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Effects of Platelet Derived Growth Factor on the Peritoneum

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Long term peritoneal dialysis results in peritoneal fibrosis, angiogenesis and loss of ultrafiltration capacity in a proportion of patients. The molecular mechanisms of this process are not clear. Platelet derived growth factor (PDGF) is known to stimulate smooth muscle proliferation and is associated with angiogenesis and fibrosis so has a potential role in peritoneal membrane damage. We created an adenovirus that expresses PDGFb. When infected in cell culture, AdPDGFb led to a significant increased expression of PDGFb in the supernatant as measured by ELISA. We infected 20 Sprague Dawley rats with AdPDGFb, and compared this to 12 rats infected with control adenovirus (AdDL). Animals were sacrificed on days 4, 7, 14, and 28 after a 4 hour peritoneal equilibrium test using 4.25% Dianeal®. Animals treated with AdPDGFb displayed transient ultrafiltration dysfunction 4 days after infection (net UF = -1.1 ml in AdPDGFb treated animals compared to +8.75 ml in control animals, p=0.01). By 7 days, this ultrafiltration dysfunction had resolved. Histologically, the AdPDGFb treated animals displayed remarkable submesothelial thickening with cellular proliferation and angiogenesis. Fibrosis was less dramatic. These changes had generally resolved 28 days after infection. Transient over expression of PDGFb in the peritoneum leads to cellular proliferation and angiogenesis. Fibrosis and ultrafiltration dysfunction were minimal and appeared to be limited to early time points. Histological changes resolved by 28 days after infection. Although PDGFb had significant histological effects on the peritoneum, the changes were not similar to those observed in patients on long term peritoneal dialysis.