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Experimental model for CAPD studies in the rabbit

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Introduction

Continuous Ambulatory Peritoneal Dialysis (CAPD) is a well established technique for treatment of patients with renal failure.

In CAPD approximately 2 liters of a hypertonic dialysis solution containing dextrose and different electrolytes is administered intraperitoneally. The solution is left to dwell for 6 hours during which electrolytes and degradation products (ie. urea and creatinine) diffuses from the blood to the dialysis solution across the peritoneal membrane, which thus serves as a dialysis filter. After 6 hours the peritoneal cavity is drained and a new amount of dialysis solution is instilled.

CAPD is preferable to hemodialysis for both practical and economic reasons. Most patients on CAPD are, however, forced to discontinue this treatment due to repeated attacks of infectious peritonitis (*Golper et al.* 1989).

Peritonitis in CAPD has been attributed to drainage of immunoglobulins, complement, other opsonins, direct irritation or to functional impairment of peritoneal macrophages and of polymorphonuclear granulocytes (PMN) due to unphysiological dialysis solutions (*Vas* 1989).

In order to study and improve peritoneal dialysis, it is of relevance to develop animal models suitable for long term CAPD.

Most animal studies of peritoneal dialysis utilize either singular injections or short term dialysis-schedules, often without catheter application (*Maher et al.* 1978, *Dunham et al.* 1981, *Albert et al.* 1984).

In two animal models (*Gotloib et al.* 1982, *Traina et al.* 1986) rabbits were used to mimic the clinical situation. In these studies it was found necessary to omentectomise the rabbits prior to the catheter application in order to avoid wrapping and occlusion of the catheter. In both models the cranial end of the catheter was brought out through the skin behind the ears of the animal, resulting in a high number of tunnel infections. Furthermore, this catheter application necessitated fixation of the animal for the entire observation and dialysis period.

The aim of the present study was: To create a model, which minimizes the obstacles described above, and which allows simultaneous, repeated, and rapid CAPD-treatment of several animals, and to evaluate the histopathological, biochemical and clinical changes induced by the technical and surgical procedures per se in non-uremic animals.

Material and methods

Animals:

Fifty-six rabbits (female french loops) of conventional quality weighing between 2.2 and 4.7 kg obtained from an authorized local breeder were used. The rabbits were kept in quarantine for 2 weeks and treated with sulphabenxpyrazine in a NaOH-solution (The Hospital Pharmacy, Odense, Denmark) in the drinking water in order to eliminate any ongoing infections. The animals were housed under controlled conditions (temperature 21 ± 1°C, relative humidity 55 ± 5 %, 12/12 hour light/dark cycle, air changed 16 times/h through filter), 1 animal per cage, fed approximately 130 g of laboratory chow daily (Altromin no. 3123) and given water ad libitum, all in accordance with Danish legislation.

Ten animals served as controls. From the operation until autopsy the catheters of these rabbits were heparinised every 36

hours with 2.5 ml 500 IU/ml heparin-solution. Apart from the dialysis these animals were handled like the others.
The remaining animals (46 rabbits) were exposed to different dialysis fluids (Dianeal® 1.36 % and 3.86 % (Baxter, USA) and 87b (The Hospital Pharmacy, Odense University Hospital, Denmark) with the addition of 1 IU heparin/ml) 3 times a day.

Anesthesia

The rabbits were pre-medicated with 1 mg Atropine and 0.1 ml/kg Hypnorm® (fentanyl/fluanison, Janssen Pharma, Germany) s.c. For anesthesia 2 mg/kg Stesolid® (Diazepam, Dumex, Denmark) i.v. and 0.25–0.40 ml Hypnorm® i.v. were used.

Surgical technique and post surgical care

The fur on the abdomen and the neck was clipped and the skin was disinfected with Iobac® Vet (5 % iodine solution, Ciba Geigy, Switzerland) and 70 % ethanol. A modified Tenckhoff® catheter (Hedima Aps, Tåstrup, Denmark) for adult humans with one dacron cuff, was inserted through a small midline incision close to the umbilicus and directed caudally. The fascia and muscle layers were closed with a purse string suture and the dacron cuff was sutured to the fascia, leaving the cuff outside the peritoneal cavity. The external part of the catheter was tunneled subcutaneously to the neck where a skin incision was made. A silver coupling (crafted by the lock-smith, Odense University Hospital) (Fig. 1) containing a silicone membrane, was connected to the catheter, thus forming a closed system with the peritoneal cavity. Before connection the catheter was filled with a heparin solution (500 IU/ml). Both skin incisions were closed with continuous sutures using 4–0 Dexon® S or 4–0 Dexon® Plus, leaving the catheter totally covered by the skin.
After the operation Temgesic® (buprenorphine, Reckitt & Colman, GB) 0.05 mg/kg was given s.c. as an analgetic and for reversal of the anesthesia. The rabbits were allowed to recover under an infrared light before being returned to their cages. Pre- and postoperatively 0.2 ml/kg of Borgal® (sulfadoxin 200 mg -trimetoprim 40 mg/ml, Hoechst, Germany) was given as antibiotic cover.
During the first 7 days after the operation the catheters were heparinised (2.5 ml, 500 IU/ml) every 36 hours, but no dialysis was performed allowing the tissue to heal properly.

