GROWTH FACTORS AS NOVEL BIOCOMPATIBILITY MARKERS IN CHILDREN ON CHRONIC DIALYSIS

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INTRODUCTION

Inflammation, immune deficiency and enhanced apoptosis are features characteristic for chronic kidney disease (CKD), aggravating with the dialysis commencement and the use of bioincompatible materials, such as dialyzer membranes and peritoneal fluids. Both hemodialysis (HD) and peritoneal dialysis (PD) influence multiple phenomena, such as stress reaction, cell migration, apoptosis or oxidative stress. The variety of those processes justifies continuous search for perfect markers of dialysis biocompatibility.

First candidates are growth factors, the important players in the accommodation to stress conditions and markers of cell damage. Among these, the cytoprotective epidermal growth factor (EGF), as well as the stress-responsive growth differentiation factor (GDF)15, may be of paramount value as indices of response to stress conditions in patients on chronic dialysis. However, none of them has been tested for their applicability as biocompatibility markers in that population – either in children or in adults.

Survivin is a newly discovered anti-apoptotic protein, not assessed in the CKD population yet, irrespective of the patients' age.

Taking into account the complexity of above mentioned reactions, characteristic for renal replacement therapy, we decided to explore whether peritoneal dialysis or hemodialysis, and especially a single HD session, may have an effect on such parameters as EGF, GDF15 or survivin, in children with end stage renal disease (ESRD).

THE AIM OF OUR STUDY WAS TO:

1. assess the serum concentrations of EGF, GDF15 and survivin in children on chronic peritoneal dialysis and on chronic hemodialysis,
2. evaluate the impact of a single hemodialysis session on their levels,
3. analyze their potential applicability as bioincompatibility indices.

MATERIAL

Seventy one patients enrolled in the study were divided into 3 groups:

- 22 children (12 girls, 10 boys; median age 10y) on automated peritoneal dialysis (APD) (Baxter, Home choice)
- 19 patients (10 girls, 9 boys; median age 13.5y) hemodialyzed (HD) on polysulfone membranes
- 30 children (16 girls, 14 boys; median age 10y) with primary nocturnal enuresis and normal kidney function, who served as controls.

METHODS

Blood samples were drawn after an overnight fast from peripheral veins in APD patients and in controls, in HD patients – from the afferent line of the first-use dialyzer both before starting a single session and after finishing it. Samples were clotted for 30 minutes, centrifuged at room temperature for 10 minutes, and then serum was stored at -20°C until assayed. Serum concentrations of EGF, GDF15 and survivin were evaluated by commercially available ELISA kits (R&D Systems). Each sample was tested in duplicate and arithmetical mean was considered a final result. Measurements were performed according to the manufacturer's instructions, results were calculated by reference to standard curves.

In all patients hsCRP, as a marker of inflammation (assessed by nephelometry, Dade Behring), was evaluated.

Results are expressed as median values and interquartile ranges. Multiple comparisons and comparisons in pairs were evaluated by using nonparametric tests (Kruskall–Wallis, Mann-Whitney U, Wilcoxon). Statistical analysis was performed using the package Statistica ver. 10.0. A p value < 0.05 was considered significant.

RESULTS

The median values of GDF15 and survivin were significantly increased, whereas the EGF concentrations - significantly diminished, in children on dialysis vs. controls. The GDF15 and survivin levels were higher in HD than APD patients, in contrast to the EGF median values, elevated in APD children compared to the HD ones. The serum concentrations of survivin have diminished after a single HD session to the values comparable to those in APD patients. Contrarily, the level of GDF15 has increased, thus after the HD session it remained higher than in children on peritoneal dialysis. Likewise, a single HD session has raised the EGF concentrations to such levels that they became slightly, but significantly higher than the values in APD children.

CONCLUSIONS

1. The elevated levels of stress-responsive GDF15 and anti-apoptotic survivin show the stimulation of both inflammatory and apoptotic activities on chronic dialysis.
2. The decreased concentrations of cytoprotective EGF point at the inefficiency of protection against bioincompatible materials in that group of patients.
3. The diversity between APD and HD values, as well as the impact of a single HD session, on the concentrations of examined parameters, suggest that GDF15, EGF and survivin may serve as new biocompatibility markers in children on chronic dialysis.

Figure 1 EGF serum concentrations in examined groups.

