EXPERIMENTAL STUDY

Effects of alpha-tocopherol on acute pancreatitis in rats

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ABSTRACT

BACKGROUND: Acute pancreatitis is a disease with high morbidity and mortality, despite all the advances in technology. The overall mortality rate of acute pancreatitis is 10%, whereas the mortality rate in infected necrotizing pancreatitis is approximately 35%. In this study, we aimed to establish acute pancreatitis in rats in order to try out the alpha-tocopherol treatment protocol and to reveal the results biochemically and histopathologically.

METHODS: Twenty-four male male Sprague–Dawley rats weighing between 300 and 350 g were used in the study. In Group 1, 80 µg/kg of normal saline was subcutaneously injected into eight rats; in Group 2, 80 µg/kg of cerulein was subcutaneously injected into eight rats; and in Group 3, 80 µg/kg of cerulein was subcutaneously injected into eight rats. In addition, 30 mg/kg of alpha-tocopherol was intraperitoneally injected into eight rats.

RESULTS: The mean Schoenberg score, serum amylase, and lipase and Neutrophil Gelatinase-Associated Lipocalin (NGAL) levels were statistically significantly higher in Group 2 than in Group 1. The mean Schoenberg score and serum amylase and lipase levels were statistically significantly lower in Group 3 than in Group 2.

CONCLUSION: In this experimental study rat model of cerulein-induced acute pancreatitis, 30 mg/kg of alpha-tocopherol was injected intraperitoneally to examine its effect on pancreatitis. The improvement was observed in the histopathological examination of pancreatic tissues. We think that alpha-tocopherol may have a therapeutic effect on pancreatic tissue.

Keywords: Alpha-tocopherol; pancreatitis; rat.

INTRODUCTION

Acute pancreatitis is an acute non-bacterial inflammation in which the pancreas is autodigested by its regurgitated own enzymes when they are in the active form and which can regress clinically and histologically.[1] Acute pancreatitis is a disease with high morbidity and mortality, despite all the advances in technology.[2] Acute pancreatitis may have a broad spectrum of pathologic findings, ranging from mild interstitial edema to severe hemorrhagic gangrene and necrosis. Similarly, clinical manifestations may occur in varying degrees, ranging from mild abdominal pain to hypotension, fluid sequestration, metabolic disturbances, and sepsis. The overall mortality rate of acute pancreatitis is 10%, whereas the mortality rate in infected necrotizing pancreatitis is approximately 35%.[3]

Respiratory complications are the leading cause of mortality in the short term in 95% of cases.[3]

In experimental pancreatitis models, studies are still being conducted to examine the efficacy of various therapeutic agents on treatment and to determine the parameters that can be used in measuring this efficacy. Cerulein is a cholecystokinin analog that leads to bile reflux into the pancreatic duct and thus pancreatitis by relaxing the sphincter of Oddi and stimulating the gallbladder contraction.[4] Cerulein has

Cite this article as: Özgül H, Tatar C, Özer B, Aydın H, Sarı S, Peltek Özer S. Effects of alpha-tocopherol on acute pancreatitis in rats. Ulus Travma Acil Cerrahi Derg 2018;24:1-6.

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Ulus Travma Acil Cerrahi Derg 2018;24(6):1-6 DOI: 10.5505/tjtes.2018.30413 Submitted: 16.12.2017 Accepted: 16.04.2018 Online: 10.12.2018

been administered by the intravenous, subcutaneous, and intraperitoneal routes in experimental pancreatitis models.[5,6]

In this study, we aimed to establish acute pancreatitis in rats in order to try out the treatment protocol and to reveal the results biochemically and histopathologically.

MATERIALS AND METHODS

This experimental study was approved by the Ethics Committee of Bezmialem University Faculty of Medicine. It was carried out at the Experimental Animals Laboratory of Bezmialem University. Twenty-four male Sprague–Dawley rats weighing between 300 and 350 g (standard pelleted diet) were used in the study. Twenty-four rats were randomly divided into three groups of equal numbers.

Group 1: 80 µg/kg of normal saline (an equivalent volume of cerulein) was subcutaneously injected into eight rats 6 times at 1-hour intervals.

Group 2: 80 µg/kg of cerulein was subcutaneously injected into eight rats 6 times at 1-hour intervals.

Group 3: 80 µg/kg of cerulein was subcutaneously injected into eight rats 6 times at 1-hour intervals. In addition, 30 mg/kg of alpha-tocopherol was intraperitoneally injected into eight rats 2 times at 1-hour intervals.

