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Serum GDF-15 associated with cognitive dysfunction in end stage renal disease on maintenance hemodialysis

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Objectives: Cognitive dysfunctionecline is known to be more common in hemodialysis patients than in the general population. Interest in serum markers that reflect cognitive function has recently increased. In this study, The correlation between cognitive dysfunction and growth differentiation factor 15 (GDF-15) in hemodialysis patients was analyzed.

Methods: A retrospective study was conducted on hemodialysis patients aged ≥18 years. Cognitive function was evaluated by the Korean version of the Mini-Mental Status Examination (K-MMSE), and based on the K-MMSE score, the patients were divided into group A (normal, ≥24 points) or group B (cognitive dysfunction, <24 points). The concentration of serum GDF-15 was measured in blood samples collected before hemodialysis. The expression of GDF-15 as the result of increased uremic toxins was confirmed in HT22 cells and in a C57BL/6 uremic mouse model.

Results: A total of 92 hemodialysis patients were included in the study (group A, normal, n = 59 and group B, cognitive dysfunction, n = 33). In group B, serum GDF-15 was statistically significantly higher (7500.42 pg/mL, P = 0.001) than group A. In univariate and multivariate regression analysis, the K-MMSE score decreased as serum GDF-15 increased (r = −0.337, P = 0.001). In logistic regression analysis, when serum GDF-15 was >5408.33 pg/mL, the risk of scoring <24 points on the K-MMSE was increased by 2.912 times (P = 0.047). After HT22 cells were treated with indoxyl sulfate, a uremic toxin, cell survival was decreased and GDF-15 expression was increased in a concentration-dependent manner, respectively. Additionally, GDF-15 expression in mouse brain tissue under uremic conditions after ischemia-–reperfusion was significantly increased compared with the sham mice.

Conclusions: Serum GDF-15 is related to cognitive dysfunction in hemodialysis patients and may be helpful in screening for cognitive dysfunction in hemodialysis patients.

Table 1.

Table 1. Correlation between the MMSE score and clinical parameters

	r	P value
GDF-15	-.337	**0.001***
Age	-.435	**0.000***
BMI	.149	0.158
Total protein	.185	0.077
Albumin	.259	**0.013***
Total cholesterol	.030	0.804
BUN	.191	0.068
Serum creatinine	.258	**0.013***
Total calcium	.042	0.690
Phosphorus	.348	**0.001***
Sodium	.093	0.376
Potassium	.257	**0.013***
Total CO_2	-.122	0.255
C-reactive protein	-.257	0.014
B2-MG	-.077	0.468
Homocysteine	.121	0.257

BMI, body mass index; GDF-15, growth and differentiation factor 15; BUN, blood urea nitrogen; CRP, C-reactive protein; B2-MG, beta-2 macroglobulin. Significant P values are indicated using *.

Figure 1.

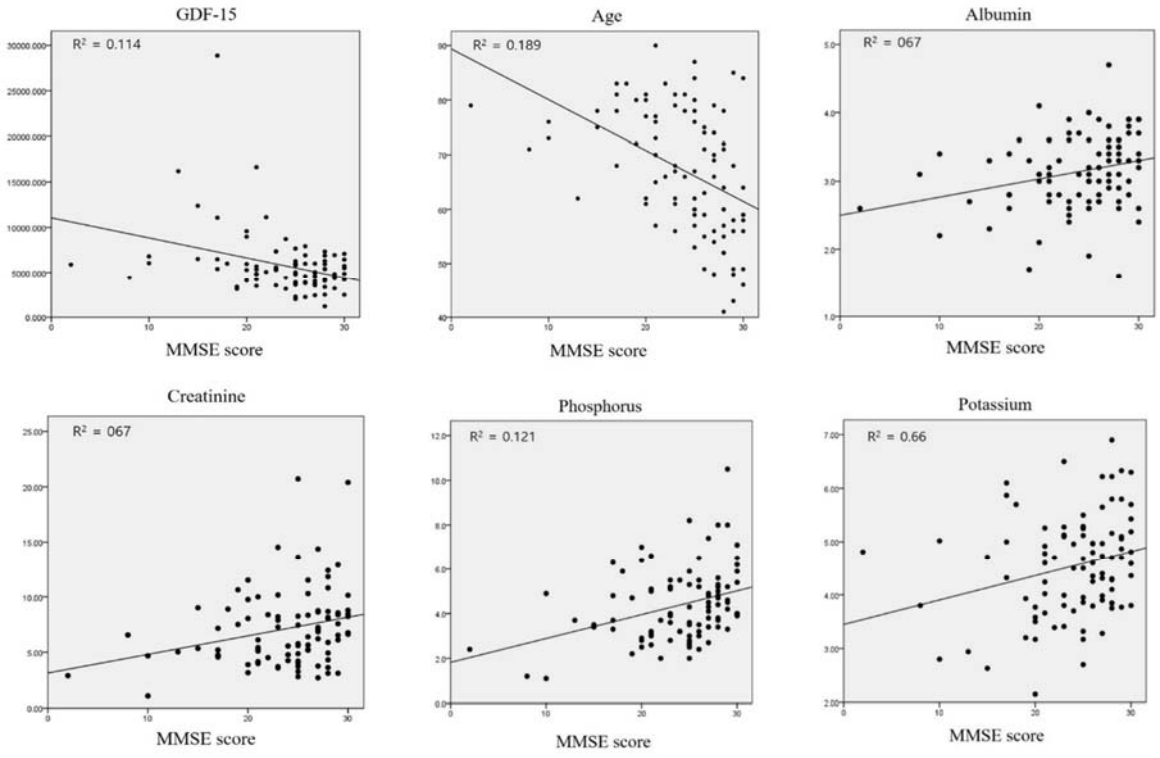

Figure 1. Correlation of K-MMSE score with clinical parameters