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## **COX-2 Inhibition Largely Prevents Peritoneal Worsening in Rat PD Model**

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Introduction - Peritoneal dialysis (PD) is associated with an inflammatory response of the peritoneal membrane, with new vessel formation and fibrosis, and loss of ultrafiltration capacity. Since cyclooxygenase (COX)-2 is involved in inflammation and angiogenesis, we investigated the effects of COX-2 inhibition in a chronic rat PD model. Methods - During 4-5 weeks, 10 ml conventional PDF was daily instilled via an intraperitoneal catheter connected to a subcutaneous vascular access port. Half of the PDF treated animals (n=8) and half of the control rats (n=8) received via oral gavages the selective COX-2 inhibitor celecoxib (20 mg/kg/day), and half of PDF treated (n=8) and control animals (n=8) received only the vehicle (PEG solution). Control animals didn't have an indwelling catheter, nor received PDF instillations. Before sacrificing the animals, a 90 min PET-test was performed and net ultrafiltration determined. Cells were quantified from PET fluids and peritoneal tissues excised for morphological analysis. Results - Net ultrafiltration volume decreased from 10 ml in both control groups towards ~6.5 ml in the PD-PEG group (p<0.01). Treatment of the PD group with celecoxib completely prevented this drop in ultrafiltration towards 9.7 ml (PD-PEG vs PD-Celecoxib: p<0.01). Furthermore, a strong induction of peritoneal vessels and submesothelial fibrosis was found in the PD-PEG group compared to both control groups (p<0.01), which was significantly reduced 30-50% in the PD-celecoxib group (PD-PEG vs PD-Celecoxib: p<0.05). PDF instillation induced a strong peritoneal influx of leukocytes and a regenerative response of the mesothelium, along with increased values of MCP-1, VEGF and hyaluronan, all however not significantly reduced by celecoxib treatment. Conclusion - We conclude that COX-2 inhibition improves ultrafiltration capacity and reduces angiogenesis and fibrosis in a chronic rat PD model. Our results encourage therapeutic blockage of COX-2 in human CAPD patients.