EXPERIMENTAL STUDY

Effect of L-carnitine on regeneration in experimental partial hepatectomy model in rats

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ABSTRACT

BACKGROUND: In cases of major liver resections or ischemic damage made by the pringle maneuver, agents that increase regeneration or manage ischemic reperfusion injury have become a fascinating topic for researchers. The aim of this study is to see how systemic L-carnitine, an antioxidant with thorough research behind it, affects liver regeneration after major hepatectomy in a rat experimental hepatectomy (two-thirds liver resection) model.

METHODS: The liver regeneration was evaluated in this study using a rat hepatectomy model developed in the General Surgery Clinic of Health Sciences University, Umraniye Education and Research Hospital's Laboratory. In the experiment, 15 male and 15 female Wistar Albino rats weighing between 250 and 300 g were used in a way that the genders were mixed. In each group, three groups were formed, including male and female rats randomly selected and ten rats. Gcontrol: 70% hepatic resection + intraperitoneal 0.9% saline, GSham: After laparotomy, the abdomen was closed again without any procedure, Gcarnitine: 70% hepatic resection + intraperitoneal 100 mg/kg L Carnitine was applied. It was applied systemically to GSham and Gcarnitine groups and the same procedure was applied to rats for 4 days at the same time without any restrictions. On the 5th day, the abdomen was entered with relaparotomy after sacrification and liver regeneration was evaluated macroscopically and recorded in the forms developed for each subject. Later, liver tissue was resected and microscopically recorded by measuring mitotic index, binuclear hepatocyte, gall duct proliferation, dilation in central veins, and cell proliferation in the parenchyma. The results obtained were evaluated statistically.

RESULTS: According to the results, the L-carnitine group had a statistically significant increase in overall regeneration scoring after hepatectomy in the histopathological assessment as compared to the control group.

CONCLUSION: It is thought that L-carnitine, whose many positive effects have been shown experimentally and clinically, has a positive effect on liver regeneration and immunohistochemical researches is required to elucidate this pathway.

Keywords: Hepatectomy; L-carnitine; liver; regeneration.

INTRODUCTION

The liver is the largest solid organ in the human body and it is located in the upper right quadrant of the abdomen, where it performs a variety of metabolic functions. An adult's average weight is around 1.5 kg.[1] The liver's vital role in metabolism can often result in cell damage, which is compensated for by cell regeneration. The liver lobule, which is located around the central vein and has a millimeter structure, can reach up to 2 mm in length, and has a number of 50,000–100,000 in healthy adults, is the basic unit in this function. During the metabolic function of the liver, the central veins provide the passage of metabolized products to the hepatic veins and then to the systemic circulation through the vena cava. There are small gall ducts between neighboring cells, these ducts are poured into the gall ducts and provide the gall circulation.[2–5]

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Despite its critical role in metabolism, the liver's cell proliferation and/or regeneration is extremely slow, with a mitosis rate in hepatocytes of <0.01% in normal cell proliferation.[6] When the liver mass reaches a certain percentage of the total body mass, depending on the species and age, cell proliferation ends.[7] This rate, on the other hand, is much faster in toxicity caused by viruses or chemical agents that infect the liver, or in toxicity caused by major liver resections. At this point, the two-stage liver resection, namely, the ALLPS procedure (Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy), which will be discussed in more detail below, is one of the best examples to be given in this respect.[8] The liver regenerates to larger sizes in about a week after surgical ligation of the portal vein and subsequent liver division in this method. Another non-surgical condition is non-alcoholic fatty liver disease (NAFLD) and cirrhosis, which decreases the functional capacity of the liver. In terms of NAFLD, rates of up to 25% have been reported in society, and the same rate can be given higher for cirrhosis and other viral hepatitis. While major liver resection is tolerated in healthy individuals, it is vital to compensate for the resection to be performed especially in individuals with chronic liver disease. Resections to be made at this point are more limited and hepatic regeneration is more important since liver failure that may develop at this point can result in serious morbidity and high mortality.[9–11]

Regeneration in patients with functional or surgical liver diseases, especially after major liver resections and living donor liver transplantation, is critical and remains an unsolved issue.[12] Since liver failure after such resections can result in severe morbidity and even mortality. Only by can the liver's regeneration capacity can this condition be managed. Many agents are still being studied in terms of liver regeneration effect from this perspective.

