Activity of urine arylsulfatase A in brain-dead graft donors is a predictor of early and late graft function

Aktywność arylosulfatazy A w moczu dawców narządów ze śmiercią mózgu jako czynnik progностyczny wczesnej i późnej funkcji przeszczepu

Summary

Human lysosomal arylsulfatase A (ASA) is a member of the sulfatase family. Arylsulfatase A is required to degrade sulfatides. Sulfatides occur in the myelin sheets of the central and peripheral nervous system. In this study we evaluated the urine activity of lysosomal enzyme arylsulfatase A in brain-dead donors as a marker and predictor of short - and long-term renal allograft function.

We analyzed data from kidney recipients who received organs from brain-dead donors. Data from 40 donors and 68 recipients were analyzed.

Urine activity of arylsulfatase A in graft donors correlated positively with creatinine clearance in graft recipients after transplantation: significantly after 30 days ($R_s=0.38$, $p=0.004$) and after 3 years ($R_s=0.38$, $p=0.03$), and with borderline significance after 14 days ($R_s=0.25$, $p=0.08$) and after one year ($R_s=0.23$, $p=0.07$).

The results of this study suggest that arylsulfatase A has a protective effect on kidney allograft, and the urine activity of this enzyme in kidney donors correlates positively with graft function.

Keywords: arylsulfatase A • graft • kidney
We analyzed activity of tubular lysosomal enzyme ASA in urine of brain-dead donors before organ taking. In recipients we examined early and long-term kidney function. Early graft function was assessed as the necessity of hemodialysis treatment in the first week after kidney transplantation. Patients who required hemodialysis in this period were diagnosed with delayed graft function (DGF). Long-term kidney function was assessed as the level of serum creatinine at 1, 2, 3, 4 and 5 years after kidney transplantation. Estimated glomerular filtration rate (eGFR) was determined by the CKD-EPI formula using the calculator of the National Kidney Foundation.

**STATISTICAL ANALYSIS**

We used Statistica 10 software (StatSoft, Poland) for statistical analysis. As the Shapiro-Wilk test showed that the distributions of most of the assessed quantitative variables were significantly different from normal (p<0.05), we used non-parametric Spearman’s rank correlation coefficient (Rs) for the statistical analysis.

**RESULTS**

Clinical characteristics of the renal donors are shown in Tables 1, 2.

Urine activity of arylsulfatase A in graft donors correlated positively with creatinine clearance in graft recipients after transplantation: statistically significant after 30 days (Rs=0.38, p=0.004) and after 3 years (Rs=0.38, p=0.05), and with borderline significance after 14 days (Rs=0.25, p=0.08) and after one year (Rs=0.23, p=0.07) (Fig. 1).

**DISCUSSION**

Brain death triggers a complex cascade of molecular and cellular events including the release of various proinflammatory mediators, leading to a pronounced inflammatory state. The triggering stimulus of this phe-
In our study we analyzed the activity of urine arylsulfatase A in brain-dead graft donors as a predictor of early and late graft function. This activity correlated positively with creatinine clearance after transplantation. These results suggest protective activity of arylsulfatase A in kidney allografts.

Arylsulfatase A is required to degrade sulfatides. Sulfatides, such as galactosylceramide 1-sulfate, occur abun-
dantly in the myelin sheets of the central and peripheral nervous system and in glandular epithelial tissues of mammals. Sulfatides of more complex structure have been found in the kidney [6]. In the human renal cell carcinoma line SMKT-R3, high levels of sulfatides including gangliotriosylceramide-II sulfate were observed [8,9]. In addition, complex sulfatides have been recognized to rank among the strongest ligands for natural killer receptor-p1. This membrane protein, with an extracellular Ca2+-dependent lectin domain, is expressed on natural killer cells that display innate immunity [1]. More recently it has been shown that intracellular sulfation of lactosylceramide suppresses the expression of integrins [7] Sulfatides show structural, and possibly physiological similarities to gangliosides. Kidney dysfunction might be correlated with changes in sulfatides, the major acidic glycosphingolipids in this organ. In protein-overload nephropathy mice, the level of sulfatide in serum decreases as the disease progresses.

Acute kidney dysfunction lowers the level of sulfatide in serum through downregulation of CST gene expression in lipoprotein-producing organs such as the liver [16]. Reduction of serum sulfatide level in patients with end-stage renal disease was detected prior to induction of hemodialysis therapy [11]. Kidney function itself also seems to be associated with regulation of sulfatide level in serum and lipoprotein-producing organs. Hypoxia in brain death donors may reduce activity of arylsulfatase. Bhattacharya et al. analyzed the effect of hypoxia on arylsulfatase B activity [2]. Hypoxia, like N-acetylgalactosamine-4-sulfate (arylsulfatase B) silencing, significantly increased the total cellular sulfated glycosaminoglycans and chondroitin-4-sulfate content. The results of this study suggest that arylsulfatase A has a protective effect on kidney allograft and the urine activity of this enzyme in kidney donors correlates positively with graft function.

References


The authors have no potential conflicts of interest to declare.