PORTAL TRİAD OKLÜZYONUNDA İNTESTİNAL İSKEMİ

İNTESTINAL ISCHEMIA IN PORTAL TRIAD OCCLUSION

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Özet

Çalışmadaki amacımız geçici portal triad oklüzyonunda iskemiye bağlı intestinal değişiklikleri ve serum D (-) laktat seviyelerini deneysel olarak araştırmaktır. Tavşanlarda 90 dakika portal triad oklüzyonu (PTO) yapıldı. Arteria mezenterika süperior (AMS) ve vena mezenterika süperior (VMS) kan akımı dopler ultrasound ile ölçüldü. Aynı zamanda D (-) laktat seviyeleri ve histopatolojik inceleme için intestinal doku örnekleri alındı. Portal triad oklüzyonundan sonra ASM ve VSM kan akımları düştü, serum D (-) laktat seviyeleri sürekli arttı. Aynı zamanda portal triad oklüzyona bağlı olarak gelişen mukozal değişiklikleri histopatolojik olarak gözledik. Sham kontrol grubunda anlamlı değişiklikler olmadı. Deneysel çalışmamız geçici portal triad oklüzyonunun intestinal iskemik değişiklikler oluşturduğunu gösterdi. Çalışma, PTO artışının süresi boyunca intestinal iskemik değişikliklerin arttığını gösterdi. Bu yüzden morbidite ve mortaliteyi düşürmek için portal triad oklüzyonundan sonra intestinal fonksiyonlar dikkatli değerlendirilmelidir.

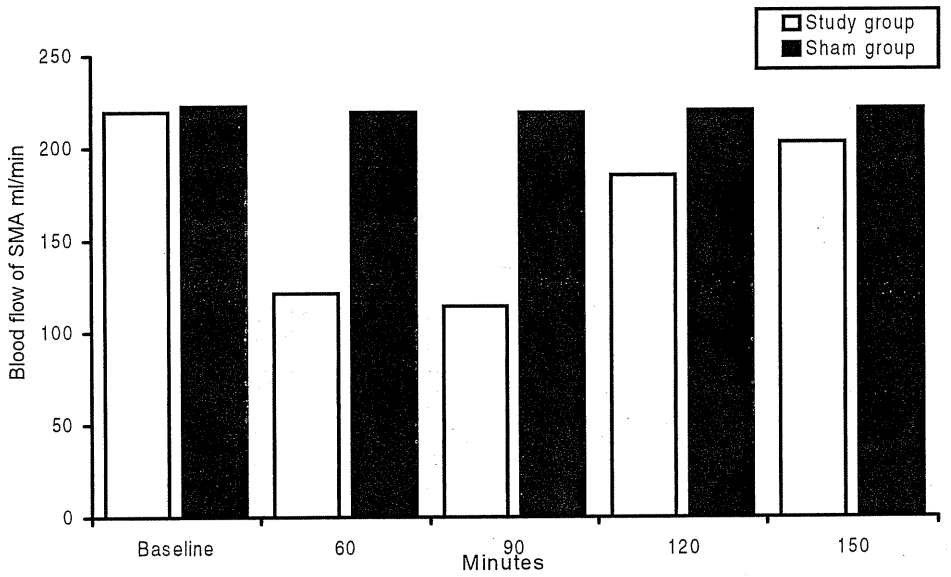
Anahtar kelimeler: *Portal triad oklüzyonu, D (-) laktat*

Summary

To investigate intestinal ischemic alterations and serum D(-) lactate levels due to transient portal triad occlusion (PTO) an experimental study was performed. Rabbits underwent 90 minutes of portal triad occlusion. Superior mesenteric artery and vein blood flows were measured by doppler ultrasound. In addition, histopathological examination was performed. At the same time, blood samples were obtained for determination of D(-) lactate levels and intestinal tissue samples for histopathological examination. After portal triad occlusion, superior mesenteric artery and vein blood flows were decreased and serum D(-) lactate levels were increased progressively. Intestinal mucosa showed ischemic changes after portal triad occlusion. In the sham operated group, there were not any significant changes in serum D(-) lactate levels, intestinal mucosa and blood flow. Our experimental study demonstrated that transient portal triad occlusion produced intestinal ischemic alterations. In the present study, it was shown that intestinal ischemic changes correlated with duration of PTO. Thus intestinal functions must be evaluated carefully after portal triad occlusion to decrease morbidity and mortality.