Decapitation was performed 7 hours after the first injection of cerulein.

Biochemical Analysis

Approximately 7–8 cc of blood was obtained from each rat heart after decapitation and was kept at room temperature for 40 min. Then, the serum was separated by centrifugation at 3500 rpm at +4°C for 10 minutes. For amylase, lipase, Neutrophil Gelatinase-Associated Lipocalin (NGAL), myeloperoxidase (MPO), AST, and ALT, 0.5 cc of serum was placed into Eppendorf tubes to the biochemistry laboratory. It was measured according to the International Federation of Clinical Chemistry and Laboratory Medicine with the Roche Preanalytical Modular System device. The results of the groups were compared statistically to each other. A p-value <0.05 was considered statistically significant.

Histopathological Examinations

After decapitation, the rats were laparotomized with a median incision. Pancreatic tissue was removed for histopathological evaluation. Specimens were fixed with a 10% formaldehyde solution. Pancreatic tissue sections were stained with the hematoxylin–eosin stain and examined under the light microscope. Edema, inflammation, vacuolization, and necrosis in pancreatic tissue were assessed using a score range of 0–4 (Schoenberg index) (Table 1). Moreover, pancreatic tissues of the groups with acute pancreatitis were stained with immunohistochemical stains. Myeloperoxidase staining demonstrated neutrophil infiltrates in pancreatic tissues. Neutrophil infiltration in pancreatic tissues was shown with the staining of IL-8 (also called neutrophil-activating peptide).

Statistical Analysis

The SPSS 16.0 statistical software package (SPSS Inc., Chicago, USA) was used for statistical analysis. Categorical variables were expressed as number and percentage. Numerical variables were expressed as the mean and standard deviation. If numerical variables were normally distributed, the one-way analysis of variance was used to compare more than two independent groups. If numerical variables were not normally distributed, the Kruskal–Wallis test was used to compare more than two independent groups. Subgroup analyzes were performed by the Tukey test (parametric test) and the Mann–Whitney U test (non-parametric test), and they were interpreted by the Bonferroni correction. A p-value <0.05 was considered statistically significant.

RESULTS

Amylase

The mean serum amylase level was 1537.00±123.26 in Group 1, 3316.13±432.49 in Group 2, and 2531.38±433.93 in Group 3. The mean serum amylase level was statistically significantly higher in Group 2 than in Group 1 (p<0.001). The mean serum amylase level was statistically significantly lower in Group 3 than in Group 2 (p<0.001) (Table 2).

Table 1. Schoenberg's scoring[10]

	Edema	Inflammation	Vacuolization	Necrosis
0	No	No	No	No
1	Diffuse expansion of interlobar septa	Periductal	Periductal (<5%)	1–4 necrotic cells*
2	1 (+) Diffuse expansion of interlobular septa	Parenchymal (<50% lobules)	Focal (5%–20%)	5–10 necrotic cells
3	2 (+) Diffuse expansion of interacinar septa	Parenchymal (51%–75% lobules)	Diffuse (21%–50%)	11–16 necrotic cells
4	3 (+) Diffuse expansion of intercellular septa	Parenchymal (>75% lobules)	Severe (>50%) 27	>16 necrotic cells

*(microscopic field). 2–5 = mild pancreatitis. 5–8 = moderate pancreatitis. 8 and above = severe pancreatitis.

Table 2. Statistical results of biochemical parameters

	Group 2	Group 3	Group 1	p
	Mean±SD	Mean±SD	Mean±SD	
Aspartate aminotransferase	196.63±162.96	155.88±29.42	128.38±22.83	0.161
Alanine aminotransferase	75.50±14.73	78.13±10.59	74.75±12.71	0.859
Amylase	3316.13±432.49$^{\#¥}$	2531.38±433.93$^{*¥}$	1537.00±123.26$^{*\#}$	<0.001
Lipase	3459.63±500.60$^{\#¥}$	2450.38±808.69$^{*¥}$	216.38±81.81$^{*\#}$	<0.001
NGAL	14.43±5.13$^{¥}$	10.37±2.38	6.77±1.48$^{*\#}$	0.001
Myeloperoxidase	14.39±1.77	14.90±1.92	12.71±2.16	0.088
Pathology score	5.38±0.52$^{\#¥}$	3.50±0.53$^{*¥}$	0.50±0.53$^{*\#}$	<0.001

*Different from Group 2. #Different from Group 3. ¥Different from Group 1. NGAL: Neutrophil Gelatinase-Associated Lipocalin; SD: Standard deviation.

