

## MESENTERIC ARTERY OCCLUSION IN THE GUINEA-PIG : TISSUE PROTECTIVE EFFECT OF ILOPROST

B.Şükrü BOZKURT, M.D., Orhan BAYRAM, M.D., Emin ERSOY, M.D., H.Ercüment TEKİN, M.D.,  
Erhan ONUK, M.D., Z.Sevim ERCAN\*, Ph.D.

Gazi University, Faculty of Medicine, Department of General Surgery and Pharmacology\*,  
Ankara, Turkey

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**SUMMARY :** *The tissue protective effect of intravenous 0.1 ng/kg/min Iloprost for 30 minutes infusion was elevated in guinea-pigs subjected to ligation of a branch of arterial mesenterica superior for 4 hours.*

*In the control group only sham operation was performed. In the first group 0.1 ml/min saline and in the second group Iloprost 0.1 ng/kg/min was infused for 30 minutes. In the first and second groups after abdominal incision was made a branch of arteria mesenterica ligated for 4 hours. In all groups, blood samples was taken by cardiac puncture for the determination of creatine phosphokinase and alkalen phosphatase and dissected mesenteric vascular beds were transferred for the light microscopic examination.*

*Creatine phosphokinase and alkalen phosphatase activitie<sup>e</sup> are found to be increased significantly in the blood samples of mesenteric artery ligated group when compared with that of controls. Iloprost pretreatment significantly prevents the increase in the enzyme activiivies.*

*In the ligation group oedema, congestion and necrotic changes were observed at the mucosa of small bowel while oedema and slight necrosis were observed in Iloprost pretreated group according to microscopic examination.*

*The results of the present study indicate that Iloprost at low concentrations protect the tissue damage induced by lysosomal enzymes.*

**Key Words :** *Iloprost, Mesenteric Artery Occlusion, Tissue Protective Effect.*

### INTRODUCTION

It is well known that prostacyclin (PGI<sub>2</sub>), is a powerful inhibitor of platelet aggregation and induces a potent vasodilator effect. It has been shown that PGI<sub>2</sub> induces a protective effect in several models of hypoxia / anoxia (3, 6, 9). Stable analogue of PGI<sub>2</sub>, Iloprost has a pharmacological profile like PGI<sub>2</sub> (12, 13) have been shown to produce an anti-

arrhythmic effect (1, 8). The protective effect of Iloprost has also been described in myocardial strips exposed to anoxia (2), restraint-cold stress - induced gastric damage in rats (19), angiotensin II-induced rat lung oedema (17), in isolated rabbit kidney exposed to anoxia (18). The tissue protective activity of Iloprost has successfully been applied in kidney transplantation in pig (5) and Iloprost has a beneficial effect on functional recovery in the isolated rat heart after 24 hours of hypothermic arrest (4). New

clinical studies indicate the beneficial effect of Iloprost in peripheral arterial occlusive diseases, Raynaud's phenomenon, cardiopulmonary bypass and coronary heart disease (11).

The present study was undertaken to investigate whether Iloprost has a tissue protective activity in the mesenteric circulation in which one branch of mesenteric artery occlusion was applied.

### MATERIALS AND METHODS

Adult guinea-pigs of both sexes weighing 300-400 g were anaesthetised with sodium pentobarbital (30 mg/kg iv). Femoral artery was dissected and cannulated for the infusion of saline and Iloprost. Blood samples were taken by cardiac puncture for the determination of creatine phosphokinase and alkaline phosphatase.

After abdominal incision was made a branch of arteria mesenterica superior was dissected and prepared for ligation.

In the first group, saline infusion was made for 30 min with an infusion pump at constant flow (0.1 ml/min) and then artery ligation was applied for 4 hours. After this period blood samples were taken from the heart, tissue samples were taken from the mesenteric vascular bed for biochemical and pathological examination.

In the second group, Iloprost at the dose of 0.1 ng/kg/min was infused for 30 min before ligation and the same experimental procedure was repeated as mentioned above.

The activities of creatine phosphokinase and alkaline phosphatase were measured according to the methods of Oliver (10) and Bassey - Lawry - Brock (16) respectively.

Dissected mesenteric vascular beds were transferred to a beaker containing formaldehyde (10 %) for light microscopic examination.

The results were statistically analysed by using Student's t-test.

### RESULTS

Creatine phosphokinase and alkaline phosphatase activities are found to be increased significantly in the blood samples of the mesenteric artery ligated group when compared with that of controls. The creatine phosphokinase activity in the control group was found to be  $126.8 \pm 16.4$  IU/L while it was found to be  $247.6 \pm 18.6$  IU/L in the group that mesenteric artery ligation is applied for 4 hours.

