EXPERIMENTAL STUDY

The effects of dexmedetomidine on liver injury in rats with experimental sepsis: A histopathological and immunohistochemical study

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ABSTRACT

BACKGROUND: In the rat sepsis model, the protective effect of dexmedetomidine (Dex) in sepsis-induced tissue injuries by reducing inflammation is still unclear. Research is ongoing to determine whether Dex modulates sepsis-induced tissue injury. The aim of this experimental study was to investigate the effect of Dex on liver injury in sepsis rats histopathologically and immunohistochemically.

METHODS: In this study, sepsis was induced in rats by a 10 ml/kg E. coli injection, and the protective efficacy of Dex against liver damage was investigated through histopathological and immunohistochemical findings by the intraperitoneal administration of 100 µg/kg Dex.

RESULTS: In our results, the most striking and basic morphological changes in the liver tissues of sepsis group rats were neutrophil leukocyte infiltrations in and around the vessels. In Dex-treated groups, neutrophil leukocyte infiltrations were more prominent, and marked dilatations were observed in the vessels. The fact that inflammatory reactions were more prominent in the Dex-treated groups was thought to be related to the increase in vascular permeability due to Dex's vasodilation effect.

CONCLUSION: According to the histopathological and immunohistochemical findings obtained in the present study, we conclude that Dex did not alleviate sepsis-induced liver inflammation in a rat sepsis model.

Keywords: Dexmedetomidine; E. coli; histopathology; liver; rat; sepsis.

INTRODUCTION

Sepsis is a systemic inflammatory response of the body to infectious agents and is a clinical syndrome that can lead to organ failure and death. In sepsis, both the activation of the coagulation mechanism and the disruption of endogenous anticoagulant and fibrinolytic mechanisms cause thrombosis in the microvascular circulation and tissue ischemia, resulting in tissue damage and multiple organ failure.[1] While sepsis cases in which one or more organ failures occur are called severe sepsis, the deterioration of hemodynamic stability characterized by intravascular volume loss is called septic shock.[2] The liver is the most vulnerable organ in which dysfunction occurs in cases of sepsis. It is stated that dysfunctions occur as a result of circulatory disorders, bacterial toxins, neutrophil leukocyte infiltration, and the release of cytokines.[3] Despite significant advances in the understanding of the pathophysiology of sepsis, advances in hemodynamic monitoring tools, and various measures taken, it is still one of the main causes of morbidity and mortality in critically ill patients.[4] In studies conducted, while the overall in-hospital mortality rate was 12.5%, the

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mortality rate in septic shock cases was recorded as 34.3%.[5]

Dexmedetomidine (Dex) is a potent α-2 adrenergic agonist with sedative, analgesic, sympatholytic, hemodynamic, and diuretic properties.[6] It has been reported that there are potential anti-apoptotic and anti-inflammatory effects of Dex.[7] Moreover, it has been shown that Dex's anti-inflammatory effects improve the survival rate in clinical reports of patients with severe sepsis.[5] It has been increasingly used in the clinic for anxiolysis, analgesia, sedation, and anesthetic-sparing effects.[6] Myeloperoxidase (MPO) activity, an indicator of tissue neutrophil infiltration, is often detected in association with a variety of lung pathologies, the most common being interstitial lung disease.[8]

In the presented study, we aimed to examine the effect of Dex on secondary liver injury in early sepsis by histopathological and immunohistological (MPO activity) examinations.

MATERIALS AND METHODS

The study was carried out with the permission of Van Yuzuncu Yil University Animal Experiments Local Ethics Committee (25/08/2024, 2024/08-08). In the study, 32 healthy male Wistar albino rats weighing 260–290 g, obtained from the mentioned local ethics committee, were used. All animals were kept under ideal conditions (21±1°C, 40–70% humidity, 12/12 day-night cycle). They were fed with standard rat chow and tap water.

Experimental Protocols

Rats were randomly divided into four groups, and each group was numbered from their tails. Three groups were infected with Escherichia coli (E. coli) to induce sepsis (endotoxemia).

• Control group: In this group, 10 ml/kg saline (SF) was administered intraperitoneally (i.p.).