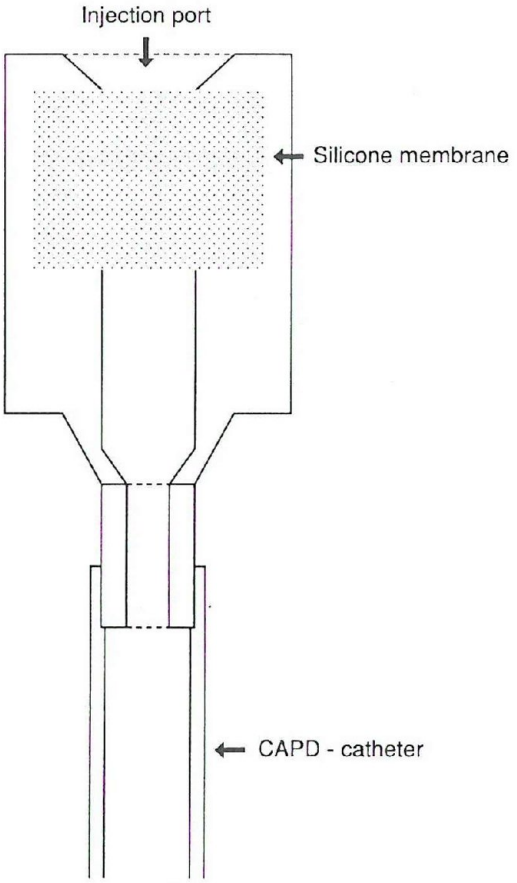

Fig. 1. The silver coupling.

Dialysis technique and procedure

From the seventh day on the rabbits were

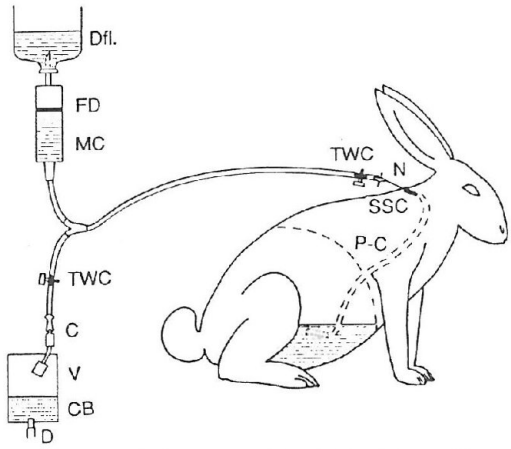

Fig. 2. The CAPD system for rabbits. The pediatric measuring-chamber is inserted just beneath the dialysis fluid container. Dfl. = dialysis fluid, FD = floating disc., MC = measuring chamber, TWC = tree way tap, N = needle, SSC = subcutaneous silver coupling, P-C = peritoneal catheter, C = connector, V = valve, CB = collecting bag, D = drain.

dialysed for a period of 4 weeks. Fluid exchanges were carried out three times a day, six days a week with 30 ml of dialysis fluid per kg bodyweight. The average dwell time was approximately 8 hours.

For the CAPD-procedure, specially constructed Y-shaped plastic-tubes (Codan-Steritex, Denmark) (Fig. 2) with a bag for the dialysate and two 3-way taps for heparinising and sample-collection, were used. A measuring-chamber containing a floating disc which had volume-indicator- and shutter-function, preventing air- and over-infusions, was interposed in the y-system.

During the exchange of dialysis solutions (which lasted less than one hour) the rabbits were placed in 6 separate and adjacent boxes which prevented them from chewing or disconnecting the tubings. An opening in the box allowed access to the head of the rabbit and the subcutaneous silver-coupling (Fig. 1), which was penetrated by needles with bended tips (Port-A-Cath®, Pharmacia, Sweden), thus preventing stamping of the silicon membrane.

The dialysis-fluids were pre-heated to a temperature of 37°C and hung in a heated locker during the entire procedure.

Dialysate was permitted to drain by gravity for a period of at least 20 minutes into the collecting-bag placed on the floor.

The dialysis fluid (30 ml/kg) was infused after drainage of the peritoneal cavity within a period of 10 minutes. Before disconnecting the peritoneal-catheter was filled with 2.5 ml of a heparin solution (500 IU/ml) through the 3-way tap to prevent fibrin clotting.

Clinical observation

Food consumption, the volume of the dialysate and its macroscopic appearance, the infusion time and the behaviour of the rabbits were registered three times a day. Body weight and rectal temperature of the animals were measured pre-surgically and every afternoon in the observation period.

Laboratory tests were performed as illustrated by Table 1. Effluent leukocytes were counted in a hemocytometer (Fuchs-Rosenthal) by phase-contrast microscopy. Differential of hundred leukocytes were counted in Wright's stain smears distinguishing between mononuclear and polymorphonuclear amphophil leukocytes only. Lactate-dehydrogenase was analysed according to the recommendations of The Scandinavian Committee on Enzymes (1974) using a Cobas® Bio spectrophotometric centrifugal analyser

Table 1. Laboratory tests performed during the study. T and D are total and differential white cellcounts, LD is lactate-dehydrogenase, and Hb is hemoglobin.