Lipase

The mean serum lipase level was 216.38±81.81 in Group 1, 3459.63±500.60 in Group 2, and 2450.38±808.69 in Group 3. The mean serum lipase level was statistically significantly higher in Group 2 than in Group 1 (p<0.0001). The mean serum lipase level was statistically significantly lower in Group 3 than in Group 2 (p=0.016) (Table 2).

NGAL

The mean serum NGAL level was 6.77±1.48 in Group 1, 14.43±5.13 in Group 2, and 10.37±2.38 in Group 3. The mean serum NGAL level was statistically significantly higher in Group 2 than in Group 1 (p=0.002). There was no statistically significant difference between Groups 2 and 3 in terms of the mean serum NGAL level (p=0.074) (Tables 2, 3).

MPO

The mean serum MPO level was 10.37±2.38 in Group 1, 14.39±1.77 in Group 2, and 14.90±1.92 in Group 3. There was no statistically significant difference between Groups 1 and 2 in terms of the mean serum MPO level. There was no statistically significant difference between Groups 2 and 3 in terms of the mean serum MPO level (p=0.088) (Tables 2, 3).

Histopathological Findings

In our study, pancreatitis was proven histologically in all 16 rats (Groups 2 and 3) in which it was planned to be established with subcutaneous injection of cerulein (80 µg/kg). Histopathological examinations revealed fat necrosis, interstitial edema, vacuolization, and polymorphonuclear cell infiltration in the groups with acute pancreatitis compared with the control group.

In our experimental rat model of cerulein-induced acute pancreatitis, neutrophil infiltration, vacuolization, fat necrosis, and edema in pancreatic tissue were evaluated by histopathological examination (Schoenberg index).[7] The mean Schoenberg score was 0.50±0.53 in Group 1, 5.38±0.52 in Group 2, and 3.50±0.53 in Group 3. The mean Schoenberg score was statistically significantly higher in Group 2 than in Group 1 (p<0.001). The mean Schoenberg score was statistically significantly lower in Group 3 than in Group 2 (p<0.001) (Tables 2, 3).

Table 3. Subgroup analyzes

	Group 2 vs Group 3	Group 1 vs Group 2	Group1 vs Group 3
	p	p	p
Amylase (IU/mL)	0.001	<0.001	<0.001
Lipase	0.016	0.001	0.001
NGAL	0.074	0.002	0.006
Pathology score	0.001	0.001	0.001

NGAL: Neutrophil Gelatinase-Associated Lipocalin;

Moreover, pancreatic tissues of the groups with acute pancreatitis were stained with immunohistochemical stains. Myeloperoxidase staining demonstrated neutrophil infiltrates in pancreatic tissues. Neutrophil infiltration in pancreatic tissues was shown with the staining of IL-8 (also called neutrophil-activating peptide).

DISCUSSION

Pancreatitis is mainly caused by the auto-digestion of the pancreatic tissue resulting from the abnormal activation of pancreatic enzymes.[8,9] In the course of acute pancreatitis, systemic inflammatory conditions besides localized events occur. Oxygen free radicals play an important role in the pathogenesis of acute pancreatitis.[10]

Impaired microcirculation is also one of the important steps in the pathogenesis. There is an increase in the permeability of the endothelial layer of arterioles and venules. As a result, edema and microhemorrhages occur in the tissue due to extravasation of plasma and erythrocytes.[11] Willemer

et al.[12] showed that interstitial edema occurred due to the PNL accumulation in pulmonary capillary vessels, damage to alveolar epithelial cells, and increased vascular permeability in cerulein-induced experimental acute pancreatitis model in rats. They also reported that these findings peaked at 12 hours and completely disappeared at 84 hours. For this reason, they emphasize the importance of early treatment. In many experimental studies, edematous pancreatitis has been established, and it has been aimed to prevent systemic complications.[13–17]

Although different methods are used in experimental models of acute pancreatitis, an increase in pancreatic secretion is one of the most preferred methods for the pathophysiology of acute pancreatitis. Cerulein has been successfully used in many experimental studies with this effect.[7,10] The effect of cerulein on the pancreas is dependent on the dose and duration. Cerulein dose and duration of administration are determined according to the form of pancreatitis to be created.[13,18,19] Strowski et al.[18] created an experimental model of acute edematous pancreatitisin rats where 10 µg/kg of cerulein was administered five times at 1-hour intervals. Konturek et al.[20] created an experimental model of acute edematous pancreatitisin rats where 10 µg/kg of cerulein was administered subcutaneously.

