Nano particles: What are they doing in Peritoneal Dialysis

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1. Drug delivery: increased efficiency, targeted delivery
2. Imaging: Contrast/Fluorescent markers (tracking)
3. Blood purification/drug removal
4. Diagnostic chips (antigen/disease detection)
5. Implantable biosensors: detecting gene sequences

- Nanosize (2-12 nm)
- Improves solubility of poorly water soluble drugs
- Prolong half-life
- Sustained drug release
- Targeted drug delivery
- Bind Plasmid DNA efficiently
- Protects DNA from DNase
- Biocompatible
- Excellent cellular uptake
TGF-β1-siRNA delivery with nanoparticles inhibits peritoneal fibrosis

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Gene therapies may be promising for the treatment of peritoneal fibrosis (PF) in subjects undergoing peritoneal dialysis (PD). However, a method of delivering treatment genes to the peritoneum is lacking. We attempted to develop an in vivo small interfering RNA (siRNA) delivery system using liposome-based nanoparticles (NPs) to the peritoneum to inhibit PF. Transferring growth factor-TGF-β1-siRNA encapsulated in NPs (TGF-β1-siRNAs/NPs) dissolved in PD fluid was injected into the peritoneum of mice with PF three times a week for 2 weeks. TGF-β1-siRNAs/NPs knocked down TGF-β1 expression significantly in the peritoneum and inhibited peritoneal thickness with fibrous changes. TGF-β1-siRNAs/NPs also inhibited the increase of expression of a smooth muscle actin-positive myofibroblasts. These results suggest that the TGF-β1-siRNA delivery system with NPs described here could be an effective therapeutic option for PF in subjects undergoing PD.


Distribution of siRNAs-NPs in the peritoneum. Immunofluorescence analyses of intraperitoneally injected Cy3-labeled siRNAs-NPs and siRNAs alone in the peritoneum. DAPI, 4',6-diamidino-2-phenylindole.

TGF-β1-siRNA delivery with nanoparticles inhibits peritoneal fibrosis

**Representative immunofluorescence staining and quantitative analyses of TGF-β-positive cells in peritoneum tissue sections in each group.**

**Effects of TGF-β1-siRNAs-NPs on peritoneal fibrous thickness.** Quantitative analyses of peritoneal thickness in each group. Each group: n = 6, values are the mean ± s.e. (error bars) of at least three independent experiments. NS, not significant; *P < 0.05; **P < 0.01.

TGF-β1-siRNA delivery with nanoparticles inhibits peritoneal fibrosis

Knockdown of TGF-β1 expression in the peritoneum and inhibition of TGF-β1 expression in peritoneal drainage fluid by TGF-β1-siRNAs-NPs. TGF-β1 concentration was measured by ELISA in the peritoneal drainage fluid in each group. Each group: n = 6.

Nanotechnology and aden-associated virus-based decorin gene therapy ameliorates peritoneal fibrosis


Representative hematoxylin and eosin images showing abdominal wall parietal peritoneum thickness in treated and untreated animals.

Measurements of effects of GNP- and AAV-mediated decorin (dn) gene therapy on parietal peritoneum thickness. *P < 0.001. #P = NS.

Immunohistochemistry showing levels of α-smooth muscle actin (SMA) in treated vs. untreated animals

Quantitative real-time PCR showing differential change in α-SMA, transforming growth factor (TGF)-β, and VEGF expression in parietal peritoneum of treated vs. untreated animals. *P < 0.001 vs. control and *#P < 0.01 vs. dcn gene therapy via AA V and GNP.

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RESEARCH ARTICLE NANOMEDICINE
Liposome-supported peritoneal dialysis for detoxification of drugs and endogenous metabolites
Vincent Forster, Rea Deborah Signorell, Maurizio Roveri and Jean-Christophe Leroux

• Report Nano-sized liposome-based dialysis medium that increases clearance efficiency of low–molecular weight ionizable solutes and that could be used to treat various intoxications. This system is unique in that it concentrates the toxic compounds in the liposomal core and therefore generates a virtual sink in the PD fluid.
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Concept of LSPD: Weak bases, including drugs ("D") or ammonia (NH$_3$), diffuse from the blood to the peritoneal space and into the acidic interior of the transmembrane pH gradient liposomes. They become protonated (OH$^-$ and NH$_4^+$, respectively) in the liposome’s aqueous core, where they remain trapped because the diffusion of the protonated species through the phospholipid membrane is hindered.