Test:	Day:
Blood glucose	10, 17, 24, 31
White cellcounts (T and D), Hb and LD of dialysate-samples	10, 17, 24, 31
Total protein of a 24 hours dialysate-sample	10–11, 17–18, 24–25, 31–32
Bacteriological examinations	9, 30, 35

(Hoffmann-La Roche, Switzerland). Effluent hemoglobin was measured spectrophotometrically following centrifugation of the sample at 415 nanometers with absorption at 380 and 450 nanometers as background. Protein was measured spectrophotometrically in well mixed pools of 24 hours effluent from each animal at 540 nanometers using Biuret®-reagent. Calibration was performed against Standard Reference material 927 from National Bureau of Standards (NBS).
Day 9 and day 30, samples of dialysate were taken for bacterial cultivation. Extra bacteriological tests were performed in case of cloudy dialysate or in case the rabbits showed any clinical signs of peritonitis.
Pilot investigations demonstrated, that peritonitis showed certain clinical characteristics: An initial body-temperature peak which only lasted one day, after which the dialysate became purulent with a concomitant increase of viscosity and finally a decline of dialysate volume. In prolonged or severe cases a reduced food consumption was followed by a decrease in body weight.
These observations lead to the empirical definition of the diagnosis "peritonitis", being the simultaneous fulfillment of at least two of the three following criteria: 1. *Temperature exceeding 40.2°C* (normal range for control animals: 37.8–40.1), 2. *Weight-loss of more than 5 % in 5 days,* or *reduced food consumption* and 3. *Turbid dialysate.* Rabbits who ceased eating were euthanised and autopsied. Peritonitis was not treated with antibiotics.

Autopsy
During autopsy on day 35 or earlier in case of peritonitis, the catheter and the subcutaneous catheter-tunnel were inspected. The abdominal cavity was described macroscopically and any sign of peritonitis or infection as fibrin, adhesions, purulent exudate, hemorrhage and sclerosis were noted. An autopsy score was calculated based on the degree of the different manifestations at eight different sites (0 = no changes, 1 = edema, 2 = fibrin and 3 = adhesions or hemorrhage). Maximum autopsy score achievable was 24 point.
Specimens of the peritoneal membrane covering liver, spleen, diaphragm, omentum and abdominal wall were obtained for light microscopy (LM) and scanning electronmicroscopy (SEM) examinations. The specimens were fixed within one minute after stop of blood circulation.

Light microscopy (LM)
Tissue for LM was fixed in 4 % buffered formalin, processed conventionally to paraffin sections and stained with hematoxylin and eosin. Examinations of the histological sections were performed by one of the authors (MHM). The morphologic changes were classified as none, mild or severe on the basis of changes in the mesothelial cell-layer and the number of inflammatory cells present.

Scanning electron microscopy (SEM)
After fixation overnight with 2.5 % glutaraldehyde buffered to pH 7.2 with phosphate buffered saline (PBS), fixative vehicle 300 mOsm, the specimens were rinsed in PBS, dehydrated in ethanol, subjected to critical point drying, mounted on stubs, and coated by sputtering with a thin layer of gold (150 Å). The preparations were examined and photographed with a JEOL EM 100CX with SEM unit. Specimens covered with mesothelium, 5×3×2 mm, of the liver and the spleen were used for the SEM examinations. The evaluation was performed as a blind study by one of the authors (JC).

Statistical analyses:
Data were compared with Student's paired t-test (figures distributed normally) and Mann-Whitney's (Wilcoxon's) non-parametric test (Non-normally distributed figures). Confidence intervals were determined by means of the t-distribution. Correlations were estimated with parametric correlation analysis. Statisticall significance was accepted at $p < 0.05$.

Results

Peritonitis and tunnel infections

The incidence of peritonitis was 37 % in the CAPD-group, whereas no cases were seen among control rabbits.

Four of the CAPD-treated rabbits were euthanised pre-scheduled due to severe peritonitis. No tunnel infections were observed neither in the CAPD- nor in the control-group.

Table 2. The different bacterial species detected in the dialysate. n = number of animals. In seven incidents more than one type of bacteria was observed.

	Number of positive cultures	
Species	Healthy n = 29	Peritonitis n = 17
Micrococcus sp.	3	10
Staph. aureus	1	1
Staph. epid.	1	1
Strept. sanguis		2
α-hem. strept.	1	3
P. aeruginosa		2

Bacteriology

Bacteria were detected in the dialysate from 12 of the 17 rabbits with clinical peritonitis, while no growth of bacteria were demonstrated in 4 cases. One animal was not examined bacteriologically after peritonitis developed. The bacterial species found are shown in Table 2. In seven incidents more than one type of bacteria was observed.

Five of the rabbits without clinical peritonitis had a positive bacterial cultivation – three of which were rendered at repeated examinations. In the last two cases the bacteria were isolated at autopsy and the test could consequently not be repeated.

Biochemical parameters

The biochemical data (Table 3 and Fig. 3) showed considerable inter- and intra-individual variance. The dialysate contained more leukocytes than normal human dialysate during CAPD. Dialysate from clinic-

Table 3. Comparison of biochemical findings in dialysed, non-infected rabbits and animals with peritonitis. Figures are mean (95 %-confidence intervals). LD is lactate dehydrogenase, PMN is percentage of polymorphonuclear amphophil leukocytes in dialysate leukocytes. n = number of measurements.