The data obtained from many comprehensive experimental studies show that oxygen free radicals are produced as important mediators in the pathogenesis of many tissue injuries.[7,9,10,19,21] Oxygen free radicals are involved in both the initial and later stages of the pathophysiology of acute pancreatitis.[7,10,22] For this reason, experimental studies have been carried out to remove the efficacy of oxygenfree radicals in acute pancreatitis. In our study, 80 µg/kg of cerulein was subcutaneously injected into the rats six times at 1-hour intervals to create an experimental model of acute pancreatitis. Acute pancreatitis was created histopathologically and biochemically in the cerulein-treated groups (Groups 2 and 3). When these groups (Groups 2 and 3) were compared with the control group (Group 1), histopathological evaluations and biochemical measurements were found to be statistically significant (Table 3).

In experimental models of acute pancreatitis, serum amylase, and lipase levels were used as parameters to show the formation of pancreatitis.[10] Serum amylase levels are elevated in acute pancreatitis, acute exacerbation of chronic pancreatitis, perforated and penetrating peptic ulcer, postoperative period of upper abdominal surgery, pancreatic duct obstruction, acute alcohol intake or poisoning, salivary gland diseases, and advanced chronic renal insufficiency. The serum amylase level begins to rise within 3–6 hours in acute pancreatitis. Its urinary level begins to increase 6–10 hours after its serum level is increased. This alone has very little meaning. The amylase–creatinine clearance ratio (ACCR) is calculated. An ACCR greater than 5% suggests acute pancreatitis.[23] We did not use this ratio because we also used lipase levels and histopathological evaluations in our study. Serum lipase levels are elevated in acute pancreatitis, perforated and penetrating peptic ulcer, and pancreatic duct obstruction. Lipase level can remain high until 14 days after the amylase level returns to normal.[23]

While NGAL was initially characterized by its presence in neutrophil lysosomes, it was later observed that NGAL was expressed in various tissues, such as renal tubular epithelium, colon, prostate, and breast. Lipocalin (NGAL) is synthesized from the cells under stress. Infection, inflammation (synthesized from the secondary granules of active neutrophils), ischemia, and neoplastic transformation enhances NGAL expression.[24,25] In our study, the mean serum NGAL level was statistically significantly higher in Group 2 than in Group 1, whereas there was no statistically significant difference between Groups 2 and 3 in terms of the mean serum NGAL level.

MPO is found in large quantities in neutrophils. This enzyme, stored in azurophilic granules of these cells, is responsible for killing of pathogenic microorganisms. These granulocytic cells engulf microorganisms via phagocytosis and break down and digest pathogens by producing reactive oxygen species, such as superoxide and hydrogen peroxide.[26,27] In our study, there was no statistically significant difference between Groups 1 and 2 and between Groups 2 and 3 in terms of the mean serum MPO level (Table 3).

It has been reported that superoxide dismutase and catalase reduced the ultrastructural and biochemical injury associated with cerulein-induced acute pancreatitis in rats. According to the authors, active neutrophils secrete oxygen radicals and cause endothelial injury.[17,28]

In a study by O'Donovan et al.[29] conducted in an experimental rat model of cerulein-induced acute pancreatitis, endothelial cell injury, and edema formation were detected in pancreatic tissue, and this event was thought to be related to neutrophils. In experimental pancreatitis models, acute pancreatitis showed the same morphological characteristics with that in humans. A clinical condition was also established to be biochemically similar to that in humans by increased serum amylase and lipase levels. It was also seen that non-fatal pulmonary injury occurred in acute pancreatitis and was similar to that in humans.[29]

Alpha-tocopherol has a protective effect on membrane stabilization and an inhibitory effect on lipid peroxidation. It is also known as an antioxidant. It easily wedges between the membrane phospholipids due to its high lipid solubility and reduces unsaturated fatty acids with 20 carbon atoms. Thus, it prevents lipid peroxidation in biomembranes caused by oxygen free radicals. Moreover, alpha-tocopherol is converted into alpha-tocopheryl quinone by combining with oxygen free

radicals, and thus it undertakes the free radical scavenging process.

