of 2 cm × 2 cm × 2 cm. The resulting pancreatic tissue specimens were kept in 10% formalin (Sigma Aldrich, St. Louis, Mo, USA) solution for 24-36 hours and fixed. After the fixation process, the pancreatic tissue specimens were processed with a tissue processor (Shandon Citadel 2000, Thermo Fisher Scientific Inc., Germany), undergoing dehydration (increasing ethanol series, Merck KGaA, Darmstadt, Germany), staining (xylol, Merck KGaA, Darmstadt, Germany), and paraffin (soft and hard paraffin, Merck KGaA, Darmstadt, Germany) embedding processes. After paraffin embedding, pancreatic tissue samples were embedded in tissue embedding cassettes with the use of a paraffin dispenser for tissue embedding (Leica 1125H Leica Biosystems, Germany). Sections of a thickness of 4-5 μm were obtained from paraffin blocks of pancreatic tissue using a rotary microtome (Leica RM2525, Leica Biosystems, Germany) and dried on slides. After drying, pancreatic tissue sections were stained with hematoxylin and eosin using routine histological staining (Leica Biosystems, 5020ST, Germany) (Merck KGaA, Darmstadt, Germany).

Immunohistochemical Analysis

In our study, a TUNEL (terminal deoxynucleotidyl transferase dUTP nick end labeling) test HRP-DAP kit (ab206386, Abcam, UK), primary insulin antibody (ab181547, Abcam, UK), and secondary antibody (goat anti-rabbit IgG H&L HRP, ab97051, Abcam, UK) kits were used. Sections of 2-3 μm were obtained from paraffin blocks of pancreatic tissue using a rotary microtome and transferred onto positively charged slides. A Bond MAX IHC/ISH (Leica Biosystems, Australia) instrument was used in accordance with the manufacturer's manual for the obtained pancreatic tissue sections. Pancreatic tissue sections were incubated with primary and secondary antibodies for 60 minutes. Sections incubated with antibodies were subsequently incubated with diaminobenzidine chromogen (DAB Chromogen, Abcam, UK) and stained with Hematoxylin (Merck KGAa, Darmstadt, Germany).

Semi-Quantitative Analysis

A pancreatic tissue histopathological damage score (PHDS) was calculated based on cells with pyknotic nuclei, and edema and vascular congestion in the islets of Langerhans, consistent with the histopathological examination of pancreatic tissue sections in studies of pancreatic tissue toxicity due to radiation exposure (Table 1).[28-30] Thirty different regions per section were evaluated by 2 histopathologists blinded to the treatment groups.

MAIN POINTS

- The effects of ionizing radiation on human health are becoming more and more of a concern.
- Oxidative stress caused by ionizing radiation is involved in the pathogenesis of pancreatic β-cell damage and contributes to the development of diabetes mellitus.
- Reducing oxidative stress can protect β-cells from damage.
- Coenzyme Q10 has been suggested as a treatment for many chronic diseases and as a preventative against ionizing radiation toxicity.
- Coenzyme Q10 is an antioxidant with direct benefits on glycemic control, insulin secretion, and β-cells.

Table 1. Pancreas Histopathological Damage Score Values

Score	Findings
Cells with pyknotic nuclei	
0	"5%
1	6%-25%
2	26%-50%
3	>50%
Edema	
0	<5%
1	6%-25%
2	26%-50%
3	>50%
Vascular congestion	
0	<5%
1	6%-25%
2	26%-50%
3	>50%

Table 2. Immunopositivity Scoring

Score	Findings
0	<5%
1	6%-25%
2	26%-50%
3	>50%

Apoptotic cells exhibiting anti-insulin and TUNEL positivity as determined using immunohistochemical methods were scored as presented in Table 2. Twenty-five different regions per section were examined by 2 histologists blinded to the experimental groups.

Statistical Analysis

Pancreatic tissue histopathological damage scores, immune-positive cell scores, and all data from semi-quantitative analyses were analyzed using Statistical Package for the Social Sciences (SPSS) 20.0 software (IBM Corp., Armonk, NJ, USA). Nonparametric data from semiquantitative analyses were presented as median and 25th and 75th percentiles. The Kruskal–Wallis test was used to determine whether the data were significantly different. The Bonferroni-corrected Mann–Whitney *U*-test was used to evaluate the differences between the groups. In evaluating the differences between the data, *P* values <.05 were deemed significant.