• Sepsis group: 10 ml/kg Escherichia coli (E. coli) derivatives of different cultures were administered i.p.

• Sepsis + Dex group-1 (T0-SD): 10 ml/kg E. coli derivatives of different cultures were administered i.p. Immediately afterwards, 100 mcg/kg dexmedetomidine (Sedadomid 200 mcg/2 ml, Koçak Farma, Istanbul, Turkey) was administered i.p.

• Sepsis + Dex group-2 (T5-SD): 10 ml/kg E. coli derivatives of different cultures were administered i.p. At the 5th hour after the procedure, 100 mcg/kg dexmedetomidine was administered i.p. to rats that were thought to be in sepsis according to the Murine Sepsis Score.

The experiment was terminated 8 hours after the induction of sepsis (E. coli injection) in all rats. For this purpose, rats were anesthetized with 50 mg/kg ketamine (Ketalar 1 ml: 50 mg, Pfizer, Istanbul, Turkey) and 10 mg/kg xylazine (Xylazinbio 2%, Bioveta, Czech Republic) via i.p. injection. Animals were sacrificed by the cervical dislocation technique and necropsied; tissue samples were taken from the liver and fixed in a formaldehyde solution.

Histopathological Examination

Tissue samples obtained from the livers of all groups were fixed in 10% buffered formaldehyde solution. Paraffin blocks were prepared after routine tissue follow-up. Sections of 4–5 µm thickness were taken from the paraffin blocks and stained with hematoxylin-eosin (Thermo Shandon, USA). Slides were examined under a light microscope. Pathologists blinded to the study groups scored each section for tissue injuries. Liver sections were evaluated according to the severity of neutrophil leukocyte infiltration, dilatation of the sinusoids, and vasculitis and dilatation in the portal veins. Each item was graded using the following scale: Slight = minimal damage; Moderate = moderate damage; Severe = severe damage.[9]

Immunohistochemical Examination

In the immunohistochemical examination, the expression of myeloperoxidase (MPO) was determined using the streptavidin/biotin immunoperoxidase kit (Histostain-Plus Bulk Kit; Zymed, South San Francisco, CA, USA) according to the streptavidin peroxidase method (ABC). After the sections were taken on adhesive slides and passed through the xylene and alcohol series, the sections were washed with phosphate buffer solution (PBS) and incubated in 3% H_2O_2 for 20 minutes for inactivation of endogenous peroxidase. The sections were placed in the antigen retrieval solution (citrate buffer), covered, and then heat-treated twice for 20 minutes. After this, they were taken out of the oven and allowed to reach room temperature. The tissues were washed again with PBS and blocked by protein blocking (non-immune serum) for 20 minutes.

A primary anti-MPO rabbit polyclonal antibody (Thermo Scientific, MA, USA) was added to the tissues and incubated overnight at +4°C. After that, the sections were washed with PBS and incubated for 20 minutes at room temperature with the biotinylated secondary antibody. The sections were washed again with PBS and then kept in streptavidin-peroxidase for 20 minutes. After washing with PBS, diaminobenzidine (DAB) was added and incubated for 1–2 minutes. All tissues were then stained with Mayer's hematoxylin for 1–2 minutes and washed in tap water. The sections were passed again through the alcohol and xylene series and were then covered with Entellan. Negative controls were used to confirm staining. These slides were reacted with PBS instead of primary antibodies. Sections were examined and photographed under a light microscope (Nikon 80i-DSRI2). Each item was graded using the following scale: Slight = minimal damage; Moderate = moderate damage; Severe = severe damage.

Statistical Analyses

Statistical evaluations were performed using IBM SPSS Sta-

tistics for Windows (version 22.0; IBM Corp., Armonk, NY, USA) and GraphPad Prism for Windows (version 6.0; Boston, MA, USA). The histopathological and immunohistochemical findings were analyzed using the Kruskal–Wallis test, followed by the Mann–Whitney U test to define the diversity among the groups.