Key words: *Portal triad occlusion, D(-) lactate*

Figure 1. *Blood Flow Superior Mesenteric Artery*



Introduction

Portal triad occlusion (PTO) produces dramatic alterations in systemic hemodynamics and hepatic functions (1). The pathophysiology of systemic hemodynamics is unclear; however it is suggested that it was linked to ischemia of the liver as well as alteration of the splanchnic venous drainage resulting in intestinal ischemia (2). The severely traumatized liver and elective hepatic resection (during segmental or lobar liver resection) could require temporary vascular occlusion to prevent exsanguination during surgical operation (3-6). Another indication for PTO is liver transplantation. Liver transplantation is becoming common place at many institutions for the treatment of end stage liver disease and ischemia reperfusion is an unavoidable process in transplantation (7). D(-) lactate is a product of bacterial metabolism. Mammalian tissues do not produce it and metabolize it very slowly. Therefore, the D(-) lactate that is released will pass through the liver unchanged and appear in the peripheral blood in early stages of the disease(8,9). The aim of this experimental study is to investigate the intestinal ischemic changes occured after PTO.

Figure 2. *Boold Flow of Superior Mesenteric Vein*

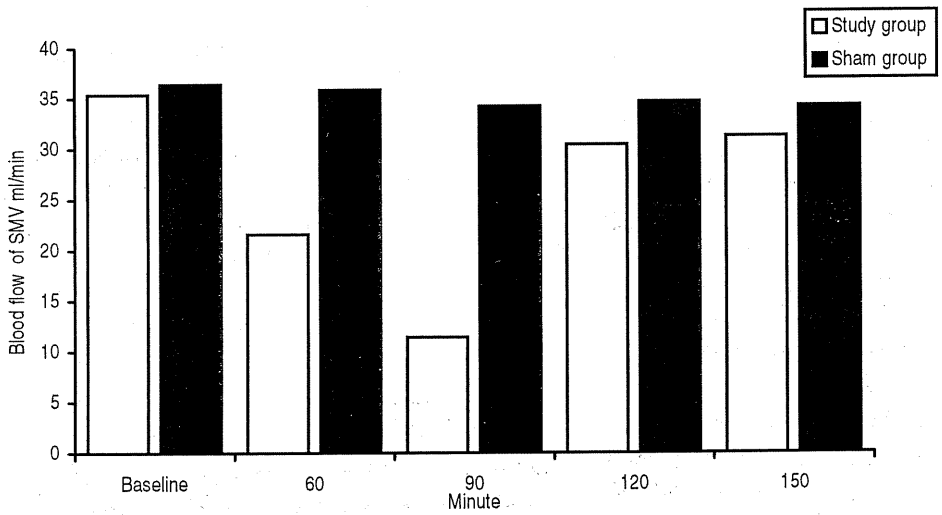
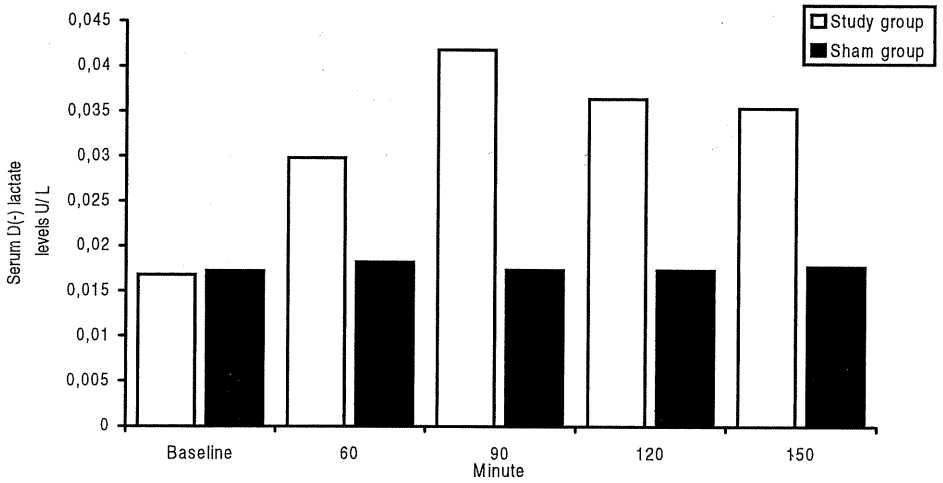