Jiang et al.[30] showed that alpha-tocopherol and tocotrienol-rich fraction reduce oxidative stress, ameliorate inflammation and fibrosis, and down-regulate the mRNA expression of TGF-β1 and collagen-α1 in chronic pancreatitis.

Li et al.[31] investigated the effects of alpha-tocopherol on pancreatic fibrosis and survival in rats with experimental chronic pancreatitis. They reported that alpha-tocopherol treatment elevates the survival rate, extenuates fibrosis, and increases relative pancreatic weight in the chronic pancreatitis model.

It has been reported that the oral administration of alpha-tocopherol significantly ameliorated the symptoms of diabetic nephropathy.[32]

Previous studies have highlighted the potential of using alpha-tocopherol for cancer chemoprevention.[33] However, several studies indicated that alpha-tocopherol might be ineffective in the prevention of prostate cancer, lung cancer, and breast cancer.[34–38]

In our experimental rat model of cerulein-induced acute pancreatitis, 30 mg/kg of alpha-tocopherol was injected intraperitoneally at 1-hour intervals 2 hours after the first injection of ceruleinin to examine its effect on pancreatitis. While the serum amylase, lipase, and NGAL levels and the mean Schoenberg score were statistically significantly h igher i n Group 2 than in Group 1, the serum amylase and lipase levels and the mean Schoenberg score were statistically significantly lower in Group 3 than in Group 2.

In this experimental study, we aimed to establish an acute pancreatitis model in rats, to reveal the natural process of acute pancreatitis, and to examine the efficacy of th e ag ent wh ich can be tried in treatment. We observed that acute pancreatitis developed as both histopathological and laboratory findings in rats after subcutaneous injection of cerulein. In an experimental model of acute pancreatitis, it was seen that the serum lipase, amylase, and NGAL levels increased significantly s tatistically, the serum MPO level did not increase significantly statistically, and the serum amylase and lipase levels decreased significantly statistically in the rats given alpha-tocopherol. In addition, the improvement was observed during the histopathological examination of pancreatic tissues. These findings s uggest t hat alpha-tocopherol may have a positive effect on treatment.

Conclusion

In conclusion, we think that alpha-tocopherol may have a therapeutic effect on pancreatic tissue. However, new studies need to be conducted with this regard.

Conflict of interest: None declared.