RESULTS

Histopathological Findings

The normal histological appearance of the liver was observed in the control group (Figures 1A and B). The most remarkable morphological changes in the sepsis group were the accumulation of neutrophil leukocytes in the central veins, portal areas, and sinusoids (acute hepatitis), but no significant dilatation of the sinusoidal capillaries was observed (Figures 1C and D). Furthermore, migration of accumulated neutrophil leukocytes from the vessel wall to the parenchyma was observed in the lumen of the vessels, especially in the portal areas (Figure 1C). Infiltration of mononuclear cells in these areas was detected very rarely. In the T0-SD group, the most striking morphological changes were more numerous accumulations of neutrophil leukocytes in the central veins, portal areas, and sinusoids, along with marked dilatation in these vessels (Figures 1E and F) compared to the morphological changes observed in the sepsis group. Morphological changes in the T5-SD group were milder compared to the changes observed in the T0-SD group (Figures 1G and H). The scores for morphological changes in the liver tissue are summarized in Table 1.

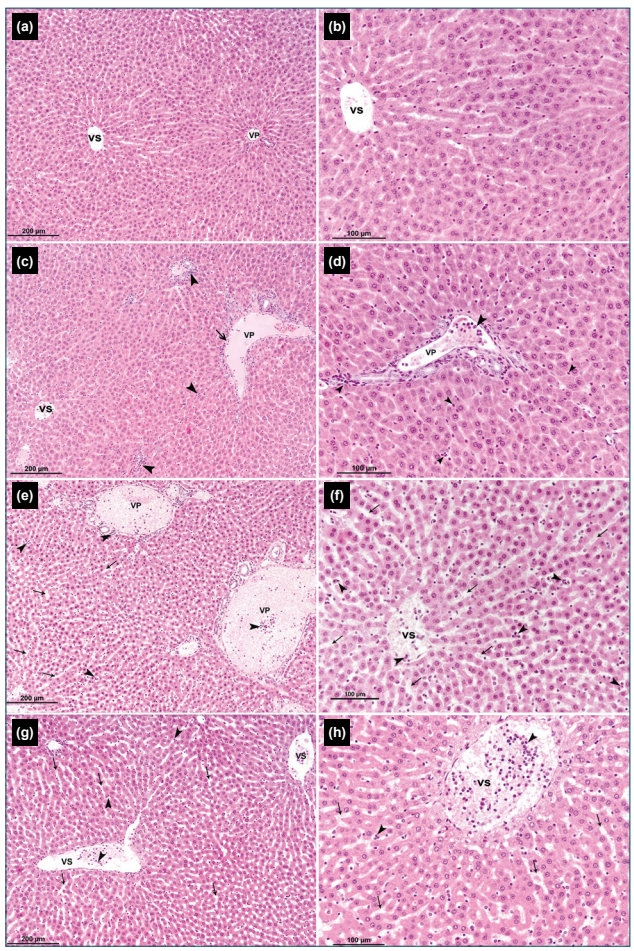

Figure 1. E. Coli-induced septic liver lesions in the rat model. Representative histochemical staining in liver tissue sections (Hematoxylin Eosin Staining) micrographs of experimental groups. Control group: Showing the normal histological appearance of the liver **(a,b)**. Sepsis group: Showing the accumulation of neutrophil leukocytes (arrow heads) in the central veins (VS), portal areas (VP) and sinusoids, but note the absence of dilatation of the sinusoidal capillaries, and migration (arrow) of neutrophil leucocytes (leucodiapedesis) from the portal vein wall into the sinusoids **(c, d)**. T0-SD group: Note that neutrophil leukocyte infiltrates (arrow heads) are more numerous in this group than in the sepsis group, and there is also the vasculitis and dilatation of sinusoidal capillaries (arrows), central veins (VC) and portal veins (VP) **(e, f)**. T5-SD group: Note that the morphological changes observed in the T5-SD group are milder than those observed in the T0-SD group **(g,h)**. Bars=200 µm, 100 µm.

Immunohistochemical Findings

No significant immunoreactivity for MPO was observed in the control group (Figure 2A). However, moderate positive reactions for MPO were observed in sinusoidal neutrophil leukocyte accumulations in the liver tissue of sepsis group rats (Figure 2B). In T0-SD group rats, strong positive reactions for MPO were noted in liver tissue when compared with the sepsis group (Figure 2C). In T5-SD group rats, immunoreactions were milder compared to the T0-SD group (Figure 2D).