Partial hepatectomy specimens are generally preferred to show regeneration. Mice and rats are the most commonly used experimental animals as experimental models in studies. The reason for this is that they are more suitable for operation, their cost and maintenance are easier, and they can be produced under suitable conditions.[13–16] Experimental liver resection models are a good method to investigate these agents, and positive results are reported with different agents in the literature.[17–19]

L-carnitine is a 3-methyl amino acid that has a structure that is very similar to that of choline. It is a small and water-soluble vitamin-like substance that stands for hydroxy-trimethylammonium butyric acid. The key role of the L-carnitine molecule in metabolism is to prevent ROM formation, free radical detoxification, and, most significantly, oxidative stress protection.[20] L-carnitine performs this complex role by transforming long-chain fatty acids to acylcarnitine during the transition to the mitochondrial matrix. Another important function is the role that it plays in ketone metabolism, which is crucial for metabolism's energy production. This task is basically the conversion of branched-chain amino acids (leucine, isoleucine, and valine) into energy.[21]

In the literature review, there was no study on the effect of L-carnitine (3-hydroxy-4-N-trimethyl ammonio butanoate), which is physiologically synthesized in tissues, whose positive effects have been presented experimentally in different studies after flap surgery and whose effect has been proved in clinical use, on liver regeneration.[22] Based on this context, the objective of the study is to examine the effect of systemic L-carnitine, which has a wide place in the literature as an antioxidant, on liver regeneration after major hepatectomy in experimental hepatectomy (two-thirds liver resection) model developed in rats.

MATERIALS AND METHODS

The Work Plan

In this study, liver regeneration was evaluated in the hepatectomy model developed in rats obtained from the laboratory of the General Surgery Clinic of the University, with the permission obtained from Health Sciences University Animal Experiments Ethics Committee (SBÜ-HADYEK), dated July 2, 2018 and numbered 46418926–774.99. The Council of Europe's prescribed guidelines was followed when preparing experimental animals.

Experimental Animal Material

In the research, 15 male and 15 female 30 Wistar Albino rats weighing between 250 and 300 grams were used in a way that the groups were mixed in terms of gender. The rats were kept in cages of three rats per cage until the experiment was completed. The rats were kept in 12-h light-dark cycles at a constant temperature and humidity of 24±2°C room temperature. All of the subjects were fed standard laboratory feed and drinking city water. Six-h fasting was provided before the surgery.

Determining the sample size in the study, by alpha 0.05 and beta 80%, based on similar experiments in the literature, the minimum number of animals was composed by calculating with the power calculator. Accordingly, three groups were formed, each group consisting of ten rats selected randomly, male and female rats:

Group I (Sham Group)

The abdomens of the rats in the sham group were closed without any treatment after laparotomy.

Group II (Control Group)

Animals underwent 70% hepatic resection and were given intraperitoneal 0.9% saline.

Group III (Carnitine Group)

About 70% hepatic resection and intraperitoneal application of 100 mg/kg L-carnitine was performed.

The experiment was conducted at X University's Experimental Animal Laboratory. T.C. performed biochemical analyses at X University X Training and Research Hospital, and histopathological and morphological examinations at X University X Training and Research Hospital. It was planned to be installed in the Pathology Laboratory of the Ministry of Health's Sancaktepe Training and Research Hospital.

Anesthesia Type

The subjects were fasted the night before surgery, and the operations were done in the first half of the day. The surgeries were carried out under general anesthesia. Doses of the anesthetics used were administered at a dose of 0.25 ml/100 mg body weight, at a concentration of 50 mg/ml Ketamine HCL and Xylazine HCL at a concentration of 20 mg/ml. Within the scope of preparing anesthetic agents and appropriate laboratory measures, general anesthesia was administered intraperitoneally from the right lower quadrant of each subject's abdomen and left to spontaneous breathing.