REFERENCES

1. Elkan H. Ratlarda cerulein ile oluşturulan deneysel akut pankreatit modelinde N asetilsistein ile metilprednisolonun etkileri [Uzmanlık Tezi]. Adana: Çukurova Üniversitesi; 2006.
2. Austin JL, Reber HA. Pathophysiology of acute pancreatitis. Surgical disease of pancreas. Washington: Lea & Febiger; 1987. p. 377–85.
3. Yeo CJ, Cameron J. Acute pancreatitis. In: Zuidema GD, editor. Shackelford's surgery of the alimentary tract. Philadelphia: Saunders; 1991. p. 19–36.
4. Manuel A, Manso PD, Jose I, San R. Cerulein induced acute pancreatitis in the rat. Dig Dis Sci 1992;37:364–8. [CrossRef]
5. Yonetci N, Sungurtekin U, Oruc N, Yilmaz M, Sungurtekin H, Kaleli I, et al. Is procalcitonin a reliable marker for the diagnosis of infected pancreatic necrosis? ANZ J Surg 2004;74:591–5. [CrossRef]
6. Um SH, Kwon YD, Kim CD, Lee HS, Jeen YT, Chun HJ, et al. The role of Nitric oxide in Experimental Cerulein Induced Pancreatitis. J Korean Med Sci 2003;18:520–6. [CrossRef]
7. Schoenberg MH, Büchler M, Gaspar M, Stinner A, Younes M, Melzner I, et al. Oxygen free radicals in acute pancreatitis of the rat. Gut 1990;31:1138–43. [CrossRef]
8. Deveny ZJ, Orchord JL, Powers RE. Xanthine oxidase activity in mouse pancreas: effects of caerulein-induced acute pancreatitis. Biochem Biophyd Res Commun 1987;149:841–5. [CrossRef]
9. Wisner J, Green D, Ferrell L, Renner I. Evidence for a role of oxygen derived free radicals in the pathogenesis of caerulein induced acute pancreatitis in rats. Gut 1988;29:1516–23. [CrossRef]
10. Dobrowski A, Gabryelewicz A, Wereszczynska U, Chyczewski L. Oxygen-derived free radicals in cerulein-induced acute pancreatitis. Scand J Gastroenterol 1988;47:1245–9. [CrossRef]
11. Watanabe O, Baccino FM, Steer ML, Meldolesi J. Supramaximal caerulein stimulation and ultrastructure of rat pancreatic acinar cell: early morphological changes during development of experimental pancreatitis. Am J Physiol 1984;246:457–67. [CrossRef]
12. Willemer S, Feddersen CO, Karges W, Adler G. Lung injury in acute experimental pancreatitis in rats. I. Morphological studies. Int J Pancreatol 1991;8:305–21.
13. Steer ML, Meldolesi J. The cell biology of experimental pancreatitis. N Eng J Med 1987;316:144–50. [CrossRef]
14. Closa D, Bulbena O, Rosello-Catafau J, Fernandez-Cruz L, Gelpi E. Effect of prostaglandins and superoxide dismutase administration on oxygen free radical production in experimental acute pancreatitis. Inflammation 1993;5:563–71. [CrossRef]
15. Jaworek J, Jachimczak B, Tomaszewska R, Konturek PC, Pawlik WW, Sendur R, et al. Protective action of lipopolysaccharidesin rat caerulein-induced pancreatitis: role of nitric oxide. Digestion 2000;62:1–13.
16. Nonaka A, Manabe T, Tobe T. Effect of a new synthetic ascorbic acid derivative as a free radical scavenger on the development of acute pancreatitis in mice. Gut 1991;32:528–32. [CrossRef]
17. Guice KS, Miller DE, Oldham KT, Townsend CM Jr, Thompson JC. Superoxide dismutase and catalase: A possible role in established pancreatitis. Am J Surg 1986;151:163–9. [CrossRef]
18. Strowski MZ, Sparmann G, Weber H, Fiedler F, Printz H, Jonas L, et al. Caerulein pancreatitis increases mRNA but reduces protein levels of rat pancreatic heat shock proteins. Am J Physiol 1997;273:G937–45.
19. Steer ML, Rutledge PL, Powers RE, Saluja M, Saluja AK. The role of oxygen-derived free radicals in two models of experimental acute pancreatitis: effects of catalase, superoxide dismutase, dimethylsulfoxide, and allopurinol. Klin Wochenschr 1991;69:1012–7. [CrossRef]
20. Konturek PC, Dembinski A, Warzecha Z, Ihlm A, Ceranowicz P, Konturek SJ, et al. Comparison of epidermal growth factor and transforming growth factor-beta1 expression in hormone-induced acute pancreatitis in