In addition, a scoring system was used to assess the degree of MPO immunoreactivity in liver tissue (Table 2).

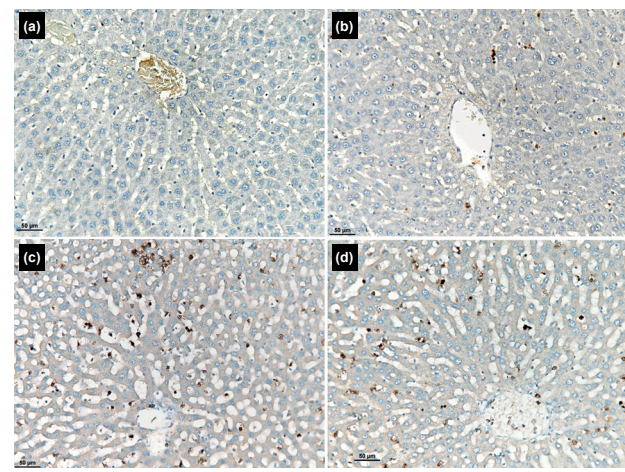

Figure 2. Representative immunohistochemical (MPO) staining in liver tissue micrographs of experimental groups. Control group: Note that there is no significant immunoreactivity for MPO in the control group **(a)**. Sepsis Group: Moderate positive reactions for MPO **(b)**. T0-SD Group: Note that strong positive reactions for MPO when compared with sepsis group **(c)**. T5-SD group: Milder immunoreactions compared to T0-SD group **(d)**. Bars=50 µm.

Table 1. The histopathological effects of Dex on liver injury (affected rats/total number of rats)

Changes/lesions in livers	Control	Sepsis	T0-SD	T5-SD	P values
Infiltration of neutrophil leukocytes	-/8[b]	8/8[a]	8/8[c]	8/8[a]	
Slight	–	–	–	–	
Moderate	–	6	1	4	*
Severe	–	2	7	4	
The dilatation of sinusoids	-/8[b]	-/8[b]	8/8[a]	8/8[a]	
Slight	–	–	–	–	
Moderate	–	–	2	5	*
Severe	–	–	6	3	
Vasculitis and dilatation in the portal veins	-/8[b]	8/8[a]	8/8[a]	8/8[a]	
Slight	–	4	–	–	*
Moderate	–	4	2	5	
Severe	–	–	6	3	

[a,b,c] Values in a row with no common superscript letter are significantly different. Values with different letters (a, b and c) in same row are significantly different. P<0.05. *; P<0.01.**

Table 2. MPO Immunoreactivity scores in liver tissue (affected rats/total number of rats)

MPO Immunoreactivity for livers	Control	Sepsis	T0-SD	T5-SD	P values
	-/8[b]	8/8[a]	8/8[c]	8/8[c]	
Slight	–	1	–	–	*
Moderate	–	7	2	4	
Severe	–	–	6	4	

[a,b,c] Values in a row with no common superscript letter are significantly different. Values with different letters (a, b and c) in same row are significantly different. P<0.05. *; P<0.01.**

DISCUSSION

In this study, the most remarkable morphological changes observed in the liver tissues of rats in the experimentally induced sepsis group were the infiltration of neutrophil leukocytes in and around the blood vessels. In the liver tissues of rats in the Dex-treated groups, neutrophil leukocyte infiltration was more prominent, and vasodilation was detected.

The effects of Dex in sepsis rats have been investigated by many researchers.[10-12] The number of studies in which histopathological findings are assessed by pathologists is believed to be limited, and their conclusions are often inadequately supported by illustrative evidence. In the present study, the effects of Dex on liver tissue in a rat model of experimentally induced sepsis were comprehensively evaluated by veterinary pathologists. Detailed histopathological findings are presented and supported with numerous demonstrative figures.[10-14] In this study, the effects of Dex on the morphological changes caused by sepsis in the liver were evaluated histopathologically and immunohistochemically by MPO activity.