After the anesthesia procedure, the subjects were weighed with a laboratory-sensitive scale and recorded in grams. After the abdominal area to be incised was shaved with a shaver, it was wiped with 10% povidone-iodine (Batticon 10% solution, Adeka İlaç Sanayi ve Ticaret A.Ş.) and covered in a sterile manner.

Establishing Experimental Hepatectomy Model in Experimental Animals

The skin, linea alba, and peritoneum were passed through the upper and sub-umbilical vertical incisions of 4 cm in the abdomen under general anesthesia and sterile conditions, and the laparotomy was completed. An additional pathology was explored in the abdomen. In a file generated for each subject, additional pathologies were documented. The liver was then mobilized after the falciform ligament was cut in the midline. According to Uzun et al.,[23] the pedicles of the liver were tied with 3/0 silk in previous studies in the literature. The median and left anterior lobes were later removed, and a two-thirds (70%) hepatectomy was performed.

Rats in Group I (Sham Group) underwent only intraperitoneal laparotomy.

Intraperitoneal SF at a dose of 1 ml/kg for rats in Group II (Control Group).

Group III (Carnitine Group) was administered 100 mg/kg L-carnitine at the same time for 4 days.

Rats were sacrificed on the 5th day using a high dose of ether anesthesia. Relaparotomy was performed on the subjects, and the entire abdomen was explored. The whole liver was removed and weighed. For pathological examinations, the residual tissue was preserved in 10% formol. The liver tissue found in formol was washed with tap water, passed through an alcohol series, dehydrated, and embedded in paraffin blocks for histopathological analysis (Fig. 1, 2).

Experiment Parameters

Morphological Parameters

As a morphological parameter, relative liver weight was measured. The ratio of this value to the whole liver weight was calculated by subtracting the remaining liver weight after partial hepatectomy from the liver weight obtained at relaparotomy. Multiplying the obtained value by 100 yielded the liver regeneration rate. The whole liver weight was accepted as 3% of the rat weight. Results are expressed as %. Relative liver weight was calculated as = [Total liver weight at relaparotomy – (whole liver weight-resected liver weight)/whole liver weight]×100. After this procedure, histopathological and immunohistochemical research was performed on the liver tissue (Fig. 3).

Histopathological Evaluation

The pathologist who evaluated the preparations in the Training and Research Hospital Pathology Laboratory was the same pathologist who evaluated the preparations in the Training and Research Hospital Pathology Laboratory. Two-

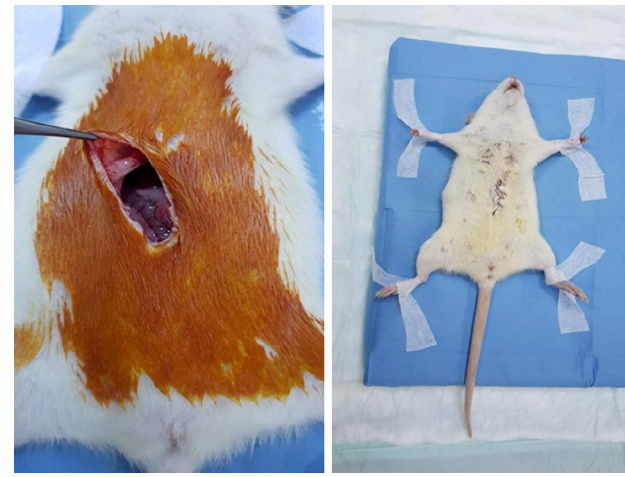


Figure 1. Anesthesia and start of the operation.