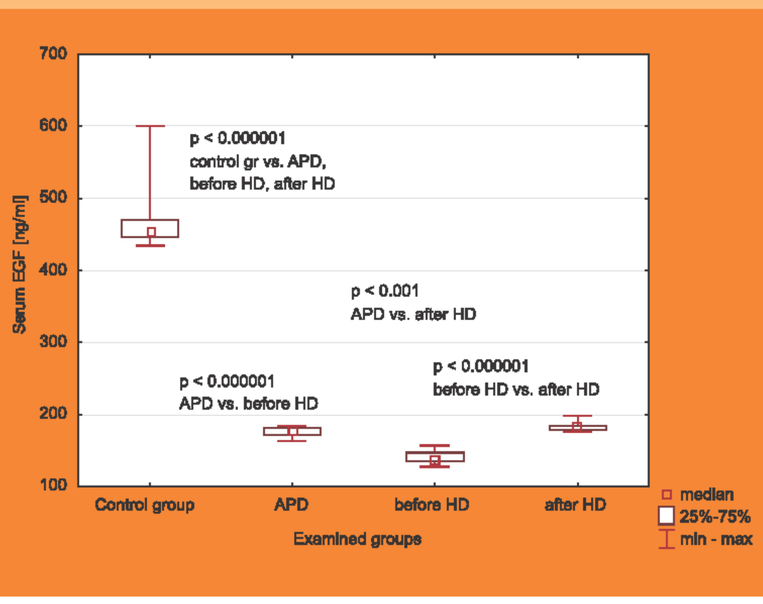


Figure 2 GDF15 serum concentrations in examined groups.

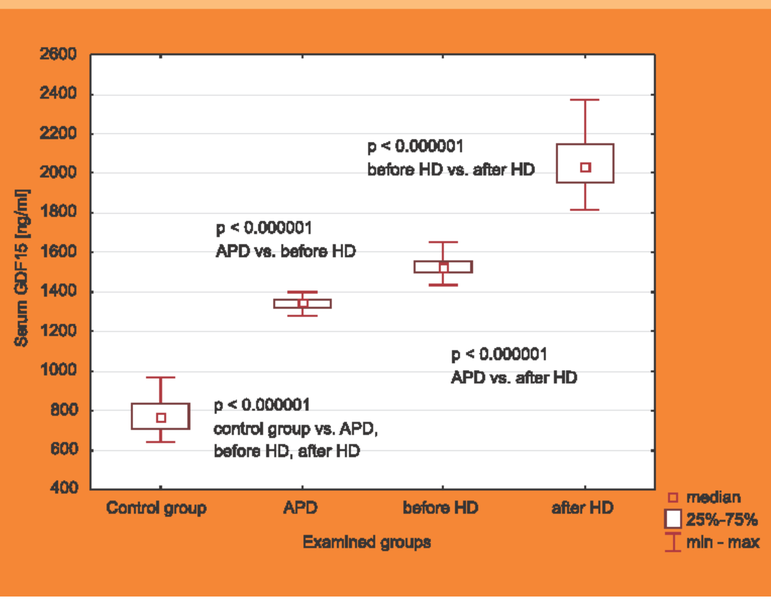
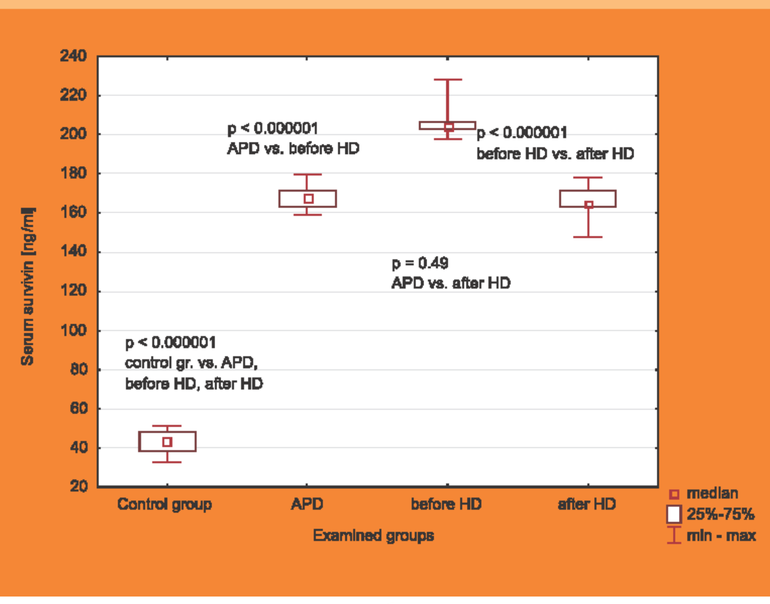


Figure 3 Survivin serum concentrations in examined groups.



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