Results

Histopathological Analysis

Examination of pancreatic tissue sections under light microscopy revealed normal structures in the islets of Langerhans [Figure 1A, Table 3, PHDS: 0 (0-1)]. Similarly, typical islets of Langerhans were observed in the CoQ10-only application group [Figure 1B, Table 3, PHDS: 0 (0-1)]. In contrast, widespread apoptotic cells with pyknotic nuclei were observed in the islets of Langerhans in the x-ray radiation group. Extensive edematous areas and vascular congestion were also present [Figure 1C, Table 3, $P < .05$, PHDS: 6 (6-7)]. On the other hand, a decrease in pyknotic cells, vascular congestion, and edematous areas was observed in the islets of Langerhans in the CoQ10 treatment group compared to the x-ray radiation group [Figure 1D, Table 3, PHDS: 3 (2-4)].

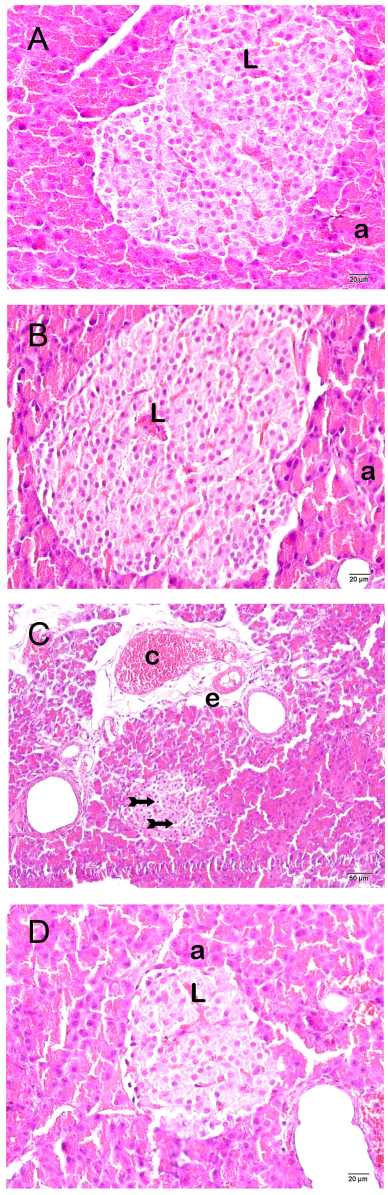

Figure 1. Representative light microscopic images of H+E-stained pancreatic tissue. Islets of Langerhans (L), A (acinus). A (×40) control group: normal endocrine islets of Langerhans (L) and exocrine acinus (ac) structures [PHDS: 0 (0-1)]. B (×40) CoQ10 group: Typical endocrine islets of Langerhans (L) and exocrine acinus (ac) structures [PHDS: 0 (0-1)]. C (×40) irradiated group: vacuolizations accompanying loss of cytoplasm in cells (tailed arrow) in endocrine islets of Langerhans (L) and edema (e) can be seen. In addition, severe vascular congestion (c) is observed [PHDS: 6 (6-7)]. D (×40) irradiated + CoQ10 group: necrotic cells in the islets of Langerhans (L) have decreased. In addition, we have shown a decrease in findings of edema and vascular congestion [PHDS: 3 (2-4)].

Immunohistochemical Results

Examination of pancreatic tissues incubated with insulin primary antibody under light microscopy revealed a large number of β cells with extensive insulin positivity in the control group and CoQ10-only administration groups [Figure 2A and 2B, Table 4, insulin positivity score: 2 (2-3) for both]. In contrast, a decrease in β-cells exhibiting

Table 3. Pancreas Histopathological Damage Score results [Median (25%-75% Interquartile Range)]

Group	Pyknotic Cells in the Islets of Langerhans	Edema	Vascular Congestion	PHDS
Control	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)
CoQ10	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)
IR	2 (2-2)*	2 (2-3)*	2 (2-3)*	6 (6-7)*
IR + CoQ10	0.5 (0-1)**	1 (1-2)***	1 (0-1)***	3 (2-4)****

