Effects of Chronic Kidney Failure and Exposure to Different Dialysis Solutions on the Peritoneal Membrane

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INTRODUCTION

Long-term peritoneal dialysis treatment using conventional dialysis solutions is associated with alterations of peritoneal morphology. Peritoneal fibrosis, hyalinising vasculopathy and angiogenesis develop and lead to membrane solute transport changes and decreased ultrafiltration capacity.

New 'biocompatible' dialysis solutions have been developed in order to prevent the alterations of the peritoneal membrane, and prolong the duration of the treatment with peritoneal dialysis. However, most of the experimental studies investigating the effects of new solutions have been done in animal models with normal kidney function, whereas the clinical studies have been challenged by the difficulty of obtaining human peritoneal specimens.

AIM

The aim of the present study was to make an extensive comparison between the changes in the peritoneum induced by the long-term exposure to a 'conventional' and a 'biocompatible' dialysis solution in a rat model with chronic kidney disease.

METHODS

Forty-four Wistar rats were grouped as follows:
- **NKF**: normal kidney function
- **CKD**: chronic kidney failure induced by 70% nephrectomy
- **CKDD**: CKD + daily peritoneal infusions with Dianeal® 4.25%
- **CKDP**: CKD + daily peritoneal infusions with Physioneal® 3.86%

After 16 weeks we performed:
- **Standard Peritoneal Permeability Analysis** adapted for rats (SPARa), using Dextran 70;
- tissue specimens were collected for light and electron microscopy:
  - **Vessel density**: anti-aminopeptidase P and anti-podoplanin immunostaining of the omentum;
  - **Fibrosis**: picro-Sirius red staining and anti-collagen I immunostaining of the omentum;
  - EM: vascular basal lamina, mesothelial cell layer.

RESULTS

Renal function after 16 weeks

	NKF N=8	CKD N=12	CKDD N=10	CKDP N=9
Removed kidney mass (%)	0	69.6+1.4*	69.5+1.0*	68.8+0.8*
Renal creat clearance(ml/min)	4.3±0.7	1.8±0.5*	2.3±0.5*	1.8±0.6*

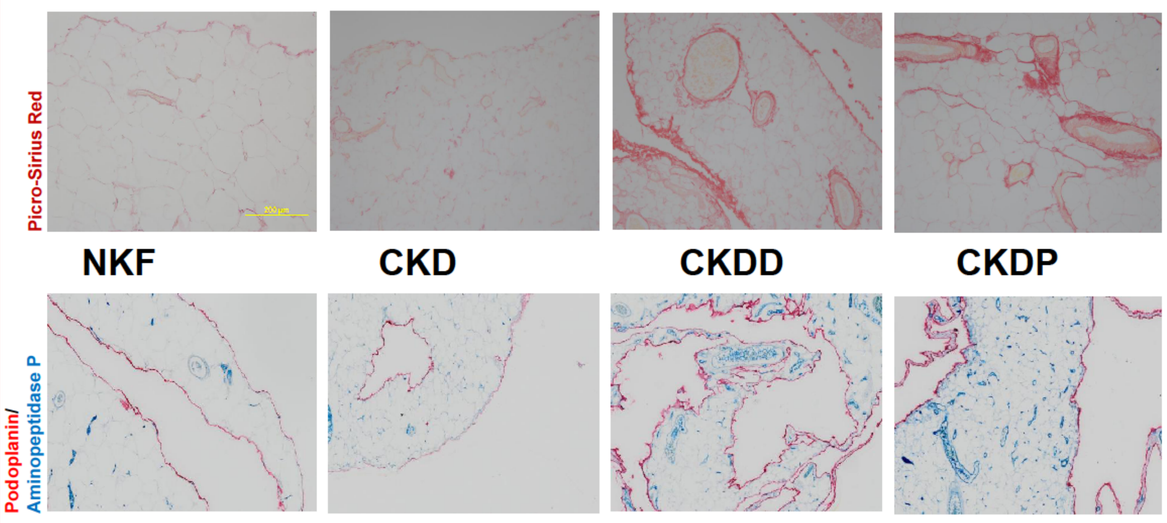
NKF: normal kidney function; CKD: chronic kidney failure; CKDD: CKD +Dianeal®; CKDP: CKD+Physioneal®.
* p<0.001 NKF vs CKD, CKDD, CKDP

Peritoneal transport parameters

	NKF N=2	CKD N=3	CKDD N=4	CKDP N=4
D/P creatinine	0.4±0.06	0.5±0.03	0.6±0.08	0.6±0.05
Glucose absorption (%)	58±6	59±1	69±1	65±3
NUFR(µl/min)	73±12	74±25	62±2	56±20