	Non-infected, Dialysed	Peritonitis
Leukocytes ($\times 10^8$/l)	19.5 (12.9–26.0) n = 136	273 (112–433) n = 20
LD (U/l)	153.5 (115–190) n = 110	781 (464–1098) n = 17
PMN (percent)	41 (38–45) n = 88	42 (27–57) n = 12
Protein (g/l)	6.1 (5.6–6.6) n = 115	17.8 (14.9–20.7) n = 24
S-glucose (mmol/l)	6.3 (6.1–6.5) n = 142	6.4 (5.8–7.0) n = 27

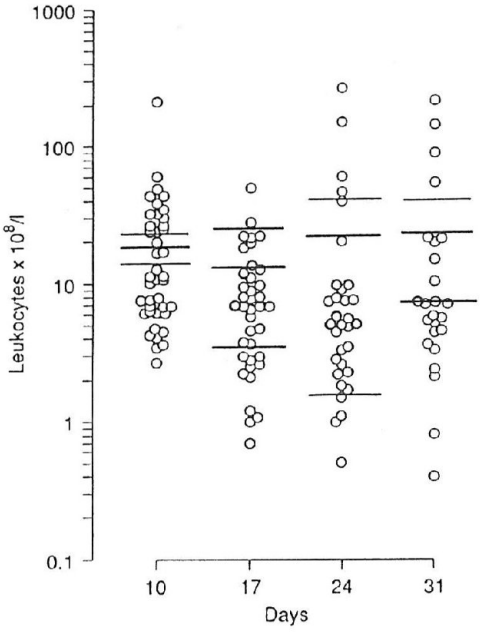

Fig. 3. Leukocyte count in dialysate (logarithmic scale) at different days during the study in non-infected animals. Counts are leukocytes × 10^8/l. Brackets illustrates mean and 95 %-confidence intervals.

Table 4. Comparison of clinical findings between dialysed, non-infected CAPD-rabbits and controls. Weight-gain is the measured difference from operation to autopsy. Figures are mean (95 %-confidence interval). n is number of measurements. N is the number of animals in each group.

	Dialysed, Non-infected	Controls
Temperature °C	39.41 (39.37–39.45) n = 721	39.29 (39.22–39.36) n = 242
Weight-gain g	270 (189–350) N = 46	307 (111–503) N = 10

ally uninfected rabbits contained (mean 95 %-confidence interval)) 19.5×10^8 (12.9–26.0) leukocytes/l, whereas human dialysate contains (median) 0.13×10^8, with an upper range of $4.58/10^8$ (*Antonsen et al.* 1991).

The protein-loss was 0.96 g/day (0.88–1.04) (mean (95 %-confidence interval)) for non-infected animals. It was not possible to calculate an indicative value of the protein-loss for the animals with peritonitis, because of sparse effluent-volume, but the dialysate protein concentration (g/l) was higher during peritonitis (Table 3).

The hemoglobin content in the dialysis effluent of the non-infected rabbits was low (1.6 mg/l (1.0–2.3)) (mean (95 %-confidence interval)) and constant during the course of the study. There was no correlation between the hemoglobin and the LD-content of the dialysate (Correlation coefficient (r) = 0.275, $p > 0.2$).

Clinical parameters

The clinical findings obtained from rabbits without clinical peritonitis were compared to those obtained from the controls (see Table 4).

Weight:

The mean body-weight (which did not differ significantly between the three groups at day one), shown in Fig. 4, increased significantly with time ($p < 0.001$) for all groups. Animals with peritonitis had a weight-gain of 115 g (57–172.7) (mean (95 %-confidence interval)) from operation to autopsy. An evaluation of the difference in weight-gain between the infected and non-infected animals is statistically inconclusive, as the diagnosis "peritonitis" was partly based upon loss of body-weight. There was no statistical correlation between peritonitis-frequency and initial body weight.

Temperature:

The mean body-temperature of the rabbits are listed in Table 4. The body-temperature was independent of dialysate leucocyte count ($r = 0.041$) and of the percentage of polymorphonuclear amphophils (PMN%) ($r = -0.189$).

Dialysate volume:

The dialysate volume was 58.1 % (56.3–59.8) (mean (95 %-confidence interval)) of the infused amount and increased during the test-period though with great variance ($r = 0.282$, $p < 0.001$). The dialysate volume varied inversely with dialysate protein content ($r = -0.663$, $p < 0.001$) and the dialysate leucocyte count ($r = -0.397$, $p < 0.001$).