Kruskal–Wallis/Mann–Whitney *U*-test with Bonferroni corrections.
*$P < .05$: versus the control group
**$P < .05$: versus the IR group
***$P \leq .037$: versus the IR group
****$P \leq .015$: versus the IR group

insulin positivity was observed in the x-ray radiation group [Figure 2A and 2C, Table 4, $P < .05$, insulin positivity score: 1 (0-1)]. The number of β-cells exhibiting insulin positivity increased in the CoQ10 treatment group compared to the x-ray irradiation group [Figure 2A and 2C, Table 4, $P = .001$ insulin positivity score: 2 (1-2)].

Light microscopic evaluation of pancreatic tissue sections subjected to the TUNEL assay in order to determine apoptotic cells in the islets of Langerhans showed an increased number of apoptotic cells exhibiting TUNEL positivity in the x-ray radiation group compared to the control and CoQ10-only application groups [Figure 3A and 3C, Table 4, $P < .05$, TUNEL positivity scores: 0 (0-0), 0 (0-0), and 2 (2-2), respectively]. In contrast, the number of apoptotic cells exhibiting TUNEL positivity in the islets of Langerhans decreased in the CoQ10 treatment group compared to the x-ray radiation group [Figure 3C and 3D, Table 4, $P = .001$, TUNEL positivity scores: 2 (2-2) and 1 (1-1), respectively].

Discussion

In the present study, CoQ10 reduced the damage and apoptosis induced by IR in pancreatic β-cells. Previous studies have reported that IR is toxic to pancreatic tissue.[1,31] Pancreatitis is regarded as a likely outcome of radiation-induced injury.[32] In line with the present study, Schoonbroodt et al[32] reported that abdominal RT causes acinar cell necrosis, cell damage in the pancreatic ducts, edema, vascular inflammation, and widespread fibrosis in the late period. Several years earlier, Du Toit et al[33] reported interstitial edema, vascular occlusion, necrosis, and mononuclear cell infiltration in the lobular structure of the pancreas, as well as decreased insulin release and necrosis of the islet cells after whole-body irradiation in animal experiments. At the same time, islet histology revealed cytocavitary network alterations of α- and β-cells that included mitochondrial destruction and increased lysosomes, along with loss of cytoplasm and edema.[33] These changes in pancreatic morphology may lead to subsequent glandular destruction, and eventually, the occurrence of pancreatic fibrosis, which involves the loss of exocrine and endocrine functions.

Ionizing radiation produces ROS,[34] which plays an important role in the cell death pathway as a signaling molecule. The overproduction of ROS can lead to inflammatory reactions by disrupting the structure of organelles.[6] Oxidative stress plays an important role in pancreatitis and pancreatic β-cell damage.[35] Due to their low content of redox buffers, pancreatic β-cells are particularly sensitive to oxidative stress.[35] Oxidative stress is characterized by the reduction of antioxidants and the increase of free radicals, which may promote and even increase the speed of the development of DM, probably due to the resultant β-cell injury.[36] Numerous studies have reported that the development and progression of diabetes are associated with insufficient biological antioxidants and the resulting oxidative stress.[25] Several studies have shown that insulinopenic DM develops following whole-body or abdominal irradiation, particularly

