Risk factors of chronic renal failure: A single-center preliminary study

Pr Lionel Rostaing, MD, PhD
Dr Asma Allal, MD

Department of Nephrology and Organ Transplantation
Toulouse University Hospital France
**Objective:** to setup rheopheresis (DFPP) to treat patients with refractory peripheral arteriopathy (early 2015)
Multidisciplinary approach

- Refractory peripheral arteriopathy: how to manage the very severe patients?

- Multidisciplinary meetings on a monthly basis:
  - Vascular surgeon
  - Vascular physician
  - Nephrologist
  - Diabetologist/diabetic foot physician
To discuss the medical files of patients with refractory peripheral arteriopathy:

- Local prostacyclin infusion?
- Hyperbaric oxygen therapy?
- Amputation?
- Is there any other option?
  - Double-filtration plasmapheresis (DFPP)?
When do we use DFPP in our unit?

- Desensitization protocols for ABOi and/or HLAi kidney-transplant recipients
- Antibody-mediated rejection
- Refractory hypercholesterolemia
- Diabetic foot with severe ischemic lesions
- Stage IV distal arteriopathy in end-stage renal-disease patients
- Age-related macula degeneration
Techniques and Disposables

- Extracorporeal circuit: central venous catheter or arteriovenous fistula
- 1st filter: plasma separation: plasma filtered with Plasmaflo OP-05W
- 2nd filter ER 4000: plasma treatment
- PLASAUTO monitoring: management of the blood circuit and the plasma circuit
- Citrate anticoagulation (on an aspiration line) and CaCl$_2$ compensation on the return venous line
- ~1.5 plasmatic volumes
- Substitution: 20 g of albumin
- No compensation for coagulation factors
- Monitoring of clinical and biological parameters, including tPCO$_2$
Circuit diagram
Lipoprotein apheresis (LA) in patients with peripheral artery disease and hyperlipoproteinemia (a).

Poller WC, Dreger H, Morgera S, Berger A, Flessenkämper I, Enke-Melzer K.


**Abstract**

**OBJECTIVE:**
Hyperlipoproteinemia(a) [Lp(a)-HLP] is a major risk factor for severe atherosclerosis. The present investigation sought to assess the effect of lipoprotein apheresis (LA) in patients with peripheral artery disease (PAD) and Lp(a)-HLP.

**CONCLUSION:**
LA improves circulation, oxygen supply, level of pain and walking distance in patients with severe PAD and Lp(a)-HLP. The frequency of revascularization procedures is strongly reduced under LA treatment.
Objectives of rheopheresis

Means:

- To improve blood flow at the microcirculation level
- To improve viscosity
- To reduce high molecular-weight molecules

Results

- Improvement in tissue oxygenation
- To accelerate wound healing
- To reduce the need for amputation
Molecules that are removed

- Fibrinogen
- Alpha-2 macroglobulin
- Cholesterol/triglycerides
- LDL, Lp(a)
- Fibronectin
- IgM
- Orosomucoid
- .........
Patients

- 6 patients with severe distal arteriopathy: of these
  - One chronic hemodialysis patient aged 67 with toes and fingers necrosis
  - One chronic hemodialysis patient aged 54 with ischemic toes on one foot
  - One type I diabetic hemodialysis patient aged 49 with ischemic toes on 1 foot plus ischemic ulcer on Achille’s heel on the other foot
  - One diabetic hemodialysis patient aged 48 with bilateral necrosis on the feet
  - One diabetic non-dialyzed (eGFR = 40 mL/min) patient aged 65 with distal necrotic lesions on both feet
  - One kidney transplant patient aged 52 with chronic kidney disease (eGFR= 30 mL/min) and a single necrotic toe
Implementation of rheopheresis in our unit

- Support from HemaT with an onsite very efficient trainer for 3 weeks
- 100% of our nursing staff are now trained
- The nursing staff are very motivated (innovative techniques)
- Very close collaboration between nurses and physicians
- No rheopheresis conducted at weekends

=> scheduling is modulated
1st patient: Mr Delv....

- Age: 66 years
- Chronic hemodialysis since 1991; HCV (+)/ RNA (+)
- 1993: 1st kidney transplantation
- 2003:
  - End-stage renal disease (chronic rejection)
  - Calciphylaxis (toes): daily hemodialysis, hyperbaric oxygen therapy: good outcome
  - Parathyroidectomy
- January 2006:
  - 2nd kidney transplantation
  - Hyperparathyroidism recurrence (Cinacalcet)
- June 2014: arterio-venous fistula setup
- August 2014: return to hemodialysis
- Nov. 2014: ligation of arterio-venous fistula because of downstream finger necrosis
Vascular history

- **Right arm:**
  - Nov. 2014: necrosis of fingers; ligation of humero-cephalic arterio-venous fistula; amputation of some fingers.