Autopsy

Autopsy scores averaged 0.2 (range 0–1) for controls and 0.4 (0–5) for the non-nfected CAPD-treated rabbits (n.s.). Rabbits with clinical peritonitis scored 9.7 (0–17), which is significantly higher than the scores of

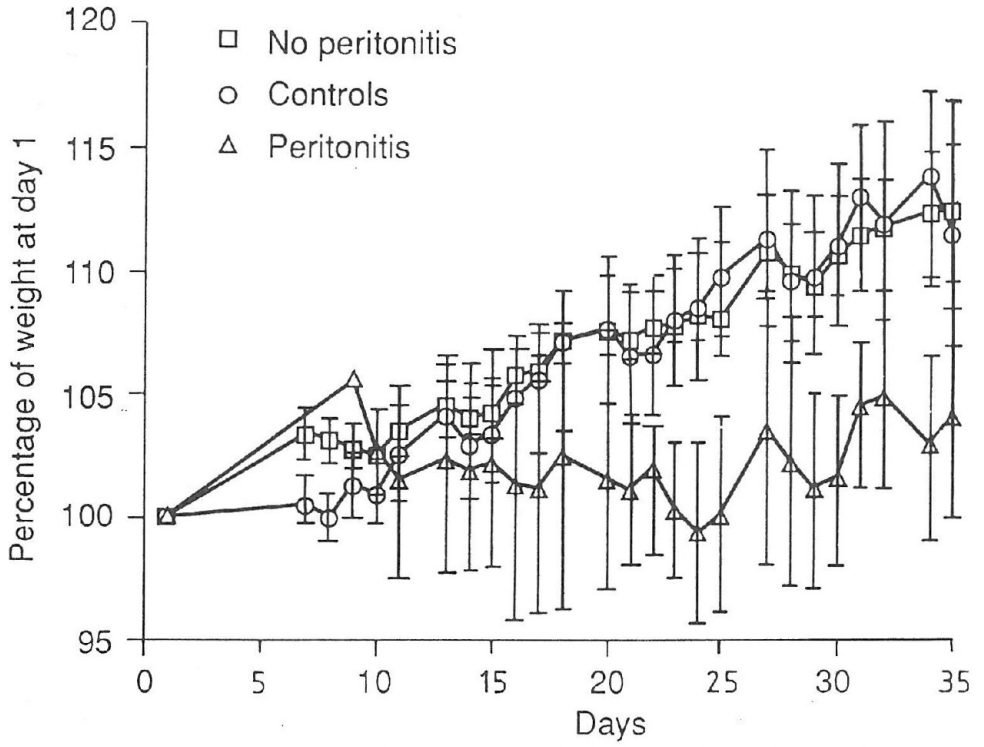

Fig. 4. Weight-gain in percentage of weight at operation. The initial weight was identical in the three groups. Figures illustrates mean and 80 %-confidence intervals.

controls and of non-infected animals ($p < 0.0.001$). Rabbits scored low when peritonitis developed late in the examination period.

Light microscopy:
In the control animals histopathological changes were found only at the omentum, where focal inflammatory reactions were observed. The dialysed non-infected animals had more severe and confluent changes at the omentum ($p < 0.05$), and non-consistent, minor degenerations of the parietal mesothelium.

Scanning electron microscopy:
In control animals all speciment from the liver and spleen had a microvillous mesothelial surface. No shrinking and detachment of mesothelial cells were observed. Attachment of leukocytes was not present on the mesothelial surface (Fig. 5A).
Thirteen of the twenty-seven dialysed animals without peritonitis had minor changes of the mesothelial surface consisting of focal areas with loss of microvilli and shrinking of the mesothelial cells (Fig. 5B). Except for the focal and sporadic occurrences of minor changes, the mesothelial surface had the same morphological appearance as in the controls.
All specimens from animals with peritonitis showed changes consisting of a diffuse attachment of leukocytes and focal detachment of the mesothelial cells (Fig. 5C).