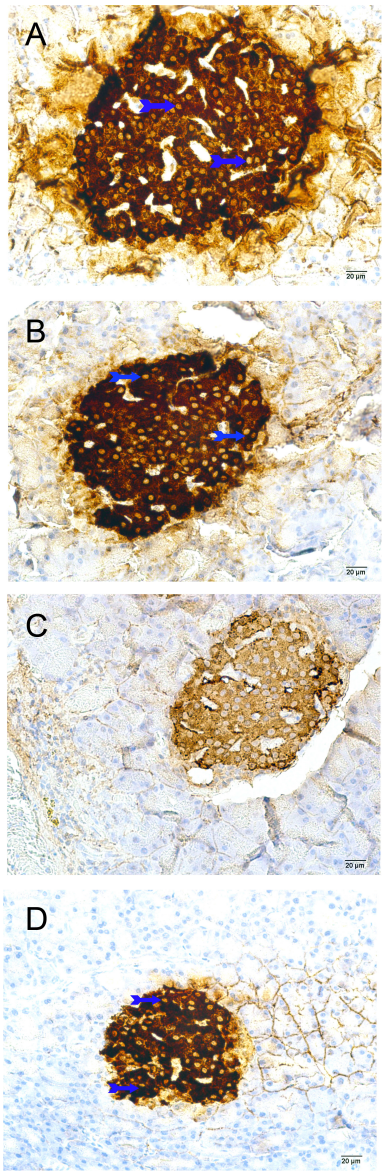

Figure 2. Representative light microscopic images of pancreatic tissue incubated with anti-insulin primary antibody. A (×40) control group: numerous cells (arrow) exhibiting extensive insulin positivity can be seen in the islets of Langerhans [anti-insulin positivity score 2.5 (2-3)]. B (×40) CoQ10 group: cells with extensive insulin positivity (arrow) can be seen in the islets of Langerhans [anti-insulin positivity score 2 (2-3)]. C (×40) irradiated group: Fewer insulin-positive cells (tailed arrow) seen in the islets of Langerhans [anti-insulin positivity score 0 (0-1)]. D (×40) irradiated+CoQ10 group: an increase in cells (arrow) with extensive insulin positivity can be seen in the islets of Langerhans [anti-insulin positivity score 2 (1-2)].

Table 4. Semi-Quantitative Analysis [Median (25%-75% Interquartile Range)] Results

Group	Anti-Insulin Positivity Score	TUNEL
Control	2 (2-3)	0 (0-0)
CoQ10	2 (2-3)**	0 (0-0)
IR	0 (0-1)*	2 (2-2)*
IR + CoQ10	2 (1-2)***	1 (1-1)***

Kruskal–Wallis/Mann–Whitney *U*-test with Bonferroni corrections.
* $P < .05$: versus the control group
** $P < .05$: versus the IR group
*** $P = .01$: versus the IR group.

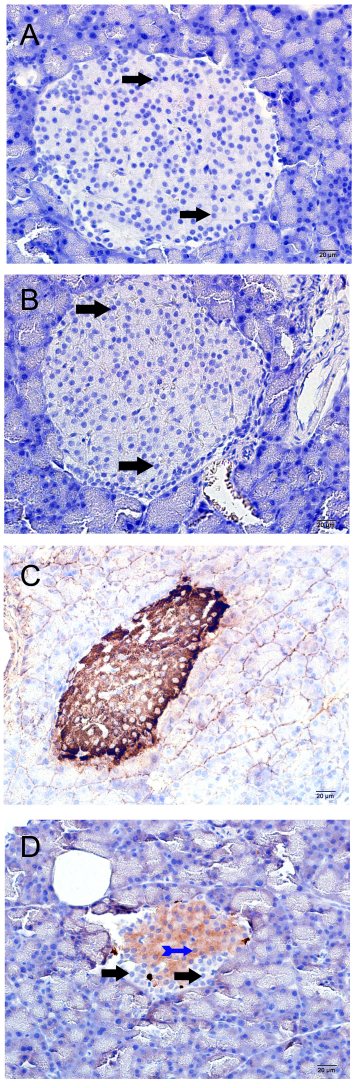

Figure 3. Representative light microscopic image of pancreatic tissue processed with the TUNEL method. A (×40) control group: normal, immune-negative cells can be seen in the islets of Langerhans [TUNEL positivity score 0 (0-0)]. B (×40) CoQ10 group: Numerous typical immune-negative cells (arrow) can be seen in the islets of Langerhans [TUNEL positivity score 0 (0-0)]. C (×40) irradiated group: Numerous immune-positive cells (tailed arrow) can be seen in the islets of Langerhans [TUNEL positivity score 2 (2-2)]. D (×40) irradiated + CoQ10 group: a decrease in immune-positive cells (arrow) can be seen in the islets of Langerhans [TUNEL positivity score 1 (1-1)].