NKF: normal kidney function; CKD: chronic kidney failure; CKDD: CKD +Dianeal®; CKDP: CKD+Physioneal®.
NUFR: net ultrafiltration rate

Morphological alterations of the peritoneum

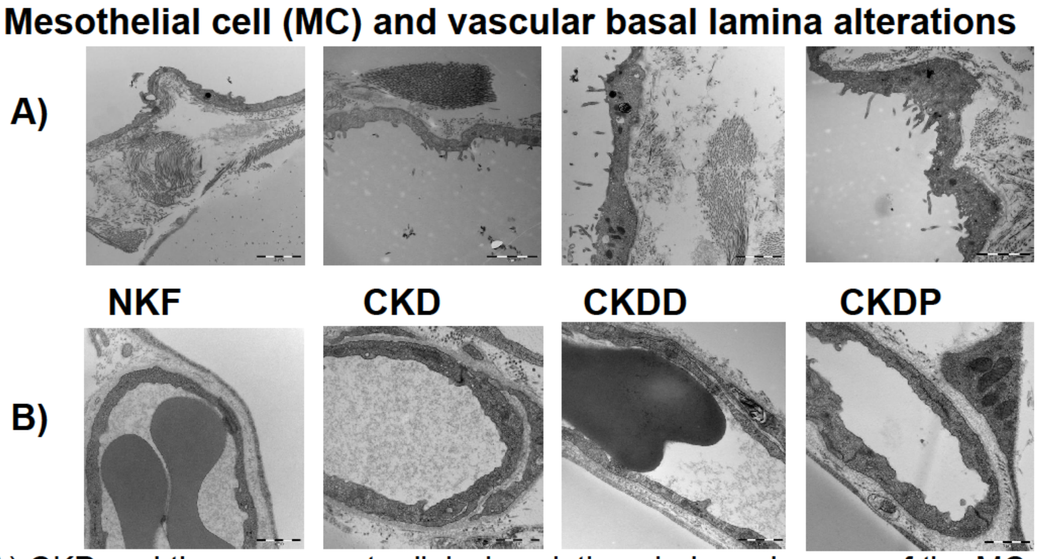


Analysis of the morphological alterations of the peritoneum

	NKF N=8	CKD N=12	CKD+exposure N=19	CKDD N=10	CKDP N=9
Vessel densities					
BV profile density	2.9 (2.2-3.8)	5.5 (4.4-6.9) *	7.0 (5.7-8.5) *†	7.3 (5.6-9.0)	7.0 (5.7-8.3)
LV profile density	0.3 (0.1-0.5)	0.6 (0.5-1.2) *	0.9 (0.6-1.2) *	0.7 (0.5-1.7)	0.9 (0.6-1.2)
Analysis of fibrosis					
Fibrosis score	0 (0-1)	3 (1-3) *	5 (4-6) *†	6 (5-7) δ	4 (4-5) δ
PSR staining (%)	1.3 (0.9-2.2)	2.8 (2.0-3.5) *	7.9 (4.4-11.8) *†	7.1 (5.3-16.6)	8.7 (4.1-11.2)
OH-proline (µg/mg tissue)	0.3 (0.2-0.5)	0.5 (0.4-1.0)	0.8 (0.4-1.3)	1.0 (0.4-1.3)	0.6 (0.2-1.1)
Collagen I (%)	-	-	14.2 (9.7-18.8)	14.8 (13.1-25.8)£	9.8 (5.9-18.5) £

Results are expressed as median and interquartile range. * p<0.05 CKD, CKDD, CKDP versus NKF; † p<0.05 CKD+exposure versus CKD; δ p<0.05 and £p=0.09 CKDP versus CKDD.BV: blood vessel; LV: lymph vessel; PSR: picro-sirius red

Mesothelial cell (MC) and vascular basal lamina alterations



A) CKD and the exposure to dialysis solutions induce damage of the MC: they show a reactive state, are enlarged, have an increased surface area of the microvilli and high number of intracytoplasmic vesicles; B) Mesenteric blood vessels: thickening and reduplication of the basal lamina induced by CKD and the exposure to dialysis solutions.

CONCLUSIONS

- **Chronic kidney failure itself induced mesothelial cell alterations, peritoneal fibrosis, new blood and lymph vessel formation, alterations of the vascular basal lamina, and high peritoneal small solute transport rates. These alterations were partially more severe after long-term exposure to dialysis fluids.**
- **A trend towards less fibrosis was present after the exposure to the 'biocompatible' solution, but no other differences were present between the two dialysis solutions.**

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