Recent studies have shown that liver dysfunction occurs in the early stages of sepsis. It has been suggested that this impairment is caused by systemic or microcirculatory disturbances, bacterial and endotoxin (lipopolysaccharide, LPS) dissemination, and the subsequent activation of inflammatory cytokines. Neutrophil infiltration is one of the earliest phenomena to develop in the liver during the progression of sepsis. Neutrophils infiltrating the liver produce potentially destructive enzymes and free oxygen radicals, which may further exacerbate acute liver injury.[3]

It has been reported that the effects of Dex on peripheral vasculature are dose-dependent, causing vasodilation at low doses and vasoconstriction at high doses.[15] Postsynaptic α2-ARs are widely present in the smooth muscle of vessels. In experimental animal studies, Dex has been reported to produce both vasodilation and vasoconstriction in cerebral arteries and venules. It has been stated that these different

effects of Dex may be related to the models used, the animal species involved, and the doses administered. It was also stated that the cerebral vasoconstriction effect of Dex is not directly related to the vascular endothelium, whereas the vasodilation effect may be endothelium-dependent and related to nitric oxide, though the exact mechanisms have not yet been fully elucidated.[16] Dex has been reported to cause hypotension and bradycardia in patients by inhibiting the release of norepinephrine in the central nervous system and causing vasodilation in peripheral vessels.[17]

In a study investigating the protective effects of Dex pretreatment against lipopolysaccharide (LPS)-induced acute liver injury in rats, different doses of Dex (3, 10, and 30 μg/kg) were administered intraperitoneally to determine the optimal dose.[18] These researchers used the highest dose of 30 μg/kg Dex in their study, as they found that Dex pretreatment provided significant dose-dependent protection against LPS-induced mortality and liver damage. Additionally, in other studies, Dex has been used intraperitoneally at doses ranging from 25 μg/kg to 100 μg/kg.[19-21]

In the study presented here, sepsis was induced in rats by administering 10 ml/kg E. coli, and 100 μg/kg Dex was administered intraperitoneally at the same time to investigate the protective activity of Dex against liver damage. In our study, the most striking and fundamental morphological change in the liver tissues of all groups (sepsis, T0-SD, T5-SD), except the control group, was neutrophil leukocyte infiltration in capillaries and venules. The observation of marked neutrophil leukocyte infiltration in the liver indicates that sepsis was experimentally induced in the study groups. However, neutrophilic infiltrations, vascular dilatation, and vasculitis were more prominent in the Dex-treated groups (T0-SD and T5-SD). In addition, while no dilatation of sinusoidal capillaries was observed in the sepsis group, significant sinusoidal dilatation occurred in the Dex-treated groups. These findings show that Dex has a dilatation effect, as recorded by Rozet.[15,16]

However, in experimental studies in which sepsis was induced and different doses of Dex (5 μg/kg IV,[13] 10 μg/kg IV,[22] 30 μg/kg IP,[23] 50 μg/kg IP,[14] and 100 μg/kg IP[20]) were administered, as far as we were able to examine, there was no information indicating that Dex caused dilatation in the vessels. In our study, significant dilatation of capillaries and venules was observed in the Dex-treated groups (T0-SD, T5-SD), whereas no dilatation was observed in the sepsis group. The fact that neutrophil leukocyte infiltration was more prominent alongside capillary and venule dilatation in the Dex-treated groups suggests that the dilatation caused by the effect of Dex increases the permeability of the vessels and facilitates the invasion of bacteria into the parenchyma, resulting in more prominent neutrophil leukocyte infiltration in Dex groups. Furthermore, neutrophil leukocyte infiltrations in the sepsis group were observed to be milder than in both the T0-SD and T5-SD groups. Neutrophil leukocyte infiltration was more prominent in the T0-SD group than in the T5-SD group, indicating that T0-SD group rats were more exposed to the dilatation effect of Dex. In our study, the dilatations observed in the liver tissue vessels of the Dex groups (T0-SD, T5-SD) are thought to be related to the administered dose (100 μg/kg, IP)

In rat models of sepsis, studies have reported that Dex has anti-inflammatory capacity. It has been suggested that Dex administration may inhibit inflammatory responses. Circulating endotoxins have been reported to induce complement activation and the release of cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-6, which may cause leukocytic infiltration in the lungs. Inflammatory mediators from leukocytes can produce hypotension, metabolic acidosis, and tissue damage, eventually leading to organ dysfunction.[24,25] It has been reported that it is still unclear whether the severity of sepsis-induced hepatic injury is modulated by Dex administration.[26] In their study, these investigators suggested that Dex attenuated the harmful effects of LPS-induced liver injury and decreased proinflammatory cytokines (IL-6 and TNF-α). However, when the TNF-α and IL-6 values, which are among the biochemical results of the study presented here, were analyzed, the values of the DST-0 and DST-5 groups were not lower; on the contrary, they were higher, although not significantly, when compared with the sepsis group. These results support our histopathological findings.