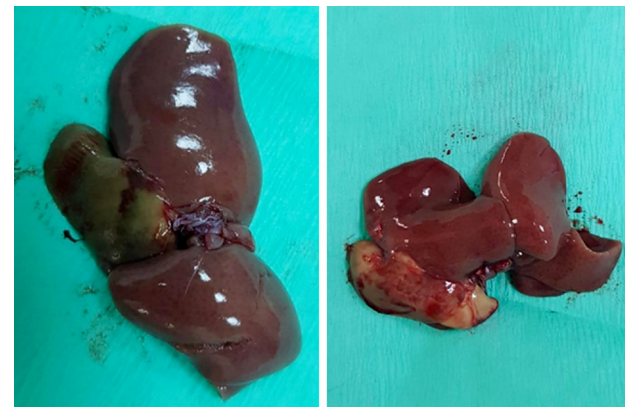
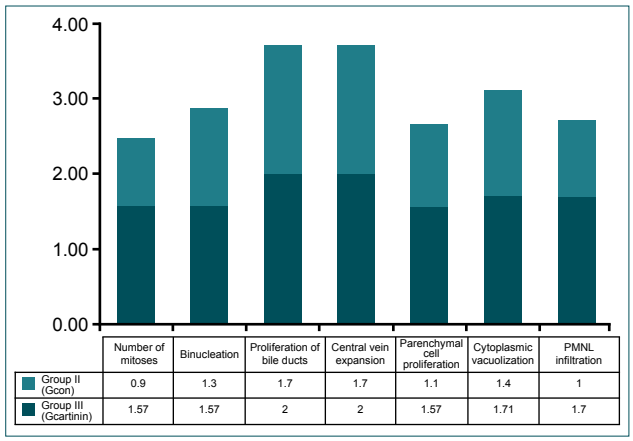


Figure 2. The piece of liver that is totally removed after sacrification.



	Number of mitoses	Binucleation	Proliferation of bile ducts	Central vein expansion	Parenchymal cell proliferation	Cytoplasmic vacuolization	PMNL infiltration
Group II (Gcon)	0.9	1.3	1.7	1.7	1.1	1.4	1
Group III (Gcartinin)	1.57	1.57	2	2	1.57	1.71	1.7

Figure 3. Macroscopic regeneration and histopathological data of carnitine and control group.

third the liver tissues were fixed with 10% formaldehyde after hepatectomy and sacrification. Two samples, approximately 1×1 cm in size, were taken from each tissue and included in routine tissue follow-up. The paraffin-embedded blocks were cut into 4–5 micron thick sections after tissue follow-up. Hematoxylin and eosin (H&E) were used to stain the sections, which were then examined under a light microscope (Nikon Eclipse Ni-U microscope).

The parameters used as indicators of regeneration in liver tissue were determined as mitosis number, presence of binuclear hepatocytes, bile ductus proliferation, dilation in central veins, irregular distribution of cell proliferation in the liver parenchyma, cytoplasmic vacuolization/hydropic degeneration in hepatocytes, and leukocyte infiltration surrounding hepatectomy.

Each sample in the preparations had its mitosis counted per 100 hepatocytes in ×40 high power fields (BBA). A total of 1000 hepatocytes (at 40 magnification in 10 BBAs) were examined for each sample, and mitosis was counted. A triple score system was used for all parameters except mitosis. If there was no parameter, it was scored as "score 0," if it was mild, it was scored as "score 1," and if it was intense, "score 2." For each subject, the total score was calculated by adding the data obtained from the subjects (Fig 4a-f).

Statistical Analysis

For statistical evaluations, the Statistical Package for the Social Sciences for Windows (22.0 version) software was used. After analyzing the distribution, the Shapiro–Wilk result was used as the basis for numerical data analysis. P<0.05, non-parametric tests, was used, and parametric tests were used when p-value was larger. The Kruskal–Wallis test was used to compare the relative liver weights obtained in the sham, control, and treatment groups. P<0.05 values were considered significant. The groups were compared one to one using Mann–Whitney U and analysis of variance Tukey tests after Bonferroni adjustment to see which groups had significance in significant parameters. P<0.05 was considered statistically significant.

The biochemical parameters specified in the ethics committee in the study could not be analyzed due to technical reasons and the inability to obtain the kits, and histopathological evaluation was made with the analysis in the control and Carnitine group. In comparison of histopathological evaluations, Mann–Whitney U, one of the non-parametric tests, and the t-test for groups independent of parametric tests were applied. It was considered statistically significant because p≤0.005.

RESULTS

After the experimental procedure, there was no mortality in the sham and control groups, but mortality developed in one rat in the carnitine group on the 1st post-operative day. A new rat was added to the group in place of this one, and the study was completed with 30 rats as expected. The study excluded the sham group, which did not receive any treatment for histopathological parameters, and compared the carnitine and control groups.