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**B. Liposome drainage from the peritoneal space to the blood of small (250 nm) and large (850 nm) liposomes.** Small liposomes entered the systemic circulation rapidly (<5 hours), only 0.2% of the total injected dose of large vesicles could be found in the plasma after 4 hours of dialysis vs 2.3% of the small vesicles could be found in the plasma, giving rise to a slightly opalescent plasma (C).

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Comparison of in vitro ammonia extraction with in vivo animal data (n=5). Data are means ± SD.

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Total ammonia removed from HD, PD, and LSPD in vitro setups after 3 hours of simulation. The LSPD extraction efficiency for ammonia after 3 hours of dialysis approached that of simulated (in vitro) HD (3.6 versus 5.5 mmol of ammonia).
In a rodent model of overdose of verapamil with LSPD, the drug was continuously removed from the systemic circulation, with an efficacy that surpassed that of standard PD. At 4 and 12 hours of LSPD, the extracted drug concentrations exceeded those obtained with the icodextrin control solution (PD) by 30- and 80-fold, respectively.

Concentrations of drugs in dialysate after 3 hours of dialysis. Drugs were administered by oral gavage at t = 0 hour (30 mg/kg, except for verapamil: 50 mg/kg), followed by the intraperitoneal injection of the dialysis fluid 1 hour later (60 ml/kg).

Recovery time of Blood Pressure after verapamil instillation and treatment with PD vs LSPD.
Redox Nano Particles effectively suppress oxidative stress by scavenging Reactive Oxygen Species.

The objective of this study was to apply RNPs as a component of dialysate to reduce oxidative stress.

Porous silica nanoparticles were combined with Redox Nano Particles (RNPs) to enhance the effective adsorption capacity of low-molecular weight compounds.

Following the administration of Chlorhexidine into the peritoneal cavity for 1 week, the ROS level significantly increased. When siRNPs were administered, the ROS level stayed the same as that of the control. The administration of low-molecular weight TEMPOL also decreased the ROS level but not to the same level as that of siRNPs.

Histological assessments by performing Masson trichrome (MT) staining of peritoneum treated with saline (2 mL) (a), Chlorhexidine gluconate (CH) (b), CH + silica-containing redox nanoparticles (c) and CH + TEMPOL (d). These solutions were administered into the peritoneal cavity once a day for 1 week. The arrows indicate the thickness of the peritoneum. Scale bars = 200 μm.
Therapeutic effect of silica-containing redox nanoparticles (siRNPs) as an additive of peritoneal dialysis (PD)–dialysate against renal failure model mice

Vehicle: 2.4 mL of 4.25% glucose solution; RNP: 2.4 mL of 4.25% glucose solution containing RNPs and siRNPs: 2.4 mL of 4.25% glucose solution containing siRNPs for 6 h (a) and 9 h (b). *p < 0.05; **p < 0.01; ***p < 0.005

Design and use of silica-containing redox nanoparticles, siRNPs, for high-performance peritoneal dialysis

- The ROS scavenging characteristic of the siRNPs prevented oxidative damage of the peritoneum in EPS model rats
- The addition of siRNPs to dialysate also improved the therapeutic efficiency of acute renal failure model mice
- No blood uptake of siRNPs was observed when they were administered into the peritoneal cavity

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A Preliminary Report on the Effectiveness of Nanotechnology Anti-Microbial Spray in Preventing Tenckhoff Catheter Exit-Site Infection

- RCT using JUC spray which consists of 2% organosilicon quaternary ammonium salt and 98% distilled water using nano technology
- the antibacterial mechanism is not fully understood.
- proposed mechanisms relate to the physical structure of the nanoparticles causing the enhanced release of antibacterial metal ions from nanoparticle surfaces which interact with and penetrate into the bacteria
- JUC spray was applied to the TC exit site to compare the incidence of ESI with the usual standard care
- A simple, safe and sustainable technique, may be less expensive
A Preliminary Report on the Effectiveness of Nanotechnology Anti-Microbial Spray Dressing in Preventing Tenckhoff Catheter Exit-Site Infection

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<tr>
<td>No</td>
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<td>31 (94%)</td>
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Future Directions

- Nanoparticles are expected to be a new multi-functional material for use in peritoneal dialysis
- Enhanced/targeted drug delivery
- Efficient IP removal of systemic drugs/toxins
- Minimal systemic absorption
- Prolong the life of peritoneal membrane
- Useful in treatment of infections

THANKYOU