in cohorts cured of childhood cancer.[10,12,13,37] While several mechanisms have been suggested to account for the radiation-induced development of diabetes, the β-cell damage caused by radiation is the most widely accepted and studied mechanism. Sarri et al[38] reported a decrease in the number of pancreatic islet β-cells and impaired insulin secretion in rats receiving a single 19 Gy dose of abdominal radiation. The increased TUNEL positivity accompanying the reduced insulin positivity in the present study suggests that β-cells in the islets of Langerhans decrease by undergoing apoptosis. In support of the present study, studies in the literature have shown the lipid peroxidation products forming in oxidative stress-related membrane damage to be involved in the occurrence of apoptosis through the activation of caspase-3 and NF-KB.[39] Yumi Imai showed that the addition of mitoQ, a derivative of endogenous CoQ10, to the diet of rats fed a high-fat diet resulted in insulin sensitivity and reduced the size of pancreatic islets.[40] Furthermore, the decrease in TUNEL positivity accompanying the higher insulin positivity in the pancreatic islets of rats treated with CoQ10 in the present study suggests a decrease in apoptosis rather than the activation of β-cells.

Oxidative stress is an important cause of cell damage. Numerous antioxidants have been proposed and studied to counter the toxic effects of oxidative stress, one of the basic effect mechanisms of IR. One of these antioxidants, CoQ10, produced endogenously and first described in 1957, has been proposed for use in the treatment of several chronic diseases and the prevention of IR toxicity.[19] Coenzyme Q10 functions as both an endogenous antioxidant and as a coenzyme involved in the electron transport chain and ATP production.[41] Therefore, it is present in all cells, particularly in soft tissues with greater energy requirements.[19] Despite being produced endogenously, lower CoQ10 levels relative to healthy individuals have been observed in conditions such as diabetes, and CoQ10 insufficiency has been linked to DM.[22,42] Coenzyme Q10 is an antioxidant shown to provide direct benefits in terms of glycemic control, insulin secretion, and β-cells.[25,43] Clinical studies have shown that it reduces fasting blood sugar by increasing insulin secretion.[44] However, not much is known about the effect of CoQ10 on insulin secretion. Although the protection of β-cells against oxidative damage is not thought to be the sole reason for increased insulin secretion, it is an important mechanism. Lim et al[27] reported that CoQ10 protected cultured insulin-producing β-cells exposed to glucotoxicity and lipotoxic conditions against oxidative damage and loss of glucose-induced insulin secretion. Lorza et al[14] showed that CoQ10 supplementation enhanced glucose tolerance and insulin sensitivity by preventing the deleterious effects of statins on the endocrine pancreas while protecting islets and β-cells against oxidative stress and death. Coenzyme Q10 supplementation under oxidative stress conditions was shown to decrease MDA levels and increase antioxidant enzymes.[18] Several studies have shown that the addition of CoQ10 to diet in varying doses, particularly in diabetic patients, significantly reduces MDA levels compared to non-diabetic individuals.[18,39] Malondialdehyde is the most important marker of lipid peroxidation.[18]

Zhao et al[23] demonstrated that CoQ10 protects astrocytes from ROS-mediated ultraviolet B (UVB)-induced damage. In addition, CoQ10 administration has been reported to protect against skin damage caused by UVB radiation.[45] In a rat study, Li Zhao et al[46] showed that CoQ10 exhibited a protective effect against cisplatin-induced

cardiotoxicity by lowering oxidative stress. In a study using UVB radiation to induce ROS stress in cultured astrocytes, Li Jing et al[47] concluded that CoQ10 is capable of protecting astrocytes by suppressing oxidative stress, preventing mitochondrial dysfunction, and blocking the mitochondria-mediated cell death pathway. Najafi et al[5] showed that CoQ10 has the potential to reduce some of the side effects of radiation on rat spermatogenesis. Mirmalek et al[39] showed that CoQ10 reduced pancreatic damage by reducing inflammation and oxidative stress in acute pancreatitis caused by L-arginine in rats. Similarly, Shin et al[24] showed that CoQ10 can ameliorate pancreatic injury and the associated pulmonary complications by inhibiting inflammatory cytokines in mice with experimentally induced acute pancreatitis. Stawiarska-Pie et al[48] confirmed that CoQ10 administration exerts a protective effect against the degenerative changes in the pancreas caused by fluoride-induced oxidative stress. The application of CoQ10 improved insulin immunoreactivity in islets and this was accompanied by a decrease in oxidative stress and apoptosis. Kang Luo et al[22] showed that CoQ10 protected mitochondria in β-cells by reducing oxidative stress caused by tacrolimus. Another study reported that CoQ10 treatment improved pancreatic β-cell function in a tacrolimus-induced diabetic rat model. Examination of mitochondria under electron microscopy revealed that the addition of CoQ10 to tacrolimus treatment increased mitochondrial size and volume, and the number of insulin granules.[27]