The macroscopic regeneration and histopathological data of carnitine and control group mean±standard deviation values and statistical analysis are summarized in Figure 3.

Evaluation of the Relative Liver Weight of the Groups

The relative liver weights were calculated by weighing the liver tissues after the rats were sacrificed. The relative liver weight in the control group (saline applied group) was determined as 29.26 12.61 in Group III (Gcarnitine) in the Carnitine group, as 32.43 24.22. The Mann–Whitney U-test was used to evaluate the data since it did not show a normal distribution. Between the two groups, there was a statistically significant difference (p=0.04).

Histopathological Evaluation

The pathology laboratory at the Health Sciences University Animal Experiments Laboratory prepared liver tissue after sacrification and evaluated it immunohistochemically. When the mitosis number, pmnl infiltration, and total score of Group II (Gcontrol) and Group III (Gcartinin) were compared histopathologically, there was a statistically significant difference between the groups. Table 1 summarizes all of the results.

DISCUSSION

In cases of significant liver resections or ischemic damage caused by the Pringle maneuver, agents that increase regeneration or decrease ischemic reperfusion injury have become a fascinating topic for researchers. By developing an experimental hepatectomy model that decreases lipid-energy metabolism and free oxygen radicals, has an important con-

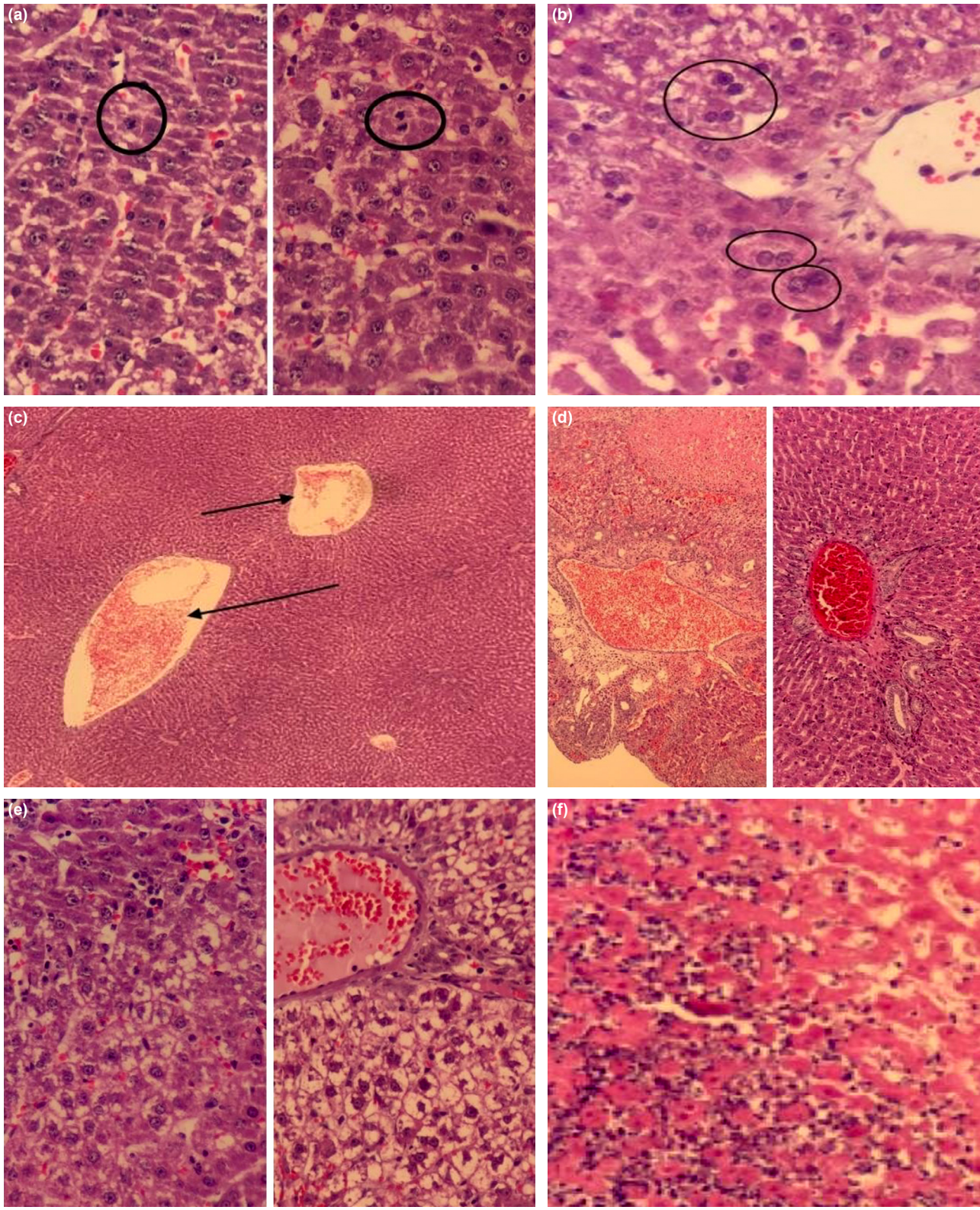


Figure 4. (a) Mitotic figures in hepatectomy surrounding areas (H&E × 400), **(b)** binuclear hepatocytes around hepatectomy surrounding areas (H&E × 400), **(c)** intensive bile ductus proliferation areas around hepatectomy areas (H&E × 100), **(d)** enlargement of central veins in areas around hepatectomy (H&E × 40), **(e)** cytoplasmic vacuolization and hydropic degeneration of hepatocytes in areas around hepatectomy (H&E × 400), and **(f)** leukocyte infiltration with dense polymorph core around hepatectomy (H&E × 200).

tribution to wound healing and is actively used in the clinic, it is investigated that the impact of L-carnitine on regeneration after major liver resection in terms of macroscopic and histopathological parameters. In the literature review con-

