Bile-associated cast nephropathy and consequent tubular damage are relevant causes of acute kidney injury (AKI) during severe liver dysfunction. The mechanisms of bilirubin-associated AKI are mainly due to tubular cell apoptosis consequent to mitochondrial dysfunction following cast formation.

Liver-type Fatty Acid Binding Protein (L-FABP) is a 15 KDa peptide belonging to free fatty acid family able to bind hydrophobic molecules including bilirubin. During liver failure, the increase of L-FABP plasma levels enhances bilirubin uptake and consequent apoptosis of tubular cells through a mechanisms dependent on megalin, the endocytic receptor located on the luminal surface of tubular cells.

**Aim of the study**

To investigate the protective role of Coupled Plasma Filtration Adsorption (CPFA) on bile cast nephropathy through L-FABP and bilirubin adsorption by the hydrophobic polystyrene resin.

**Methods**

We reported the case of a kidney transplanted patient who developed sepsis, AKI and liver dysfunction treated by CPFA (Fig. 1). We evaluated plasma levels of bilirubin and L-FABP. Renal biopsies, urine sediment, NGAL and immunoelectrophoresis were also performed at different time points.

**In vitro**, we tested:
1. static adsorption of L-FABP to the polystyrene resin; 2. Cytotoxic (XTT assay) and pro-apoptotic effect (TUNEL assay) of patient’s plasma drawn before and after CPFA on cultured human tubular cells. The role of L-FABP was confirmed in tubular cells engineered to knock-down megalin, the L-FABP receptor, by small interfering RNA (siRNA).

**Results**

A 50-year-old man was subjected to kidney transplantation with slow recovery of graft function (Fig. 2). Kidney biopsy revealed acute tubulo-interstitial and vascular rejection treated by Thymoglobulin. He then developed septic shock for Legionella with multiple organ failure (serum creatinine 5.2 mg/dl and oliguria requiring RRT; bilirubin 42 mg/dl with liver biopsy showing marked cholestasis; plasma L-FABP 52 ng/ml). Urine analysis showed the presence of tubular cells, intense positivity for bilirubin and presence of low molecular weight proteins such as alpha-1 microglobulin and retinol binding protein: urine NGAL level was 356 ng/ml. A new kidney biopsy showing bile cast nephropathy and severe tubular injury was performed. After CPFA was started, we observed an increase of urine output and a concomitant decrease of bilirubin (Fig. 3), plasma L-FABP (Fig. 4) and urine NGAL (Fig. 5) and low molecular weight proteins (Fig. 6). *In vitro*, the polystyrene resin efficiently adsorbed L-FABP (100% adsorption after 15 minutes, 75% after 10 hours) (Fig. 7). After CPFA treatment, the cytotoxic (XTT assay in Fig. 8) and pro-apoptotic (TUNEL assay in Fig. 9) effect of patient’s plasma on cultured human tubular epithelial cells were all significantly reduced. In addition, plasma-induced apoptosis was dependent on the presence of megalin, the L-FABP receptor located on tubular cell surface (Fig. 10).

**Conclusions**

CPFA may have a protective role in AKI associated with liver failure through the direct adsorption of bilirubin and L-FABP to the synthetic polystrene resin. The decrease of bilirubin and L-FABP plasma levels may limit cast formation and tubular apoptosis (Fig. 11).