Injury Induced by Somatostatin on Livers Harvested and Preserved in Eurocollins Solution for Transplantation

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Özet: *TRANSPLANTASYON AMACI İLE ÇIKARILAN RAT KARACİĞERLERİNDE SOMATOSTATİN KULLANIMINA BAĞLI GELİŞEN KARACİĞER HASARI*

Somatostatin Gastrointestinal sistemin motor ve salgı fonksiyonlarını inhibe eden bir hormondur. Aynı zamanda kolestatik etkiside bilinmektedir. Bu çalışmada somatostatin'in transplantasyon amacı ile çıkarılacak karaciğerler üzerindeki etkileri ratlarda araştırılmıştır. Somatostatin'in farmakolojik dozlarda verildiği birinci grup ratlar ile somatostatin, verilmeyen ikinci grup ratlardan çıkarılan karaciğerler Eurocollins solusyonunda saklanmış 12. ve 24. saatlerde biyopsiler alınarak histolojik inceleme yapılmıştır. Somatostatin uygulanan ratlarda karaciğerde oluşan koruma hasarının anlamlı derecede şiddetli olduğu (p<0.01) görülmüştür.

Anahtar kelimeler: Somatostatin, saklama hasarı, karaciğer transplantasyonu

Summary: *Somatostatin is a known inhibitor of the secretory and motor functions of the gastrointestinal tract. Cholestatic effect of the hormone was also established in a number of studies. Our aim was to investigate the effects of somatostatin on livers that will be harvested for potential transplantation. Livers of the somatostatin pretreated and control rats were harvested and preserved in Eurocollins solution. Following two different cold storage periods, organs were evaluated histologically. The extent of hepatic injury was found to be statistically more severe (p<0.01) within the somatostatin pretreated group compared to the control group.*

Key words: Harvest injury, liver transplantation, somatostatin

Somatostatin has been described to protect cells against different kinds of injury in animal models(1,2). In addition to its inhibitory action on gastrointestinal system secretion, somatostatin decreases portal pressure significantly(3). The peptide hormone is also a potent inhibitor of the gastrointestinal motor function.

Some experiments in rats and dogs also showed the cholestatic nature of the peptide (4,5,6). Also high doses of this drug inhibits the choleretic response to various stimuli(7).

In view of these diverse properties including reduction of splanchnic blood flow in both experimental animals and man, the effect of the chronic use of this drug on overall integrity of the liver is crucial (3,8).

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As this hormone is expected to be used in clinical practice more frequently, we planned to investigate its effects on livers that will be harvested for potential transplantation. Histological evaluation of harvested livers was used to assess the integrity of the organ following two different cold storage periods in Eurocollins solution.

MATERIALS AND METHODS

Male rats weighing between 205-240 gr were used in this experiment. They were housed 7-8 to a cage under a controlled thermal environment, allowed to feed ad libitum and exposed to a 12-hour each light and dark schedule with illumination between 8 a.m. and 8 p.m. Twenty four male rats were divided into two groups. Somatostatin with a dose of 20 microgr/kg was administered twice a day subcutaneously for eight days to one half while the remaining 12 rats received only normal saline.

Table I: Comparison of the harvesting preservation injury.

Groups	Unsignificant injury	Mild injury	Moderate injury	Severe injury
12 hr storage (somatostatin)	—	—	4	8
24 hr storage (somatostatin)	—	—	3	9
12 hr storage (control)	11	1	—	—
24 hr storage (control)	7	5	—	—

Rats were anesthetized with ether and a laparotomy through a midline incision was performed. Portal vein was cannulated by plastic tubing (18G). Thorax was opened and suprahepatic vena cava was isolated for transection. Livers were perfused with cold (4°C) Eurocollins solution through the cannulated portal vein till macroscopic evidence of uniform perfusion, simultaneously suprahepatic vena cava was transected to vent the effluent. Livers were harvested following perfusion and stored in Eurocollins solution in an ice bag. Specimens for histopathological examination were prepared after 12-hours and 24-hours of cold storage both in control and somatostatin treated groups.

Histopathological examination was done under light microscopy following hematoxylin-eosin staining.

The chi-square test was used to compare proportions in more than two groups.

RESULTS

Three categories of harvesting and preservation injury were observed in all groups. Mild injury includes spotty acidophilic necrosis, microvesicular steatosis and central hepatocanalicular cholestatis. A more serious insult results in central ballooning and cholestasis with/without cholangiolar proliferation. Severe injury shows bridging periportal necrosis, marked cholangiolar proliferation and severe hepatocyte ballooning.

Table I compares the harvesting preservation injury in two groups following 12 and 24 hours of cold storage in Eurocollins solution.

The extent of hepatic injury was statistically more severe ($p<0.01$) within the somatostatin pretreated groups compared to the control groups.

DISCUSSION

This study demonstrates that pretreatment with somatostatin significantly alters the quality of the liver harvested and stored for transplantation in rats. This injury is most likely due to the hemodynamic effect of the drug on the liver. Jenkins et al. have shown that somatostatin produced a significant increase in splanchnic vascular resistance without influencing hepatic vascular resistance, suggesting that the effects of the hormone are mediated by prehepatic splanchnic vasoconstriction(3). Significant hemodynamic alterations with decreased pulse rate and hypotension were observed in man at the start of somatostatin infusion (9). The effects of somatostatin on portal hemodynamics remain controversial. Although most studies in animals and humans have found decreases in portal tributary blood flow and pressure, others found no significant effect (10).

Schirmer et al. supported the idea of an indirect or extrahepatic mechanism of somatostatin's anti-choleretic effects. They concluded that this effect is due to the reduction in portal vein blood flow after administration of pharmacologic doses of somatostatin(11).

Injury of an organ to be transplanted may develop while it is still in the donor, secondary to preexisting disease, hypotension, compromised blood supply due to various conditions or directly as a result of toxic compounds. The term harvesting injury has been widely used to describe the non-immunologic changes in liver biopsies before or during transplantation.

In conclusion we believe that there is significant harvest injury of the liver in somatostatin treated group both at 12 and 24 hours and this could be attributed to the hemodynamic effect of the drug on liver blood flow.

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