rats. Digestion 1998;59:110–9. [CrossRef]
21. Dembiński A, Warzecha Z, Konturek PC, Ceranowicz P, Stachura J, Tomaszewska R, et al. Epidermal growth factor accelerates pancreatic recovery after caerulein-induced pancreatitis. Eur J Pharmacol 2000;398:159–68. [CrossRef]
22. Sanfley H, Bulkley GB, Cameron JL. The role of oxygen-derived free radicals in the pathogenesis of acute pancreatitis. Ann Surg 1984;200:405–13.
23. Wallach J. Interpretation of diagnostic tests. 5th ed. Boston: Little, Brown, & Co.; 1992. p. 61–3.
24. Cowland JB, Borregaard N. Molecular characterization and pattern of tissue expression of the gene for neutrophil gelatinase-associated lipocalin from humans. Genomics 1997;45:17–23. [CrossRef]
25. Soni SS, Cruz D, Bobek I, Chionh CY, Nalesso F, Lentini P, et al. NGAL: a biomarker of acute kidney injury and other systemic conditions. Int Urol Nephrol 2010;42:141–50. [CrossRef]
26. Andrews PC, Krinsky NI. Human myeloperoxidase and hemi-myeloperoxidase. Methods Enzymol 1986;132:369–79. [CrossRef]
27. Andersen MR, Atkin CL, Eyre HJ. Intact form of myeloperoxidase from normal human neutrophils. Arch Biochem Biophys 1982;214:273–83.
28. Guice KS, Oldham KT, Caty MG, Johnson KJ, Ward PA. Neutrophil-dependent, oxygen-radical mediated lung injury associated with acute pancreatitis. Ann Surg 1989;210:740–7. [CrossRef]
29. O'Donovan DA, Kelly CJ, Abdih H, Bouchier-Hayes D, Watson RW, Redmond HP, et al. Role of nitric oxide in lung injury associated with experimental acute pancreatitis. Br J Surg 1995; 82:1122–6. [CrossRef]
30. Jiang F, Liao Z, Hu LH, Du YQ, Man XH, Gu JJ, et al. Comparison of antioxidative and antifibrotic effects of α-tocopherol with those of tocotrienol-rich fraction in a rat model of chronic pancreatitis. Pancreas 2011;40:1091–6. [CrossRef]
31. Li XC, Lu XL, Chen HH. α-tocopherol treatment ameliorates chronic pancreatitis in an experimental rat model induced by trinitrobenzene sulfonic acid. Pancreatology 2011;11:5–11. [CrossRef]
32. Hayashi D, Ueda S, Yamanoue M, Ashida H, Shirai Y. Amelioration of diabetic nephropathy by oral administration of d-α-tocopherol and its mechanisms. Biosci Biotechnol Biochem 2018;82:65–73. [CrossRef]
33. Yang CS, Suh N, Kong AN. Does vitamin E prevent or promote cancer? Cancer Prev Res (Phila) 2012;5:701–5. [CrossRef]
34. Gaziano JM, Glynn RJ, Christen WG, Kurth T, Belanger C, MacFadyen J, et al. Vitamins E and C in the prevention of prostate and total cancer in men: the Physicians' Health Study II randomized controlled trial. JAMA 2009;301:52–62. [CrossRef]
35. Klein EA, Thompson IM Jr, Tangen CM, Crowley JJ, Lucia MS, Goodman PJ, et al. Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2011;306:1549–56.
36. Lippman SM, Klein EA, Goodman PJ, Lucia MS, Thompson IM, Ford LG, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2009;301:39–51. [CrossRef]
37. Lee IM, Cook NR, Gaziano JM, Gordon D, Ridker PM, Manson JE, et al. Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. JAMA 2005;294:56–65. [CrossRef]
38. Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med 1994;330:1029–35.

DENEYSEL ÇALIŞMA - *ÖZET*

Sıçanlarda alfa tokoferolün akut pankreatit üzerine etkileri

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AMAÇ: Akut pankreatit, teknolojideki tüm gelişmelere rağmen morbiditesi ve mortalitesi yüksek bir hastalıktır. Akut pankreatitte mortalite oranı tüm hastalar için %10 iken, bu oran enfekte olmuş nekrotizan pankreatitli hastalarda yaklaşık olarak %35'tir. Biz, bu çalışmada öncelikle sıçanlarda akut pankreatit oluşturmayı, alfa tokoferol tedavi protokolünü denemeyi ve sonuçları biyokimyasal ve histopatolojik olarak ortaya koymayı amaçladık.

GEREÇ VE YÖNTEM: Çalışmada 24 adet erkek sıçan kullanıldı. Grup 1: Kontrol grubu olarak sekiz sıçana birer saatlik arayla altı kez toplam 80 mikrogram/kg (cerulein ile eş hacimli) serum fizyolojik subkutan enjekte edildi. Grup 2: Sekiz sıçana birer saat ara ile altı kez toplam 80 ug/kg cerulein subkutan enjekte edildi. Grup 3: Sekiz sıçana birer saat ara ile toplam 80 mikrogram/kg cerulein ve birer saat arayla iki kez 30 mg/kg alfa-tokoferol intraperitoneal enjekte edildi.

BULGULAR: Ortalama Schoenberg skoru, serum amilaz, lipaz ve NGAL seviyeleri Grup 2'de Grup 1'e göre istatistiksel olarak anlamlı derecede yüsekti. Ortalama Schoenberg skoru, serum amilaz ve lipaz seviyeleri Grup 3'de Grup 2'ye göre istatistiksel olarak anlamlı derecede düşüktü.

TARTIŞMA: Cerulein ile oluşturulan pankreatit modelinde pankreatitin üzerine olan etkisini incelemek amacıyla 30 mg/kg alfa-tokoferol intraperitoneal olarak uygulandı. Alfa-tokoferolün pankres dokusu üzerine tedavi edici etkisi olabileceğini düşünmekteyiz.

Anahtar sözcükler: Alfa tokoferol; pankreatit; sıçan.

Ulus Travma Acil Cerrahi Derg 2019;25(1):1-6 doi: 10.5505/tjtes.2018.30413