- **Left lower leg:**
  - Diffuse mediacalcosis; numerous lesions; dry necrosis of toes; trans-tibial amputation with delayed wound healing; pain ++++

- **Right lower leg:**
  - Necrotic cutaneous lesions of four toes, plus the above disorders.
  - May 2015: rapid onset of osteoarthritis of the 1st metatarsal; ineffective antibiotherapy;
    - At this point we started DFPP sessions
Finger necrosis, downstream of arterio-venous Steal syndrome
Rheopheresis protocol

- 2.5--3 L of plasma
- 9.5--11.5 L of treated blood
- Blood flow: 60--100 mL/min
- ACDA: 1/60, then decreasing to 1/80
- ClCa: 4 cm$^3$/h, then 2 cm$^3$/h
- Substitution: 20 g of albumin during the session
- Tandem procedure with hemodialysis
DFPP program

- 1\textsuperscript{st} week: 2 sessions = 2
- 2\textsuperscript{nd} and 3\textsuperscript{rd} weeks: 3 sessions = 6
- 4\textsuperscript{th} and 5\textsuperscript{th} weeks: 2 sessions = 4
- 6\textsuperscript{th} to 23\textsuperscript{rd} week: 1 session = 16

(1 week w/o DFPP)

- At the moment: 1 session every 2 weeks

- Total: 29 sessions in 6 months
Pain, general status

- Reduction of major analgesics
  - First 2 weeks: 1 vial paracetamol/d + 1 vial of nefopam chlorhydrate/d + oxycodone chlorhydrate 5 mg/d
  - 3rd week: 1 vial of nefopam chlorhydrate/d + oxycodone chlorhydrate 5 mg/d
  - 4th & 5th week: 1 nefopam chlorhydrate on demand +/- paracetamol +/- oxycodone for cutaneous care (10 dfpp)
  - 6th week: analgesics are very rarely taken (13 dfpp)
  - At present NO analgesic, 29 dfpp

- Steady increase in dry weight; improvement of general status.
CRP at pre- and post-DFPP
Hb at pre- and post-DFPP

[Graph showing Hb levels at pre- and post-DFPP]
Fibrinogen at pre- and post-DFPP
Albumin at pre- and post-DFPP

[Graph showing albumin levels pre- and post-DFPP]
Alpha 2 macrog at pre- and post
Orosomucoid at pre- and post-DFPP

![Graph showing orosomucoid levels at pre- and post-DFPP](image-url)
Total cholesterol at pre- and post-DFPP
Triglycerides at pre- and post-DFPP
22nd May 2015 after 10 DFPP sessions
Before DFPP
June 16th 2015, 14 DFPP sessions
### tCPO$_2$ outcomes

<table>
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<tr>
<th></th>
<th>06/02/2015</th>
<th>Before DFPP</th>
<th>18/05/15</th>
<th>9 DFPP</th>
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<tr>
<td></td>
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<tr>
<td>Foot</td>
<td>5</td>
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<td>Amputed</td>
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<tr>
<td>1/3 distal leg</td>
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<td>57</td>
<td>ND</td>
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<td>1/3 distal thigh</td>
<td>44</td>
<td>82</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>
Because of these improvements, surgery could be limited:

- Trans-metatarsal amputation
- Left hand finger amputation
26/8/15, 24 DFPP sessions

26/09/15, 28 DFPP sessions
29 DFPP sessions

5/10/15

10/10/15
As of 23/10/15, DFPP every 2 weeks

01/16 / healing
DELM....AVRIL 2016
2nd patient

- Mr Len… aged 64 years
- Type II insulin-dependent diabetes
- Hypertension
- Ischemic cardiopathy (multiple stents)
- Renal artery stents
- Aorto-bifemoral bypass
- Distal arteriopathy (stage IV) with 3 months of hospitalization and vascular surgery
Patient 2 (cont’d)

- January 2015: emergency arterial femoro-popliteal bypass due to toe necrosis (right foot)

- May 2015: thrombosis and an arterial femoro-popliteal bypass, delayed wound healing, major pain, super infections.

- May 2015: last-chance treatment: DFPP, using a central venous catheter

- July 2015: had to stop DFPP because of infection around the central venous catheter. Skin lesions were partially improved, but the patient had to undergo toe amputations on both feet
19 May until 21 July: 16 DFPP sessions (3 L of plasma were treated each time)
  • 3 times/week for 2 weeks
  • 2 times/week for 2 weeks
  • 1 time/week for 5 weeks
July: DFPP was stopped due to catheter tunnelitis
End of July: toe amputation
September 2015: the patient was doing well
3rd patient

- Mrs Gran..., aged 48 years
- Type 1 diabetes
- Chronic hemodialysis for 11 months
- Distal arteriopathy (stage IV); very low tPCO$_2$ in both legs
- May 2015: right arterial femoro-popliteal bypass + right iliac artery stenting
  - However, huge pain. Thus, we decided to implement DFPP
- June 2015: rheopheresis: 7 DFPP sessions,
  - 3 times/week for 1 week
  - 2 times/week for 2 weeks
July 2015: Severe sepsis + endocarditis + distal critical ischemia of the left lower limb: transfemoral amputation

September 2015: necrosis of the right large toe; result: a favorable outcome

October 2015: good general health; no skin lesions
3rd Patient
So far....

- We treated 6 patients

  - Pt 1: 29 sessions: alleviation of pain; limitation of amputation

  - Pt 2: 16 sessions: alleviation of pain; limitation of amputation (stop because of catheter tunnelitis)

  - Pt 3: 7 sessions: alleviation of pain; limitation of amputation (stop because of sepsis)

  - Pt 4: 9 sessions: alleviation of pain; limitation of amputation

  - Pt 5: 19 sessions; still ongoing; no amputation; alleviation of pain

  - Pt 6: 28 sessions; still ongoing; no amputation; alleviation of pain
Conclusion

- DFPP is well tolerated
- Problem with vascular access in non-dialysis patients
- Spectacular results with regards to pain (soon after 5 DFPP sessions)
- Multidisciplinary approach with the major aim of avoiding/reducing amputation
- tPCO$_2$ monitoring
- Earlier DFPP treatment could be valuable
- DFPP treatment could limit the extent of amputation: thus, help rehabilitation after amputation.