Table 1. Histopathological evaluation of Group II (Gcontrol) and Group III (Gcartinin)

	Grup II (Gcontrol)	Grup III (Gcartinin)	p-value
Number of mitoses	0.9±0.31	1.57±0.78	0.026
Binucleation	1.3±0.48	1.57±0.53	0.278
Proliferation of bile ducts	1.7±0.48	2	0.121
Central vein expansion	1.7±0.48	2	0.121
Parenchymal cell proliferation	1.1±0.56	1.57±0.53	0.103
Cytoplasmic vacuolization	1.4±0.51	1.7±0.48	0.215
PMNL infiltration	1.00±0.66	1.71±0.48	0.032
Total score	9.1±2.42	12.14±1.46	0.007

ducted on this subject (PubMed, Cochrane, and EBSCO), it has not been found any study about the effect of systemic application of L-carnitine on liver regeneration, whose many positive effects have been experimentally shown today.

In human metabolism, the liver is an organ that is vital for its functions. The liver, which has many functions such as carbohydrate, lipid and protein metabolism, bile production and secretion, drug metabolism and detoxification and storage, plays a key role especially in the immune system, body energy metabolism and excretion of bilirubin. Failure of the liver may develop in pathological conditions such as infectious (bacterial-viral), immunological, cirrhosis, or cancer, and although this situation can be compensated, patients may sometimes encounter the picture of liver failure. Apart from this, a picture of failure may develop in resections made to the liver for benign or malignant reasons. In the past century, the ability to control liver failure has attracted a lot of attention of researchers and has enabled the regeneration mechanism of the liver to be discussed in detail, and finally, detailed information has been obtained in the pathophysiology of regeneration today.[24]

A thorough understanding of this pathway has aided in the development of liver surgery today. Living donor liver transplants have become increasingly common in many centers in the past two decades, especially after major liver resections. The failure of the residual liver after resections or the regeneration of liver tissue to become fully functional has become one of the key concerns of researchers, and agents that speed up the regeneration process have received a lot of attention in the literature.