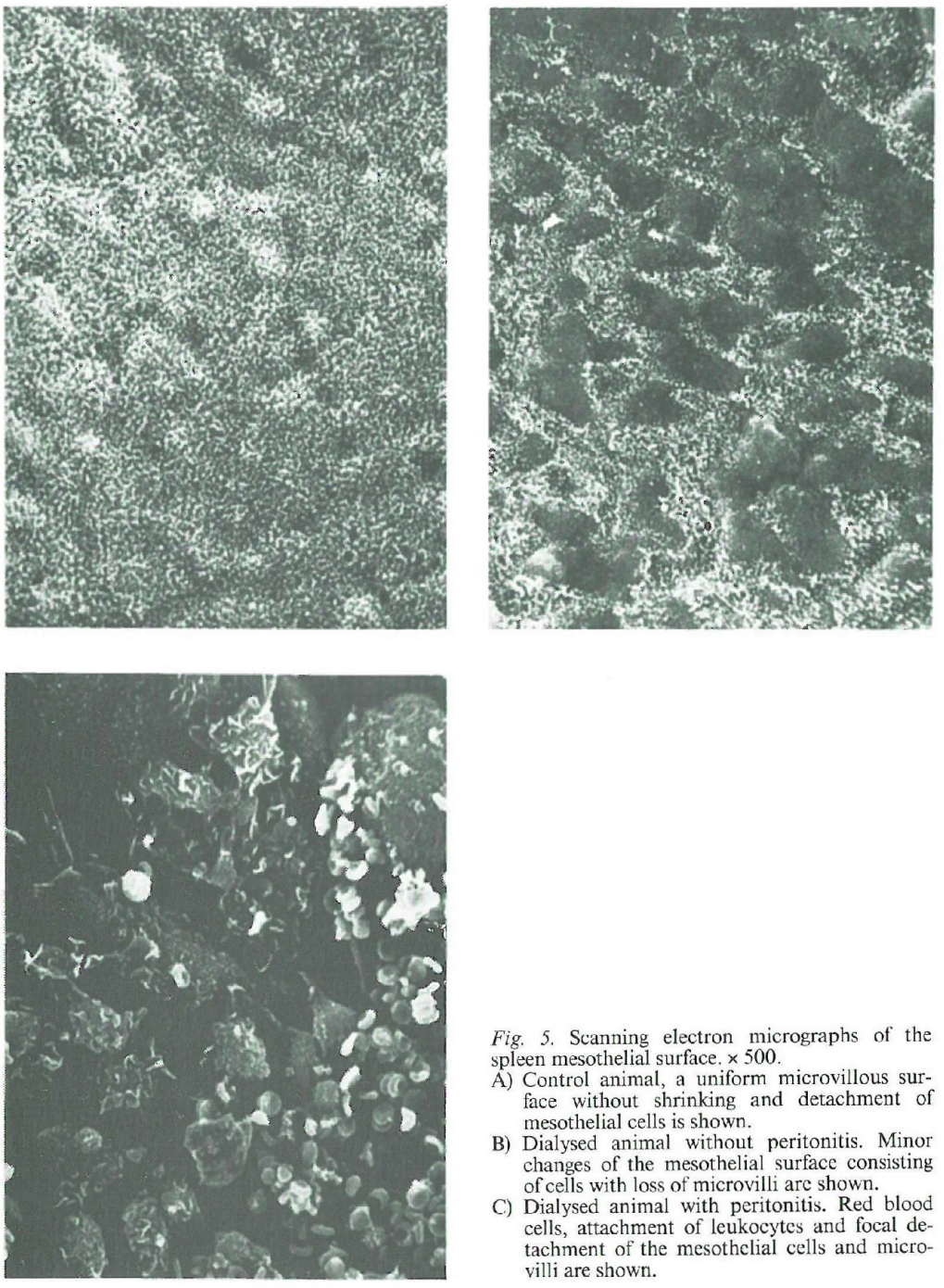

Fig. 5. Scanning electron micrographs of the spleen mesothelial surface. × 500.
A) Control animal, a uniform microvillous surface without shrinking and detachment of mesothelial cells is shown.
B) Dialysed animal without peritonitis. Minor changes of the mesothelial surface consisting of cells with loss of microvilli are shown.
C) Dialysed animal with peritonitis. Red blood cells, attachment of leukocytes and focal detachment of the mesothelial cells and microvilli are shown.

Discussion

The surgical procedure and the implantation of the peritoneal catheter in the rabbits did not cause infections. Only focal changes in the omentum were seen by LM. There were no signs of the catheter implantation affecting the well-being of the rabbits, either.

Since no incidents of omentum-wrapping were observed during our pilot investigations, we chose to omit the omentectomy in order to minimize peritoneal disturbances. Omental wrapping can be avoided by:

1. carefully directing the catheter caudally,
2. postponing dialysis for one week after operation and
3. omitting any kind of aspiration of dialysate – the abdominal cavity should be drained by gravity only.

The animals without peritonitis thrived well with significant weight-gain and no reduction of food-intake. Because of the subcutaneous connector-system, the animals were able to behave normally and move freely in their cages between the fluid-exchanges.

Peritonitis was, as in human clinic, the most important complication in this study. The peritonitis incidence of 37 % is not directly comparable to other models, as incidences were not reported in previous studies (*Gotloib et al.* 1982, *Traina et al.* 1986). The animals in these studies had a significant loss of body-weight (13 % in 14 days and 21 % in three weeks, respectively) and a high protein loss by the dialysate of 2 g/day and 1.3 g/day compared to 0.96 g/24 hrs in the present study.

Read et al. (1989) thus found that peritoneal catheters brought out through the skin, lead to infectious peritonitis within 3 weeks due to bacterial-biofilm spread along the catheter. Considering these observations and the fact that no clinical or macroscopic signs of catheter-tunnel infections developed, the subcutaneous closed-circuit system seems recommendable. Nevertheless this system necessitates one day of rest a week to reduce local edema and hyperemia of the skin at the site of needle-penetration. A mild skin-disinfection is recommended. The use of ethanol (70 %) caused skin irritation and was thus abandoned.

This study could be critized because of the use of non-nephrectomised rabbits, but we chose to work with intact animals for several reasons: The aim of the study was to test the application of the catheter and the CAPD-system and to establish an animal model for biocompatibility testing of dialysis solutions and not to examine the actual efficacy of the dialysis. Previous studies (*Gotloib et al.* 1982) have shown it difficult to keep uremic animals alive in spite of dialysis. Further more the well-being of the rabbits was of great importance.

CAPD might predispose to infectious peritonitis due to the removal of opsonins, immunoglobulins and inflammatory cells with the dialysate (*Keane et al.* 1984, *McGregor et al.* 1987, *Lamperi & Carozzi* 1986b), as well as to an impairment of the function of the peritoneal phagocytes (*Lamperi & Carozzi* 1986a, *Harvey et al.* 1988, *Bronswijk et al.* 1988, *Bronswijk et al.* 1989, *Schambye et al.* 1992), and to a direct irritation of the cells exposed to the CAPD-fluids (*Pedersen et al.* 1985, *Shaldon et al.* 1986, *Dobbie & Zaki* 1986, *Daugirdas et al.* 1986, *Yewdall et al.* 1986).

