GDP-containing PD Fluid is Involved in Peritoneal Vascularization and Fibrosis in a Chronic Inflammatory Infusion Model of the Rat

Department of Internal Medicine, College of Medicine, Kyungpook University Hospital, Department of Biochemistry, Kyungpook University[*], *Department of Pathology, College of Medicine, Yeungnam University Hospital*[†], *Baxter Health Care*[‡]

Yong-Lim Kim · Hyeog-Man Kwon · Sun-Hee Park · Eun-Gyui Lee[*] · Chan-Duck Kim
Min-Hwa Jang · Jun-Chul Kim · In-San Kim[*] · Yong-Jin Kim[†] · Min-Sun Park[‡]

Introduction : Glucose degradation products (GDPs), which are formed during heat sterilization of peritoneal dialysis fluids (PDFs), have been suggested to cause functional and structural alterations of the peritoneal membrane and be responsible for the gradual loss of ultrafiltration in PD. Application of new PDFs with reduced GDPs may ameliorate these adverse effects of GDP on the peritoneal membrane.

Aim of the study : To evaluate the effects of GDP on functional and structural stability of the peritoneal membrane.

Methods : Male Sprague-Dawley rats were divided into Group C without dialysate infusion (n=8), Group P infused with low GDP solution containing bicarbonate/lactate buffer (4.25% Physioneal, pH 7.0-7.4, n=12), and Group D infused with conventional solution (4.25% Dianeal, pH 5.2, lactate-buffer, which was adjusted to pH 7.0 by adding sterile filtered 0.1N NaOH before each exchange, n=12). In groups P and D, animals were infused through a permanent catheter with 25 mL of PDF, twice daily. In both groups, peritoneal inflammation was induced by infusing PDF supplemented with lipopolysaccharide on days 8, 9, and 10. We assessed peritoneal membrane functions and measured dialysate VEGF, TGF-β1 and βig-h3 (TGF-β induced gene) in every week after initiating PD, and the morphologic change of peritoneal tissue at weeks 8.

Results : Glucose mass transfer was lower in Group P at weeks 6 ($p<0.05$) and 8 ($p<0.01$). D/P urea was lower in Group P at weeks 8 ($p<0.05$). The TGF-β1 level was lower in Group P at weeks 4 ($p<0.05$), and 8 ($p<0.05$). The VEGF level was lower in Group P at weeks 8 ($p<0.005$). The submesothelial matrix layer of the parietal peritoneum was significantly more thickened ($p<0.05$) in Group D, and lectin-stained blood vessels on this layer were well visualized in Group D, faint in group P and undetectable in Group C. There were significantly more peritoneal blood vessels in group D ($p<0.05$). βig-h3 expression in omentum was greater in Group D compared to group P in immunohistochemistry and western blot. βig-h3 and TGF-β1 levels in dialysate effluent were correlated with submesothelial thickness ($r^2=0.196$, $p<0.05$ and $r^2=0.198$, $p<0.05$). Submesothelial thickness was also well correlated with D/D0 and D/P protein ($r^2=-0.524$, $p<0.001$ and $r^2=0.435$, $p<0.005$)

Conclusion : Using a chronic inflammatory infusion model of PD in the rat, we suggests that dialysis with GDP-containing PD fluid is associated with increased VEGF, TGF-β1 and βig-h3 production, which are involved in peritoneal vascularization and fibrosis, though the effects of different buffers cannot be excluded. Use of low-GDP solutions may therefore be beneficial in maintaining the function and structure of the peritoneal membrane during long term PD.