While regeneration in tissues such as bone marrow and skin with rapid regeneration is provided by stem cells and progenitors, this situation is different for the liver. Liver regeneration is provided by the interaction of the extracellular matrix and growth factor on a cellular basis. Again, regeneration in the liver starts with different cytokines and growth factors in undamaged normal cells secondary to resection. Many agents to accelerate this process have been experimentally studied in the literature and some examples are ACE inhibitors, different antibiotics, ursodeoxycholic acid, lovastatin, Ca channel blockers, and prostaglandins. Apart from these agents, molecules such as cytokines, growth factors, cytokine blockers, and lipopolysaccharide binders have also been researched.[25]

Liver functions, especially biochemical markers containing liver enzymes, and tests that indirectly include serum albumin, globulin, and coagulation factors come to the fore in studies evaluating liver regeneration. One of the liver function tests, serum transaminase level, has high sensitivity and specificity for identifying cell damage in the liver parenchyma. Transaminase elevation can be found in all cases where hepatocyte damage is still present as the etiological cause of the injury. In human metabolism, these enzymes are produced in tissues other than the liver, such as the pancreas, heart myocardium, and muscle. It has a low specificity for the liver in this regard. One of the liver's most essential functions is to synthesize coagulation factors, and hepatocytes produce fibrinogen, an important molecule in the final stage of coagulation. Albumin and globulin can only be synthesized in the liver. Albumin is a source of endogenous amino acids that are involved in the delivery of many molecules that are vital to human metabolism in the target tissue and the maintenance of the serum osmotic gradient. The half-life of albumin is 3 weeks, making the serum albumin level significant in the evaluation of long-term liver damage and failure that can develop. Apart from this, another marker that is used and shows that liver damage is now serious, is the prothrombin time and indirectly indicates the level of coagulation factors.[26] Our study of biochemical markers taken from each subject studied and planned, but all over the world and Turkey under the influence of COVID-19 pandemics in the process has not worked due to the problems related to mass.

Our studies looked at regeneration from a morphological and histopathological perspective. As the effective liver weight is decreased by partial hepatectomy, parenchymal and non-parenchymal cells in the residual liver tissue are enlarged morphologically. DNA replication starts in parenchymal cells and then spreads to non-parenchymal cells at this stage.[27] Within days after hepatectomy, the liver weight reaches the

optimum level for body size thanks to this mechanism. Hua-Zhong et al.[28] investigated the relationship between bile secretion and liver regeneration following partial hepatectomy in this regard. In this study, the macroscopic regeneration rate was expressed in proportion to the remaining weight after hepatectomy. In this study, the regeneration rate was found by proportioning to the total liver weight before hepatectomy and a statistically significant increase was found.[28]

L-carnitine is a water-soluble compound that facilitates the conversion of free long-chain fatty acids to acylcarnitine, as well as acting as a cofactor in the transport of long-chain fatty acids to the mitochondrial matrix, where they will be beta-oxidized for cell energy production. L-carnitine and its esters have been shown in numerous studies to have an antioxidative and free radical effect, preventing the occurrence of reactive oxygen radicals, and protecting cells from oxidative stress.[28] In the literature, positive results have been recorded in the use of systemic or local carnitine administration, in maintaining the vitality of the dorsal skin flap performed after a burn, in improving renal functions after ischemia/reperfusion injury, and in the management of doxorubicin-induced cardiomyopathy, especially in chemotherapeutic toxicity.[29] The pharmacokinetic and pharmacodynamic efficiency of 100 mg/kg/day systemic (intraperitoneal) L-carnitine was determined at the highest level in our research, and histopathologically positive results were obtained on regeneration. It is thought that this effect is due to Carnitine's reversal of fatty acids peroxided by free oxygen radicals that emerge after hepatectomy, inhibit NOS and xanthine oxidase activity, and provide cell membrane stabilization. Furthermore, it preserves cells from damage and prevents mitochondrial damage with membrane stabilization against free radicals. Thus, they increase energy production and reduce the passage of free radicals.[30,31] All these pharmacological positive effects also claim that carnitine creates a metabolically better environment for liver regeneration.

Conclusion

As a result, liver resection is preferred more frequently nowadays and multi-step procedures are applied. After anatomical or non-anatomical resection, each step has its own mortality and morbidity. Therefore, liver regeneration is of particular significance. In our research, it is determined that carnitine application after major liver resection might have positive effects on regeneration histopathologically.

