Plasmapheresis for Intractable Itch in Chronic Cholestatic Liver Disease

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Background

- Pruritus (itch) is a common complication of chronic cholestatic liver disease.

- Intractable itch can considerably reduce patients’ quality of life.

- Intractable itch, that is refractory to medical therapies, can be one of the indications for liver transplantation.

- The pathogenesis of itch in this group of patients remains uncertain.
Aims

• Primary aim
  ▪ Assess the effectiveness of plasmapheresis as a treatment modality for intractable itch, due to chronic cholestatic liver disease, that has been refractory to medical therapies.

• Secondary aims
  ▪ Assess the tolerability, safety, and acceptability of plasmapheresis in the above patient population.
Methods

• Population
  ▪ Patients with intractable itch due to chronic cholestatic liver disease (mainly primary biliary cirrhosis).
  ▪ Patients who had undergone at least 5 sessions.

• Location
  ▪ Clinical apheresis units of Belfast, Edinburgh, and Glasgow.

• Time period
  ▪ 1st of November 2008 to 31st of October 2015.
Methods

• **Medical records**
  - Demographics.
  - Exact diagnosis.
  - Medical therapies.
  - Details regarding plasmapheresis.
  - Complications of plasmapheresis.

• **Patient questionnaires**
  - Belfast and Edinburgh.
  - Assess the effectiveness and acceptability of plasmapheresis.
Results

• Population
  ▪ 19 patients.
  ▪ 17 women (89%) and 2 men (11%).
  ▪ The median age was 48 (min to max range: 20-64).

• Diagnosis
  ▪ Primary biliary cirrhosis: 16 patients (84%).
  ▪ Primary sclerosing cholangitis: 2 patients (11%).
  ▪ Microvillus inclusion disease: 1 patient (5%).
Results

- **Medical therapies**
  - The median number of therapies was 4 (min to max range: 1-7).
  - Cholestyramine, chlorphphenamine, rifampicin, colesvelam, ursodeoxycholic acid, naltrexone, SSRI, phototherapy, etc.

- **Plasmapheresis**
  - One plasma volume exchanged at each session.
  - The median number of procedures was 21 (min to max range: 6-128).
  - Documented symptomatic improvement.
Results

• **Questionnaires** (10 completed)
  - The mean pre and post plasmapheresis itch scores were 9.9 (median=10) and 3.2 (median=3.5) respectively ($Z=-2.818; p=0.005$).
  - The most frequently reported benefits from relief of itch were improved sleep, less fatigue, better mood, and enhanced social interactions.
  - All patients agreed this was an acceptable treatment option for intractable itch that had failed multiple lines of medical therapy.
Results

- **Discontinuation**
  - 13 patients discontinued plasmapheresis.
  - Reasons included:
    - Liver transplant (n=6; 32%).
    - Difficulties with venous access (n=4; 21%).
    - Death due to unrelated condition (n=1; 5%).
    - Effective alternative therapy (n=1; 5%).
    - Loss of beneficial effect (n=1; 5%).
Results

• Complications
  ▪ The procedure was generally well tolerated.
  ▪ The most frequent complication was citrate toxicity (n=13; 68%).
  ▪ Other complications included:-
    • Central venous catheter infection (n=4; 21%).
    • Hypotension (n=4; 21%).
    • Lightheadedness (n=3; 16%).
    • Line-associated thrombosis (n=1; 5%).
    • Panic attack (n=1; 5%).
Conclusion

- In this single-arm series, plasmapheresis appeared an effective, well tolerated, and acceptable treatment option for patients with intractable itch due to chronic cholestatic liver disease.
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Remaining Questions - What Exactly Are We Removing?

- Unlike the usual situation with ‘routine’ plasma exchange in autoimmune disease, any efficacy of plasma exchange in cholestatic liver disease must be due to removal of small-molecule pruritogens.

- The exact nature of the pruritogen in cholestatic liver disease remains disputed, but there is increasing evidence that bile acids are key culprits.
Circulating bile acids are highly protein bound (to HDL lipoprotein and also to albumin, $\alpha_1$ acid glycoprotein, and transferrin) and hence are predicted to be removed efficiently from the bloodstream by plasma exchange.

Efficacy for plasma exchange in cholestatic liver disease therefore makes biological sense.

Nevertheless, further work is indicated

- A sham-controlled study of plasma exchange to ensure we are not just providing an expensive placebo.
- Serial measurements of circulating bile acid levels pre and post plasma exchange.