Figure 3. *Serum D(-) Lactate Levels*



Material and Methods

Fourteen pathogen free male albino rabbits weighing 1700±50gr divided into study and sham groups each containing 7 rabbits. Then, general anesthesia was achieved by intramuscular injection of ketamine hydrochloride (50 mg/kg). The jugular vein was cannulated using polyethlene catheter. Laparotomy was performed via a midline incision, the liver was isolated from its peritoneal attachments and the liver hilum was exposed. A microvascular clip was placed across the liver hilum for 90 minutes.Then reperfusion is allowed by removing the clip. Then a transonic doppler flow probe (Toshiba SSA 270A, 7.5 mHz duplex linear transducer) was placed upon superior mesenteric artery (SMA) and vein (SMV) to investigate blood flow changes and portocaval anastomoses. The initial measurement was designated as time zero, baseline value. The control group underwent all dissections but did not receive portal triad occlusion. In both groups, blood samples taken from the jugular vein were collected to measure D(-) lactate levels to determine intestinal ischemic alterations. An equivalent volume of saline (0.9%) was infused after each blood draw. The level of the serum D(-) lactate levels was measured with a commercially available kit (D(-) lactic acid, UV-method, Boehringer Mannheim, cat no:1112821). Before the PTO, at 60^{th}, 90^{th} minutes of PTO and at 30^{th}, 60^{th} minutes after reperfusion(120 and 150^{th} min) blood samples were taken to determine D(-) lactate levels, and intestinal tissue samples for histopathological examination. At the same time, blood and tissue samples were taken from the sham group. Histopathological examination was performed to samples which were obtained at 60^{th}, 90^{th} min of ischemia and 30^{th}, 60^{th} min of reperfusion. Biopsy specimens were fixed in 10% formalin and dehydrated with alcohol and embedded in paraffin. Four-micron sections were stained with H&E and examined under ligth microscopy according to papillar atrophy in mucosa, eodema, PNL infiltration and hemorrhage. Statistical analysis was performed by using Student's t test. $P<0,05$ accepted to be significant.

Results

Prior to operation, both groups were hemodynamically stable. The sham-operated rabbits were hemodynamically stable throughout the entire study. Mean SMA blood flow showed significant changes in the study group. Blood flow was 219.5±4.5ml/min before the PTO and decreased to 114±4.5 ml/min at the end of PTO ($p<0.0001$). At the 30^{th}, and 60^{th} min of reperfusion blood flow was 185.4±5.5, 203.0±13.9 ml/min respectively ($p<0.0001$ for both). Blood flow in the sham group was 222.6±4.6 ml/min at the beginning of the study, whereas it was 219.6±3.1, 219.4±1.1, 220.4±4.6, and 221.6±3.9 ml/min at the 60^{th}, 90^{th} min of ischemia and 30^{th}, 60^{th} min of reperfusion respectively ($p>0.05$ for both) (Figure 1). In the study group the basal value of mean SMV flow decreased to 11.4±1.1ml/min at the end of PTO from 35.4±1.6 ml/min ($p<0.0001$). At the 30^{th}, 60^{th} min of reperfusion, the blood flow was 30.4±1.5 and 31.2±1.9ml/min, respectively ($P<0.05$ for both). In the sham group SMV flow was 36.6±1.1 ml/min at the begining of the study , whereas it was 35.8±1.4, 34.2±1.4, 34.6±1.1, 34.2±0.8 ml/min at the 30, 60,

