

INDOSSYL SULPHATE AND P-CRESOL SULPHATE EFFECTIVE REMOVAL BY DYVINILBENZENE RESIN IN PATIENT IN HEMODIALYSIS

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Background/aims

High serum levels of indoxyl sulfate (IS) and p-cresol sulfate (PCS), nephrovascular uremic toxins, are associated with high risk of cardiovascular disease in hemodialysis (HD) patients. IS and PCS circulate in the blood stream mainly bound to albumin (> 90%) and minimally as free solutes and accumulate in patients with chronic and terminal renal disease. The high affinity of IS and PCS for albumin makes their removal from the blood very critical through conventional dialytic techniques.

The aim of this study was to evaluate the efficacy of a symbiotic integrator and divinylbenzene resin in the reduction of serum IS and PCS levels.

Methods

In vitro: an experimental solution (3.5 L, pH 7.4) containing bovine serum albumin, IS and PCS with analogous concentrations to those of hemodialysis patients, was circulated (flow of 300 mL/min) in a closed circuit including the resin to be tested (DVB coated with polyvinylpyrrolidone and Cellulose functionalized with hexadecyl chains) for 5h. Total and free IS and PCS concentrations were quantified by tandem mass spectrometry (LC/ESI-MS/MS) every hour until the end. IS and PCS removed amount was evaluated by applying the mass balance formula and the total percentage reduction formula. The albumin concentration was evaluated by the Bradford method.

Trial: randomized placebo-controlled single blind pilot trial in HD patients. 13 patients in traditional HD were randomized to take the symbiotic NATUREN G (n = 7) or placebo (n = 6) for 2 months, and subsequently undergoing dialysis with PS-DVB resin. After enrollment of the symbiotic (T2) and after dialysis with PS-DVB (T3), routine blood count parameters and serum IS and PCS levels were evaluated at enrollment (T0).

Results

In vitro: In vitro, DVB resin is more effective in removing total IS and PCS (56%, 51%) and free (70%, 77%, Figure 1).

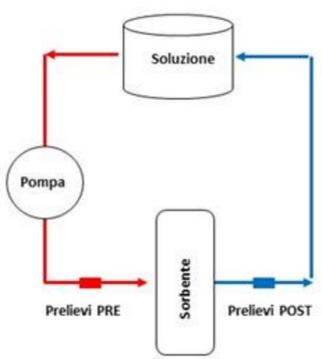
Trial: 11 patients completed the study. Early treatment with the symbiotic does not vary serum IS and PCS levels. Dialysis with DVB resin reduces serum IS and PCS levels (38% vs 27%, p = 0.04, 31% vs 23%, p = 0.02, Figure 2) compared to traditional dialysis.

Esperimenti in Vitro:

Ricircolo di una soluzione sperimentale [3,5 L contenente Albumina sierica bovina: 3,5-5 g/100ml (BSA), pCS: 40 ppm (1,2 g), IS: 30 ppm (0,72 g)] in un circuito chiuso contenente la resina da testare, mediante una pompa peristaltica ad un flusso di 300 ml/min. Durata dell'esperimento: 6 h.

Protocollo raccolta prelievi

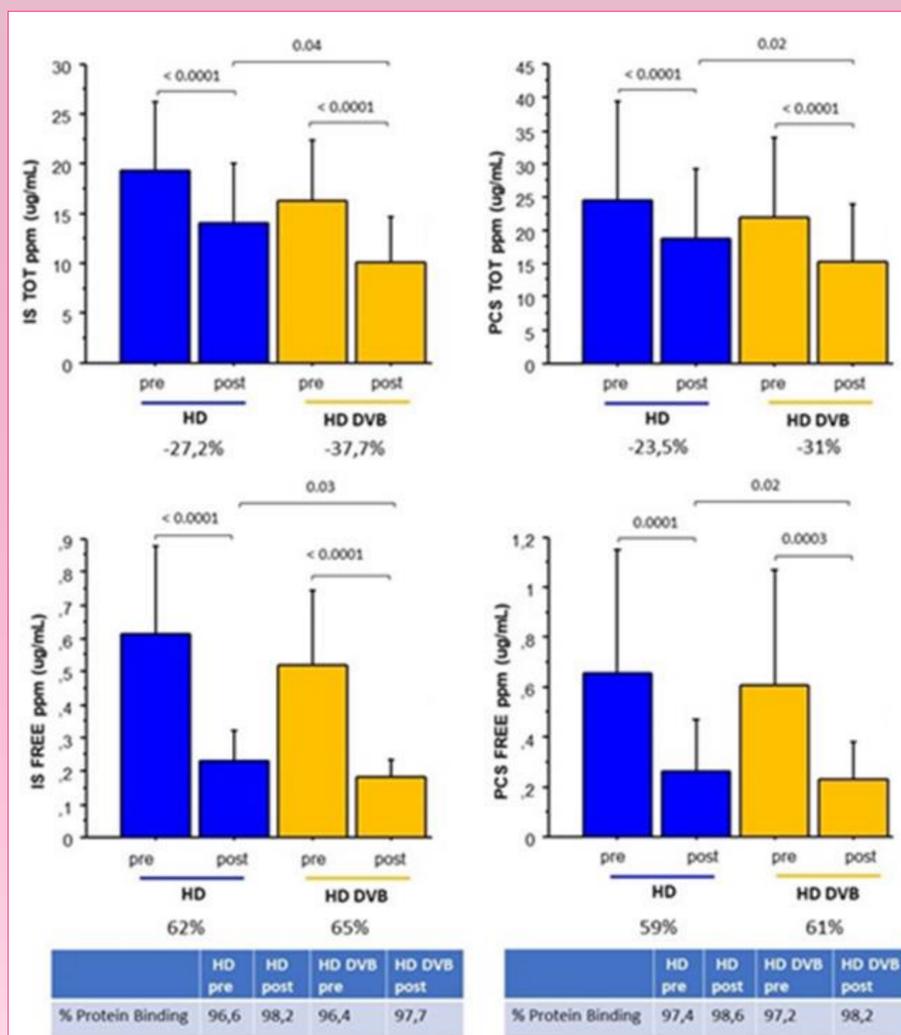
Tempi	Descrizione	Tipologia di prelievo
t ₀	Prelievo all'inizio della prova	Basale della soluzione
t ₃₀	Prelievo a 30 minuti dall'inizio	Pre / Post
t _n	Prelievo dopo ogni ora (n=1, 2..6)	Pre / Post
t _{END}	Prelievo al termine della prova	Finale della soluzione



Risultati. 2 Esperimenti di perfusione per ogni cartuccia; 18 campioni per ogni esperimento da processare e analizzare mediante HPLC-MS/MS. Mass Balance: totale quantità (g) di una molecola rimossa da una soluzione di volume noto [MB = (Ci - Cf)xVol]

Esperimento	Mass Balance IS mg (media)	Riduzione IS	Mass Balance PCS mg (medio)	Riduzione PCS	Riduzione BSA
Cartuccia DVB	Tot 42,63 Free 8,67	Tot 56% Free 70%	Tot 56,7 Free 11,65	Tot 51% Free 77%	13%
Cartuccia Cellulosa	Tot 23,4 Free 1,4	Tot 27% Free 23%	Tot 36,5 Free 6,6	Tot 30% Free 37%	10%

Figura 1



Conclusion

Dialysis with DVB reduces serum IS and PCS levels to a greater extent than traditional dialysis. To confirm the results obtained, long-term experimentation is expected in a larger series of patients.