Neutrophils contribute significantly to the development of the organism's cellular defense system.[27] In inflammatory reactions, proinflammatory cytokines secreted by neutrophil leukocytes infiltrating the pulmonary interstitium and alveolar lumen damage capillary endothelial cells.[28] When neutrophil infiltration occurs, large amounts of MPO are expressed by neutrophils. This excreted MPO passes into phagosomes and the extracellular matrix. As a result, the immune activity of MPO may indicate the degree of vascular damage and neutrophil infiltration.[29] MPO activity is a biochemical marker of neutrophil infiltration. Pre-treatment with Dex resulted in a significant reduction in lung MPO activity in the Dex groups compared with that of the ischemia-reperfusion injury group.[12] In the present study, when MPO activity in liver tissue was analyzed, it was observed that MPO activity in the sepsis group was milder than in the Dex+sepsis groups (T0-SD and T5-SD). This result showed that Dex did not reduce inflammatory reactions in the liver. It was noted that these immunohistochemical findings were consistent with histopathological findings.

In conclusion, according to the histopathological and immunohistochemical findings obtained in the present study, we conclude that sepsis-induced inflammatory reactions were induced in liver tissue, but Dex did not attenuate sepsis-induced liver inflammation in the rat sepsis model. In addition, based on the literature whose histopathological findings are evaluated below, we believe that the protective efficacy of Dex cannot be demonstrated with illustrative pictures.

Sezer et al.[11] reported that severe sinusoidal and venous congestion occurred in the sepsis group. These changes were milder in the sepsis/Dex (5 µg/kg IV) group. Marked mononuclear cell infiltration was observed in the portal areas of the sepsis group, but these cellular infiltrations were less in the Dex/sepsis group. Contrary to these investigators, neutrophil leukocyte infiltrations, which are prominent in acute bacterial infections, were observed in our study. Indeed, Wang et al.[3] reported that the inflammatory cell infiltration observed in the liver in the early stages of sepsis was composed of neutrophil leukocytes.

In a study investigating the protective efficacy of Dex (30 µg/kg IP) pre-treatment against lipopolysaccharide (LPS)-induced acute liver injury in rats, it was noted that Dex reduced morphological changes and inflammatory cytokine expression.[18] These investigators noted that significant liver tissue damage characterized by inflammatory cell infiltration and acidophilic degenerative-necrotic changes was observed in sham+LPS group rats after LPS injection, and these changes were significantly improved in the sham+LPS+Dex group. However, when the related figures in the article by these researchers are analyzed, the findings are not compatible with our figures.

In a study investigating the effects of Dex (30 µg/kg IP) on LPS-induced liver injury, it was reported that histopathological changes such as "hepatocyte necrosis, vacuolar degeneration, inflammatory cell infiltration into the hepatic sinus, and hepatocyte congestion" were observed in liver tissue.[23] It was stated that Dex attenuated these morphological changes in a dose-related manner. While "inflammatory cell infiltration," one of the histopathologic findings described in that study, was compatible with our study, other findings were not.

Zang et al.,[13] in a study investigating the protective efficacy of Dex (2.5–5 µg/kg IV) against multiple organ damage induced by experimental hemorrhage/resuscitation and endotoxemia (lipopolysaccharide) in rats, observed significant damage in the lungs, liver, and kidneys in the endotoxemic group rats. However, it was suggested that these damages were alleviated by Dex application.[13] In that article, the histopathological findings of the groups were only statistically evaluated. No textual explanation was provided, the signs used in the figures were not indicated, and the histopathological findings were not discussed. In short, the histopathological findings were not descriptive and, therefore, a comparison with our findings could not be made.