Figure 4. *Moderate Changes at 60th Min of PTO*

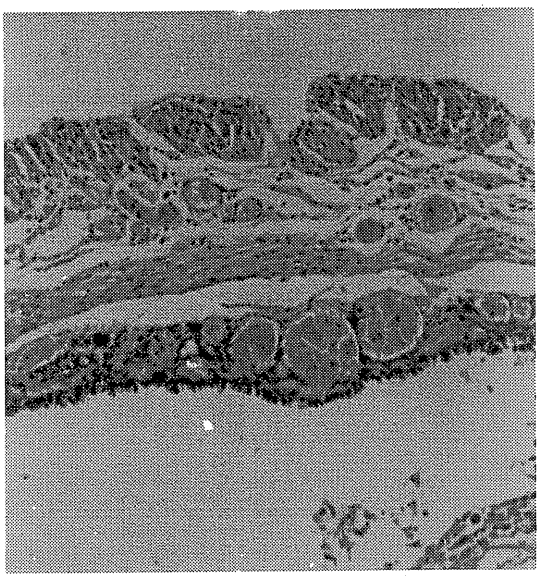
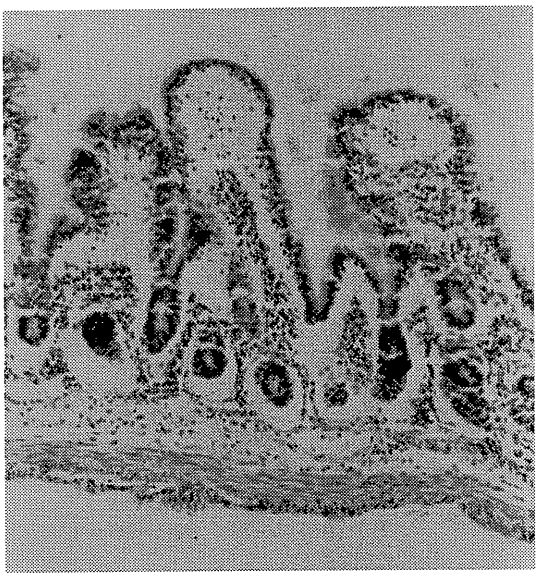


Figure 5. *Severe Changes of 90th Min of PTO*



90th min of ischemia and 30 and 60th of reperfusion (Figure 2). The differences in sham group were not significant (p>0.05 for each). In the study group, mean serum D(-) lactate levels was 0.0168±0.001 U/L at the beginning and it increased to 0.0418±0.001 U/L at the end of ischemia (p<0.0001), and it was 0.0354±0.002, 0.0326±0.001U/L at the 30th, 60th min of reperfusion respectively (p<0.001, p<0.01 respectively) (Figure 3). The differences in sham group were not significant (p>0.05). Initial tissue samples of the intestinal showed normal mucosal surfaces and serosal structures whereas edema in stroma of the villous, congestion in vessels, and PNL infiltration at 60thmin and congestion in vessels, hemorrhage, edema and PNL infiltration at 90th min (Figure 4,5).

Discussion

Protection of the liver against ischemia-reperfusion injury remains one of the major problems in traumatized liver, elective hepatic resection and liver transplantation. Temporary PTO can reduce the bleeding from liver (5,10). PTO induces not only hepatic ischemia, but additionally results in splanchnic congestion (11). Thus, stasis in the intestinal region related to occlusion of portal system to prevent bleeding, needs to be investigated. Blockage of SMV during PTO may result in obliteration of the most important drainage door of splanchnic area, which in turn causes sphlanchnic congestion. That the classical limit of 15-20 min of transient PTO described by Pringle may be exceeded resulting in surgeons to behave more freely (5,10,12-14). Lenghthening of this period, although unrecognized previously, means an increase in intestinal congestion which may cause ischemic changes in intestines. Experimental studies have showed that produce several pathologic events including splanchnic vascular congestion(1,3,11,15). In our study, the evaluation of blood flows in SMA and SMV measured by Doppler ultrasound (USG) showed that blood flow was decreased at the end of PTO from a baseline value of 219.5±4.5ml/min to 114±4.5 ml/min. Histopathological examinations showed that intestinal ischemia is unavoidable after SMV occlusion. Tissue samples showed less congestion in samples of 60th min than in samples of 90th min (Figures 4,5). These findings suggest that the longer duration of PTO the more congestion in intestines. In different studies it was shown that bacterial translocation, endotoxemia and remote organ injury, cause influence of transient PTO on intestines in human beings and it increases morbidity and mortality in conditions such as hepatic resection, liver transplantation and severe hepatic injuries (16-20). In this study, progressive histopathological changes shown in intestinal tissue, and increase in serum D(-) lactate levels, which is the early marker of mesenteric ischemia and product of bacterial metabolism (8), showed that it should not be forgetten that congestion occures in PTO causes ischemic changes. The changes in hepatic area in PTO were widely been investigated by many researchers (11,21-25).

In the light of these data, in conditions in which PTO is required, more attention must be focused on the changes in intestines.

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