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Characteristic Responses in Portal Venous Blood Flow Caused by Omental Administration of Prostaglandin E_1 in 66% Hepatectomized Rats

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Summary. **Portal venous blood flow (PVF) and systemic arterial blood pressure (SAP) were examined after prostaglandin E_1 (PGE) administration to different anatomical sites within the peritoneal cavity in 66% hepatectomized rats. The PVF increased when PGE was applied to the greater omentum at 5.0 μg/kg/min for 2 min. The magnitude of PVF response was dose dependent. The PVF responses induced in order of magnitude were in the omentum and the parietal peritoneum. No PVF increase was seen when PGE was applied to the serosal surface of the cecum or the urinary bladder. The SAP was unchanged after PGE administration.**

These results suggest that, in this hepatectomized model, omental PGE administration is efficacious in enhancing PVF without changes in SAP, and that the omentum is a better site for PGE absorption than the serosa and the peritoneum.

Key words—prostaglandin, liver, portal vein, blood flow, hepatectomy.

INTRODUCTION

Different anatomical sites within the peritoneal cavity have different capacities for the absorption of medical substances such as insulin; the greater omentum has been identified as one of the better sites for insulin absorption.[1)] Concerning the route of absorption from the greater omentum, it has been revealed that fluid and small molecules (molecular weight $<5{,}000$) pass via portal venous drainage to the liver through the gastroepiploic vein.[2)] Prostaglandin E_1 (PGE, molecular weight $=350$) has been shown to increase portal venous blood flow (PVF) by dilating the portal vascular beds,[3-5)] and the effectiveness of PGE on PVF is increased by hepatic resection.[3)]

This experiment was designed to investigate whether the peritoneal cavity has different capacities for PGE absorption by estimating PVF in partially hepatectomized rats.

MATERIALS AND METHODS

Twenty male Wistar rats weighing 300-330 g each were used. They were kept for more than one week before the experiments in a room with a light-dark cycle of 12 : 12 with lighting on from 08 : 00 h, and at a temperature of 23.0 ± 2.0°C. The animals were allowed free access to standard laboratory chow and tap water until the experiments.[6)] The experiments were performed in the afternoon between 13 : 00 and 18 : 00 h to eliminate changes associated with circadian rhythm.

The animals were anesthetized with pentobarbital sodium (45 mg/kg) intraperitoneally and depth of anesthesia was maintained with the same agent at 7.5 mg/kg, given subcutaneously every 30 min.[6)] Tracheotomy was carried out to provide a patent airway. The PVF was measured with a transit-time ultrasonic volume flowmeter (Transonic T201, Advance, NY, U.S.A.) connected to a 2 mm probe.[6)] The systemic arterial blood pressure (SAP) was recorded from the right carotid artery. Throughout the experiments, the rectal temperature was kept at 36.0 ± 0.6°C with a heating lamp.

Midline and transverse incisions were made to

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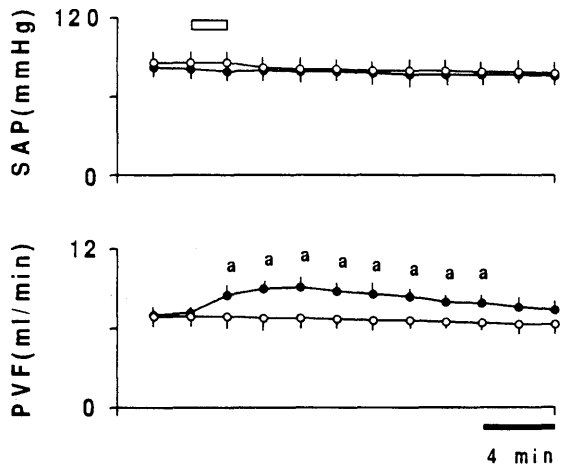

Fig. 1. Alterations in PVF and SAP after PGE application to the omentum in 66% hepatectomized rats. PGE at 5.0 μg/kg/min (●) and saline (○) were applied. A bar indicates the time of application. Values are the means ± SEM (n=6). $^{a}p<0.01$ vs ○.

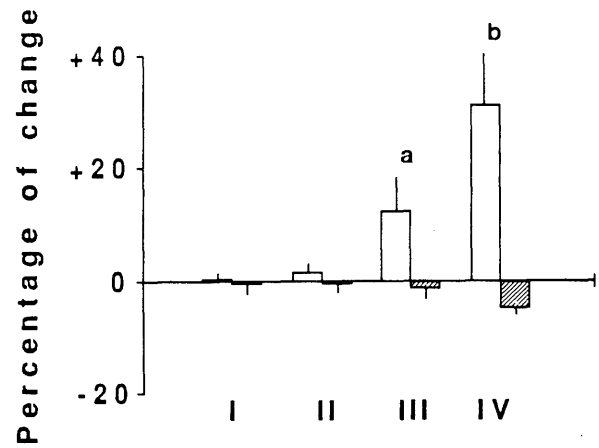

Fig. 2. Responses in PVF (opened bar) and SAP (shaded bar) 4 min after PGE application to the omentum. PGE at 2.5 (II), 5.0 (III) and 7.5 (IV) μg/kg/min were applied, and saline was used as the control (I). Values are the means ± SEM (n=6). $^{a}p<0.05$ vs I and II. $^{b}p<0.01$ vs III.

open the abdominal cavity, and the probe of the flowmeter was placed on the portal vein. The PVF and SAP were recorded with a pen recorder (SAN-EI, Type 1237, Tokyo). During the experiments, the abdomen was covered with a piece of gauze moistened with saline to prevent the viscera from drying.