Whether the incidents of infectious peritonitis in our study were preceeded by initial chemical peritonitis or they were results of bacterial inoculations independent of the exposure of the abdominal cavity to the CAPD-treatment, is uncertain, but the former is supported by the large amount of lactate dehydrogenase (LD) in the dialysate of the non-infected animals. LD is a sign of cell-lysis. The lysed cells could be leukocytes, erythrocytes or mesothelial cells. As the free hemoglobin content of the dialysate was low and constant, as the mesothelial cells appeared normal or only slightly disturbed, when visualised by light- and scanning-electron-microscopy, and as LD-content correlated significantly to the leukocyte ($r = 0.666$ $p < 0.001$), the most obvious

origin must be the leukocytes. This indicates a constant state of irritation of the peritoneum, caused by the CAPD-treatment, as it was present in all dialysate samples.

In Conclusion: A model suitable for long term peritoneal dialysis in rabbits is presented. It has several advantages compared to other models: Surgery without omentectomy and a dialysis system, which allows the animals to thrive well and move freely in their cages between examinations.

The specially constructed, disposable dialysis equipment for rabbits proved satisfactory and easily handled.

The peritonitis incidence is still a problem. Perhaps it can be further diminished by the use of a mild disinfectant, which does not destroy the natural defence and skin lipid-layer of the rabbits.

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Summary

An animal model suitable for biocompatibility studies of peritoneal dialysis solutions is presented. It permits fluid exchanges to be performed 3 times a day for at least 28 days, thus simulating Continuous Ambulatory Peritoneal Dialysis (CAPD) in humans.

The surgical procedure is lenient, without omentectomy and nephrectomy. A closed, subcutaneous placed catheter-system permits the animals to thrive well and move freely between dialysis-fluid exchanges. A Y-shaped dialysis equipment which prevents air- and over-infusion was developed and is presented.

The surgical procedure and the implanted catheter caused only minor histological changes of the peritoneum. No catheter-tunnel infections were observed.

Our findings suggest that a slight peritoneal irritation is caused by the CAPD-solutions, as non-infected, dialysed animals had a slightly higher body-temperature than controls and as the LD-content of the dialysate was high probably indicating cell-lysis.

Though peritonitis was not avoided this experimental model using rabbits was found suitable for long term CAPD studies.

Sammendrag

Langtidsperitonealdialyse (CAPD) af nyreinsufficiente patienter nødvendiggør anvendelse af en meget vævsvenlig dialyseteknik. I det foreliggende arbejde præsenteres en dyremodel (kaniner) til undersøgelse heraf. Modellen udmærker sig på flere måder:

Den tillader intraperitonealt væskeskift 3 gange i døgnet i mindst 4 uger og simulerer således CAPD hos mennesker.

Operationsproceduren er enkel, og omentektomi kan undlades.

Det subkutant lejrede dialysekateter tillader dyrene at trives normalt og bevæge sig frit mellem væskeskiftene.

Af kontrolgruppen fremgik, at selve operationen og kateteret kun giver anledning til en minimal irritation af peritonealslimhinden.

Der beskrives en specielt udviklet connector til subkutan placering og et engangsdialyse- og prøveopsamlingssæt.

Dialysevæskerne viste sig suboptimalt vævsvenlige og gav anledning til en let peritonealreaktion med øgning af kropstemperaturen hos de dialyserede kaniner og et højt indhold af laktatdehydrogenase og leukocytter i dialyseudløbsvæsken. Bakteriel peritonitis kunne ikke undgås. Trods dette finder vi, at modellen er egnet til biokompatibilitetsstudier, der er yderst vanskelige at gennemføre i den humane klinik.

Yhteenveto / K. Pelkonen

Tutkimuksessa esitellään eläinmalli peritoneaalidialyysiliuosten biokompatibiliteetin tutkimiseen. Menetelmässä voidaan vaihtaa liuos kolmasti päivässä vähintään 28 päivän ajan, joka simuloi jatkuvaa ambulatorista peritoneaalidialyysiä (CAPD) ihmisellä.

Kirurgisesti tekniikka on helppo. Tutkimuksen yhteydessä kehitettiin ihonalaisesti asennettava suljettu katetri, joka sallii eläimelle vapaan liikuskelun liuostenvaihdon välillä ja estää sekä ilman pääsyn että yli-infuusion. Katetri aiheuttaa vain vähäisiä histologisia muutoksia peritoneumissa. Katetrikanavainfektioita ei havaittu.

Merkitsevästi kohonnut ruumiinlämpö ja dialysaatin LD-pitoisuus dialysoiduilla eläimillä merkkinä soluvauriosta viittaavat siihen, että CAPD-liuokset aiheuttavat lievää peritoneaalista ärsytystä. Peritoniitista huolimatta kokeellinen kanimalli tutkimuksen tekijöiden mielestä soveltuu pitkääikais-CAPD-tutkimuksiin.

References

Albert A, H. Takamatsu, EW Fonkalsrud: Absorption of glucose solutions from the peritoneal cavity in rabbits. Arch. Surg. 1984, *119*, 1247–1251.

Antonsen S, FB Pedersen, P Wang: Leukocytes in Peritoneal Dialysis Effluents. Perit. Dial. Int. 1991, *11*, 43–47.