L-carnitine is used in different fields due to its antioxidant, anti-inflammatory, and energy metabolism regulatory effects, according to experimental and clinical research, and this study found beneficial effects on liver regeneration. However, more research is required before L-carnitine is used in clinical practice.

Ethics Committee Approval: This study was approved by the University of Health Sciences Animal Experiment Ethics Committee (Date: 28.03.2018, Decision No: 2018-02/07).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: A.T., Ö.F.Ö.; Design: A.T., A.Y., Ö.F.Ö.; Supervision: Ö.F.Ö.; Fundings: A.T.; Materials: A.T., Ö.F.Ö.; Data: A.T.; Analysis: A.T.; Literature search: A.T.; Writing: A.T.; Critical revision: A.T., A.Y., Ö.F.Ö.

Conflict of Interest: None declared.

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DENEYSEL ÇALIŞMA - *ÖZ*

Sıçanlarda deneysel parsiyel hepatektomi modelinde L-karnitinin rejenerasyona etkisi

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AMAÇ: Majör karaciğer rezeksiyonları veya pringle manevrası ile yapılan iskemik hasar durumlarında, rejenerasyonu artıran veya iskemik reperfüzyon hasarını yöneten ajanlar, araştırmacılar için büyüleyici bir konu haline gelmiştir. Bu çalışmanın amacı, arkasında kapsamlı araştırmalar bulunan bir antioksidan olan sistemik L-karnitinin, sıçanlarda deneysel hepatektomi (üçte iki karaciğer rezeksiyonu) modelinde majör hepatektomi sonrası karaciğer rejenerasyonunun nasıl etkilediğini görmektir.

GEREÇ VE YÖNTEM: Bu çalışmada, Sağlık Bilimleri Üniversitesi Genel Cerrahi Kliniği, Hamidiye Eğitim ve Araştırma Hastanesi Laboratuvarı'nda geliştirilen sıçanlarda hepatektomi modeli kullanılarak karaciğer rejenerasyonu değerlendirildi. Deneyde ağırlıkları 250 ile 300 gram arasında değişen 15 erkek ve 15 dişi Wistar Albino cinsi sıçanlar cinsiyetleri karıştırılacak şekilde kullanıldı. Her grupta rastgele seçilen erkek ve dişi sıçanlar ve her biri 10 sıçandan oluşmak üzere üç grup oluşturuldu. G Kontrol: %70 hepatik rezeksiyon + intraperitoneal %0.9 salin, G Sham: laparotomi sonrası batın herhangi bir işlem yapılmadan tekrar kapatıldı, G Carnitine: %70 hepatik rezeksiyon + intraperitoneal 100 mg/kg L-karnitin uygulandı. G Sham ve G Carnitine gruplarına sistemik olarak uygulandı ve sıçanlara aynı işlem dört gün boyunca aynı anda herhangi bir kısıtlama olmaksızın uygulandı. Beşinci gün sakrifikasyon sonrası relaparotomi ile batına girildi ve karaciğer rejenerasyonu makroskobik olarak değerlendirildi ve her olgu için geliştirilen formlara kaydedildi. Daha sonra karaciğer dokusu rezeke edildi ve mitotik indeks, binükleer hepatosit, safra kanalı proliferasyonu, santral venlerde dilatasyon, parankimde hücre proliferasyonu ölçülerek mikroskobik olarak kaydedildi. Elde edilen sonuçlar istatistiksel olarak değerlendirildi.

BULGULAR: Sonuçlara göre, L-karnitin grubu, kontrol grubuna kıyasla histopatolojik değerlendirmede hepatektomi sonrası genel rejenerasyon skorunda istatistiksel olarak anlamlı bir artışa sahipti.

TARTIŞMA: Birçok olumlu etkisi deneysel ve klinik olarak gösterilen L-karnitin'nin karaciğer rejenerasyonu üzerine olumlu etkisi olduğu düşünülmekte ve bu yolun aydınlatılabilmesi için immünohistokimyasal araştırmalara ihtiyaç duyulmaktadır.

Anahtar sözcükler: Hepatektomi; karaciğer; L-karnitin; rejenerasyon.

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