Partial hepatectomy was conducted by methods previously described.[3,7] The median and left lateral lobes, forming a unit comprising about 66%, were ligated and removed.

Prostaglandin E_1 (PGE, Ono Pharmaceutical Co., Ltd., Osaka) dissolved in saline was used. A small catheter (602-105, Dow Corning, Midland) was utilized for PGE administration. When PGE was applied to the greater omentum, the tip of the catheter was covered with the omental tissue. The tip of the catheter was also located on the anterior surface of the cecum, the urinary bladder and the umbilical portion of the parietal peritoneum. The amount of test administrations was 46 μl, and each administration was completed in 2 min with a perfusion pump. Saline was used as the control.

Data were ANOVA analyzed, and specific values were evaluated by Duncan's multiple range test.

RESULTS

PGE administration to the omentum at 5.0 μg/kg/min increased PVF in the 66% hepatectomized rats. The response reached its peak about 4-6 min after administration, and then returned to the control level within another 12 min (Fig. 1). Based on this finding, the changes in PVF 4-6 min after PGE administration were compared. However, SAP was unchanged after the PGE administration (Fig. 1).

When different doses of PGE were applied to the omentum, increases in PVF 4 min after administration were dose dependent (Fig. 2), but no significant response in SAP was evoked by PGE administration.

When PGE was applied to four different sites in the peritoneal cavity, the PVF increases induced in order of magnitude were in the omentum, the parietal peritoneum, the cecum and the urinary bladder. The SAP responses caused by PGE were similar at all sites (Fig. 3).

DISCUSSION

PGE administration to the greater omentum brought about an increase in PVF in 66% hepatectomized rats (Fig. 1). This supports the view that the intravenous administration of PGE increases PVF.[3-5] The omental PGE action on the vascular bed seemed to be specific because the PVF response caused by PGE was dose dependent (Fig. 2).

PGE applied to different sites within the peritoneal cavity showed different capacities for portal PGE action (Fig. 3). Different anatomical sites within the cavity have been shown to induce different capacities for insulin absorption.[1] This may therefore hold true

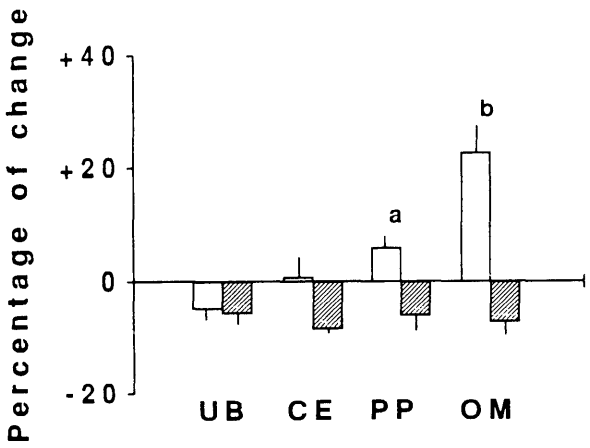

Fig. 3. Responses in PVF (opened bar) and SAP (shaded bar) 6 min after PGE application to different sites in the peritoneal cavity. PGE at 5.0 μg/kg/min was applied to the urinary bladder (UB), the cecum (CE), the parietal peritoneum (PP) and the omentum (OM). Values are the means ± SEM (n=6). $^{a}p<0.01$ vs UB. $^{b}p<0.01$ vs UB, PP and CE.

for PGE. The finding that PGE applied to the serosa failed to enhance the PVF could mean that PGE was not absorbed effectively by the serosa or that PGE was diluted to an ineffective concentration before it reached the portal vasculature.

The biological activity of PGE was reduced by 70-93% after a single circulation,[8-10] and the effectiveness of PGE on PVF was of short duration when it was administered intravenously.[3-5] However, in this study, the effects of PGE on PVF were of long duration (Fig. 1). One possible interpretation is that PGE ejected from a catheter was diffused into the omental tissue, and was then slowly released into the portal venous blood stream without inactivation by the circulation.

In spite of the fact that a reduction in SAP caused by PGE was evident when PGE was administered intravenously,[3-5] the SAP was unaffected by PGE administration (Figs. 1 and 2). This could mean that PGE slowly released into the portal circulation can be inactivated by the liver and the lungs.[8-10]

Although the exact mechanism of PGE absorption still needs to be studied, these results led us to conclude that, in the partially hepatectomized condition, omental PGE administration is very effective in enhancing PVF, and that the peritoneal cavity has different capacities for PGE absorption.

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