Bronswijk Gv, HA Verbrugh, HCJM Heezius, Jvd Meulen, LP Oe, J Verhoef: Dialysis fluids and local host resistance in patients on continuous ambulatory peritoneal dialysis. Eur. J. Clin. Microbiol. Infect. Dis. 1988, *3*, 368–373.

Bronswijk Gv, HA Verbrugh, HJ Bos, ECJM Heezius, LP Oe, Jvd Meulen, J Verhoef: Cytotoxic effects of commercial continuous ambulatory peritoneal dialysis (CAPD) fluids and of bacterial exoproducts on human mesothelial cells in vitro. Perit. Dial. Int. 1989, *9*, 197–202.

Daugirdas JT, BC Gandhi, AP McShane, DJ Leehey, AY Chan, VR Jablokow, TS Ing: Peritoneal sclerosis in continuous ambulatory peritoneal dialysis patients dialyzed exclusively with lactate-buffered dialysate. Int. J. Artif. Organs 1986, *6*, 413–416.

Dobbie JW, MA Zaki: The ultrastructure of the parietal peritoneum in normal and uremic man and in patients on CAPD. In eds. Maher JF, JF Winchester: Frontiers in Peritoneal Dialysis. Field, Rich and Ass. N.Y. 1986, pp. 3–10.

Dunham CB, LJ Hak, JH Hull, AM Mattocks: Enhancement of peritoneal dialysis clearance with docusate sodium. Kidn. Int. 1981, *20*, 563–568.

Golper G, W Geerlings, NH Selwood, FP Brunner, AJ Wing: Peritoneal dialysis results in the EDTA registry. In ed. Nolph KD: Peritoneal Dialysis, 3rd Ed. Kluwer Academic Press. Dordrecht 1989, pp. 414–428.

Gotloib L, P Crasweller, H Rodella, DG Oreopoulos, G Zellerman, R Ogilvie, H Husdan, I. Brandes, S Vas: Experimental model for studies of continuous peritoneal dialysis in uremic rabbits. Nephron 1982, *31*, 254–259.

Harvey DM, KJ Sheppard, AG Morgan, J Fletcher: Neutrophil function in patients on continuous ambulatory peritoneal dialysis. Brit. J. Haematol. 1988, *68*, 276–278.

Keane WF, CM Comty, HA Verbrugh, PK Peterson: Opsonic deficiency of peritoneal dialysis effluent in continuous ambulatory peritoneal dialysis. Kidn. Int. 1984, *25*, 539–543.

Lamperi S, S Carozzi: Defective opsonic activity of peritoneal effluent during continuous ambulatory peritoneal dialysis (CAPD): Importance and prevention. Perit. Dial. Bull. 1986a, *2*, 87–92.

Lamperi S, S Carozzi: Immunologic pattern in CAPD patients with low or high peritonitis incidence. In eds. Maher JF, JF Winchester: Frontiers in Peritoneal Dialysis. Field, Rich and Ass. NY. 1986b, pp. 550–558.

Maher JF, M Cassetta, C Shea, DC Hohnadel: Peritoneal dialysis in rabbits. A study of transperitoneal thephylline flux and peritoneal permeability. Nephron 1978, *20*, 18–23.

McGregor SJ, JH Brock, JD Briggs, BJR Junor: Relationship of IgG, C3 and transferrin with opsonising and bacteriostatic activity of peritoneal fluid from CAPD patients and the incidence of peritonitis. Nephrol. Dial. Transplant. 1987, *2*, 551–556.

Pedersen FB, N Ryttov, P Deleuran, C Dragsholt, P Kildeberg: Acetate versus lactate in peritoneal dialysis solutions. Nephron 1985, *39*, 55–58.

Read RR, P Eberwein, MK Dasgupta, SK Grant, K Lam, JC Nickel, JW Costerton: Peritonitis in peritoneal dialysis: Bacterial colonization by biofilm spread along the catheter surface. Kidn. Int. 1989, *35*, 614–621.

Scandinavian Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended methods for the determination of 4 enzymes in blood. Scand. J. Clin. Lab. Invest. 1974, *33*, 291–306.

Schambye HT, FB Pedersen, P Wang: Cytotoxicity of continuous ambulatory peritoneal dialysis (CAPD) solutions. A biocompatibility study applying human polymorphonuclear granulocytes rather than laboratory animals. ATLA 1992, *20*, 275–279.

Shaldon S, KM Koch, E Quellhorst, CA Dinarello: Hazards of CAPD: Interleukin-1 production. In eds. Maher JF, JF Winchester: Frontiers in Peritoneal Dialysis. Field, Rich and Ass. N.Y. 1986, pp. 630–633.

Traina GL, A Celardo, M Arboix, M Bonati: Experimental model for pharmacokinetic studies during continuous peritoneal dialysis in the rabbit. J. Pharm. Meth. 1986, *15*, 133–141.

Vas SI: Peritonitis. In ed. Nolph KD: Peritoneal Dialysis. 3rd Ed. Kluver Academic Publications. Dordrecht 1989, pp. 261–288.

Yewdall VMA, D Bennett-Jones, S Davies, JS Cameron: Complement activation in the peritoneal dialysate of CAPD patients. Nephrol. Dial. Transplant. 1986, *1*, 111–112.