Coenzyme Q10 was shown to increase insulin secretion in β-cells.[49] The addition of CoQ10 to metformin in a sirolimus-induced diabetic rat model was shown to significantly increase antiperoxidative enzyme levels in pancreatic islet cells, besides yielding a significant increase in insulin intensity accompanied by a decrease in oxidative stress as well as apoptosis. It also reduces sirolimus-related hyperglycemia and oxidative stress.[42] Clinical reports from Japan show that the addition of CoQ10 to the diet can reinforce β-cell function and glycemic control in DM.[21] Similarly, Folkers et al[50] indicated that the positive role of CoQ10 in diabetes was probably associated with healing in β-cells. Studies have reported that significant CoQ10 deficiency in pancreatic mitochondrial bioenergetics can lead to impairments in ATP production and insulin biosynthesis.[50] Sena et al[51] showed that the administration of CoQ10 reduced lipid peroxidation and glycated HbA1c levels in diabetic rats.

Our results suggest that CoQ10 may serve as a protective antioxidant in IR-induced pancreatic injury. The critical question here is whether CoQ10 will exhibit a radioprotective effect on tumor tissue. There have been few studies on this subject. However, Javier Frontiñán-Rubio et al[52] reported evidence suggesting that CoQ10 acts as a radiosensitizer, potentiating temozolomide-induced cytotoxicity and causing apoptosis in human glioblastoma cells with no effect on normal astrocytes. The known antioxidant CoQ10 thus acts as a prooxidant by deactivating the cell antioxidant mechanism in pathological processes and may reduce total antioxidant cell capacity.[53]

Since oxidative stress has been implicated to be a significant pathway in the pathogenesis of pancreatic β-cell damage, we investigated the antioxidant effect of CoQ10 on pancreatic β-cells. This study showed that CoQ10 exhibited protective effects in the rat pancreas exposed to abdominal IR and that insulin-positive β-cells in the islets increased, while apoptosis decreased compared to the radiation group. This study should be interpreted with some limitations in mind. First, we were unable to evaluate insulin, c-peptide, fasting plasma glucose, and HbA1C levels using biochemical methods. A second limitation of this research study is that since it is an animal study, human experiments will be required for clinical use.

Conclusion

The present study showed that CoQ10 exerted a protective effect on pancreatic β cells by suppressing inflammation and apoptosis in the acute phase in rats exposed to abdominal x-ray irradiation. Future studies may shed light on CoQ10 as a protective agent against IR-induced pancreatic β-cell damage. Further studies are needed to determine the long-term protective effect of CoQ10 in IR-induced pancreatic β-cell damage, as well as the most effective dose and duration.

Ethics Committee Approval: Approval for this experimental study was granted by the Recep Tayyip Erdoğan University Animal Experiments Ethical Committee, Rize, Türkiye (Date: 29.07.2022, Approval No: 2022/32).

Informed Consent: The present study was done with experimental animals. There is no patient participation.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – F.M., L.T.; Design – F.M., L.T.; Supervision – F.M., L.T.; Resources – T.M., S.Y.R.; Data Collection and/or Processing – L.T., T.M.,S.Y.R.; Analysis and/or Interpretation – F.M., L.T.,T.M.S.Y.R.; Literature Search – F.M.,S.Y.R.; Writing Manuscript – F.M.; Critical Review – F.M., L.T., T.M.S.Y.R.

Declaration of Interests: The authors have no conflict of interest to declare.

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