In a study investigating the effects of Dex on Gram-positive and Gram-negative bacteria (E. coli) and the effector functions of human monocyte THP-1 cells against them, it was revealed that Dex improved Gram-positive bacterial phagocytosis and killing but reduced Gram-negative bacterial phagocytosis and killing in THP-1 cells.[30] These findings support our findings related to E. coli, a Gram-negative bacterium, in our study.

CONCLUSION

In this study, it was clearly demonstrated for the first time that Dex (100 µg/kg IP) caused vasodilation in liver tissue vessels in sepsis rats. According to the results of our study and the literature we were able to review, we believe that detailed comparative studies at different doses and durations are still needed in order to use Dex more safely in patients with sepsis and to reveal the effects of Dex more clearly in the rat sepsis model.

Ethics Committee Approval: This study was approved by the Van Yuzuncu Yil University Animal Experiments Local Ethics Committee (Date: 25.08.2024, Decision No: 2024/08-08).

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Authorship Contributions: Concept: Ö.F.K., H.S.K., H.A.Ç., Z.Y., O.P.; Design: Ö.F.K., H.S.K., H.A.Ç., Z.Y.; Supervision: Ö.F.K., H.S.K., H.A.Ç., Z.Y., O.P.; Resource: Ö.F.K., H.S.K., H.A.Ç., Z.Y.; Materials: Ö.F.K., H.S.K., H.A.Ç., Z.Y.; Data collection and/or processing: Ö.F.K., H.S.K., H.A.Ç., Z.Y, O.P.; Analysis and/ or interpretation: Ö.F.K., H.S.K., H.A.Ç., Z.Y., O.P.; Literature search: Ö.F.K., H.S.K., H.A.Ç., Z.Y.,O.P.; Writing: Ö.F.K., H.S.K., H.A.Ç., Z.Y.; Critical review: Ö.F.K., H.S.K., H.A.Ç., Z.Y., O.P.

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DENEYSEL ÇALIŞMA - ÖZ

Deneysel sepsis oluşturulan sıçanlarda deksmedetomidinin karaciğer hasarı üzerine etkileri: Histopatolojik ve immünohistokimyasal bir çalışma

AMAÇ: Sıçan sepsis modelinde, deksmedetomidinin (Dex) inflamasyonu azaltarak sepsise bağlı doku hasarları üzerindeki koruyucu etkisi halen belirsizdir ve Dex'in sepsis kaynaklı doku hasarını modüle edip etmediğini belirlemek için araştırmalar devam etmektedir. Bu çalışmada, sepsisli sıçanlarda Dex'in karaciğer hasarına histopatolojik ve immünohistokimyasal olarak etkisini araştırmak amaçlanmıştır.
GEREÇ VE YÖNTEM: Bu çalışmada, sıçanlarda 10 ml/kg *E. coli* enjeksiyonu ile sepsis indüklendi ve 100 µg/kg Dex'in intraperitoneal uygulanmasıyla Dex'in karaciğer hasarına karşı koruyucu etkinliği histopatolojik ve immünohistokimyasal bulgularla araştırıldı.
BULGULAR: Bulgularımıza göre, sepsis grubundaki sıçanların karaciğer dokularında en çarpıcı ve temel morfolojik değişiklikler, damar içi ve çevresindeki nötrofil lökosit infiltrasyonlarıydı. Dex ile tedavi edilen gruplarda, nötrofil lökosit infiltrasyonları daha belirgin olup damarlarda belirgin dilatasyonlar gözlemlendi. Dex ile tedavi edilen gruplarda inflamatuvar reaksiyonların daha belirgin olmasının, Dex'in vazodilatasyon etkisine bağlı olarak vasküler permeabilitedeki artışla ilişkili olduğu düşünülmüştür.
SONUÇ: Bu çalışmadan elde edilen histopatolojik ve immünohistokimyasal bulgulara göre, Dex'in sıçan sepsis modelinde sepsise bağlı karaciğer inflamasyonunu hafifletmediği sonucuna varılmıştır.

Anahtar sözcükler: Deksmedetomidin; E. coli; histopatoloji; karaciğer; rat; sepsis.

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