Alkaline phosphatase activity in the control group is found to be  $62.4 \pm 5.6$  IU/L while it is found to be  $130.2 \pm 8.2$  IU/L in the 4 hour ligation applied group.

Iloprost pretreatment significantly prevents the rise in the enzyme activities. Creatine phosphokinase and alkaline phosphatase levels were found to be  $186.4 \pm 14.2$  and  $86.4 \pm 6.8$  IU/L respectively in the Iloprost pretreated group. The results are summarized in Table 1.

Necrosis in the mucosa of small bowel of the guinea-pig, oedema, congestion and necrotic changes were observed in ligation applied group while oedema, a slight necrosis were observed in Iloprost pretreated group according to microscopic examination Fig 1, 2.

### DISCUSSION

The results of the present study indicate that creatine phosphokinase and alkaline phosphatase one branch of mesenteric artery ligation causes an inc-

	Creatine Phosphokinase Activity (IU/L)	Alkaline Phosphatase Activity (IU/L)
Control	$126.8 \pm 16.4^a$	$62.4 \pm 5.6^d$
After ligation for 4 hours	$247.6 \pm 18.6^b$	$130.2 \pm 8.2^e$
Pretreated with Iloprost	$186.4 \pm 14.2^c$	$86.4 \pm 6.8^f$

a - b

p<0.001

b - c

d - e

e - f

p<0.05

Table 1 : Serum creatine phosphokinase and alkaline phosphatase activities before and after mesenteric artery ligation in the absence and presence of Iloprost (0.1 ng/kg/min) (Mean±S.E.M. of 8 experiments)

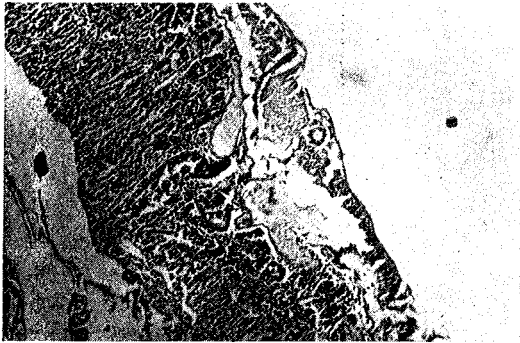


Fig - 1 : Oedema, congestion and necrotic changes in the small bowel of the guinea - pig exposed to 4hr ligation (HE)X80.

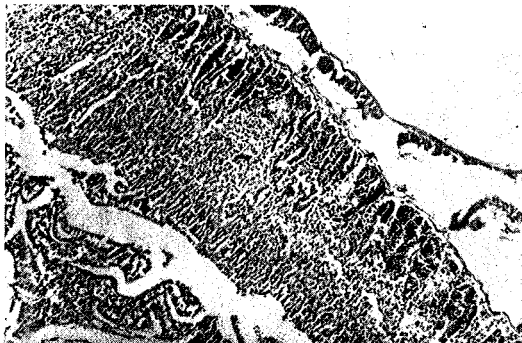


Fig - 2 : Oedema, a slight necrosis in the small bowel of the guinea-pig exposed to 4hr ligation afte. iloprost pretreatment (HE)X80.

rease in the activities of l'osomal enzymes like. Iloprost prevents the rise in creatine phosphokinase and alkalen phosphatase activity significantly. Also a slight necrosis is observed in microscopic examination in Iloprost pretreated group.

Although the mechanism of the action of Iloprost in tissue protection against ischemia is not fully understood. Prevention of ischemia induced release of catecholamines as indicated by Schrör et al (14) may be one of the mechanism contributing to its tissue protective effect. Removal of deleterious superoxide anions (7), general membrane stabilizing properties of the compound (15) and its power-

ful vasodilator action might be other factors contributing to tissue protective effects of Iloprost.

According to microscopic examination slight necrosis was observed in Iloprost pretreated group. This might be due to the increased activity of thromboxane A<sub>2</sub>, which is a powerful vasoconstrictor prostanoid.

The role of thromboxane synthetase inhibitor, UK 38485, on the pathology of mesenteric vascular bed induced by ligation is still under investigation.

Correspondence to : Dr.Şükri BOZKURT  
Gazi Üniversitesi Tıp Fakültesi  
Genel Cerrahisi Anabilim Dalı  
Beşevler  
06500 ANKARA - TÜRKİYE  
Phone : 312 - 214 10 00 / 5733

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