

Detection and adequacy assessment of erythrocyte glutathione transferase on the cycle toxin level of hemodialysis patient

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Abstract: To explore detection and adequacy evaluation of erythrocyte glutathione S transferase (GST) in hemodialysis patients on circular toxin levels, this paper divided 84 cases of long-term hemodialysis end-stage patients into 33 cases of adequate hemodialysis group (spKt/V \geq 1.3) and 51 cases of inadequate hemodialysis group (spKt/V $<$ 1.3) according to urea index value of unit chamber model (spKt/V). Take the other 50 cases of healthy physical examination people for control group, compare and analyze related clinical and biochemical indexes differences of three groups. The level of hemodialysis group GST, creatinine, high sensitivity C-reactive protein (hs-CRP), transferrin saturation (TSAT), parathyroid hormone (PTH), interleukin-2,6,8 (IL-2,6,8) and tumor necrosis factor- α (TNF- α) was significantly higher than the control group (P $<$ 0.05), and GST, IL-2, 6, 8, TNF- α level of inadequate hemodialysis group was significantly higher than adequate hemodialysis group (P $<$ 0.05). Pearson's relevant analysis showed that GST and spKt/V, IL-2, IL-6, IL-8, TNF- α have positive correlation (P $<$ 0.05) and had no correlation with creatinine, hs-CRP, TSAT, PHT (P $>$ 0.05). There was 23 patients spKt/V \geq 1.3 after adjusting the dialysis solution for 51 cases of inadequate hemodialysis patients, GST level after the adjustment was significantly lower than before the adjustment, but still higher than adequate dialysis group. It concludes that the maintenance of hemodialysis patients' level has certain relevance on spKt/V and associated inflammatory factors. Through the determination, GST can effectively response the adequate hemodialysis, which has a guiding significance on adjusting blood dialysis solution in clinic.

Keywords: Hemodialysis, erythrocyte glutathione transferase, dialysis adequacy, inflammatory factor.

INTRODUCTION

Hemodialysis is one of the most effective means for endstage renal disease patients continuing life, sufficient dialysis can protect patient's protein from loss, and plays an important role in enhancing the body's nutritional status and resistance (Chunyan *et al.*, 2011). Erythrocyte glutathione S transferase can be involved in various physiological reactions and has been known and recognized in a variety of diseases, especially with the correlation of tumor, but evaluation research is relatively less about GST as adequate hemodialysis (Minyan, 2012; Yang and Haitao, 2014). Recently, foreign scholars Dessi, *et al.* (Dessi *et al.*, 2012) has confirmed GST and inflammation in end-stage renal disease patients have certain relevance. In addition, Bonifazi, *et al.* (Bonifazi *et al.*, 2013) on GST study and kidney damage relations pointed out that GST level of the kidney patients is significantly higher than normal people, therefore both has a close relationship. Seabra (Seabra and Perianaagam, 2011) *et. al.* in their study showed that inadequate hemodialysis patients due to toxins in the body is difficult to completely clear, lead to a large number of toxins accumulation in the body, and stimulate the GST generated in great quantities, raise the level of serum GST. The above research put forward a corresponding basis for GST as adequate hemodialysis evaluation index. Based on the above foundation, this study detected and analyzed the various indexes of adequate hemodialysis

group, inadequate hemodialysis group and health group to explore detection and adequacy evaluation of GST in hemodialysis patients on circular toxin levels.

MATERIAL AND METHOD

Clinical data

Select 84 cases maintenance hemodialysis patients received from May 2011~May 2013 from The General Hospital of Shenyang Military as the research object, in which 52 cases were male, 32 cases were female, ranging in age from 38 to 78 years (mean 52.3 \pm 1.4 years old), anaphylactic purpura nephritis in 11 cases, lupus nephritis in 13 cases. Patients were divided into 33 cases of adequate hemodialysis group (spKt/V value \geq 1.3) and 51 cases of inadequate hemodialysis group (spKt/V value $<$ 1.3) according to spKt/V value. Take the other 50 cases of healthy controls for control group, in which 25 cases were male, 25 cases were female, ranging in age from 18 to 75 years (mean 49.26 \pm 2.1 years old).

Inclusion criteria of maintaining hemodialysis patients: 1) Hemodialysis time was over three months; 2) Patients in stable condition; 3) sign informed consent. Following diseased were exclusive, such as acute cardiovascular complications, recent infectious or bleeding, application of immunosuppressant for nearly three months, malignant tumor, thyroid dysfunction and patients with acute or chronic liver disease.

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Test method

After centrifugal processing on collected 3ml venous blood from subjects in the early morning without any intakes, ELISA enzyme linked immunoassay assay was used respectively to determine IL-2, IL-6, IL-8 and TNF- α level (Shanghai biological Co., LTD); immunoturbidimetry to determine high-sensitivity CRP (Suzhou Keming biological technology Co., LTD); ultraviolet spectrophotometry to determine GST (America B&G company); Hitachi 7600-020 automatic biochemical analyzer to determine creatinine, hemoglobin, TSAT, PTH.

Hemodialysis adequacy evaluation index

Include patient's clinical situations, weight loss situation, Kt/V value, single room Kt/V value (spKt/V) = $-\ln(R-0.008t) + (4-3.5R) UF/W$. spKt/V value ≥ 1.3 was hemodialysis adequacy.

STATISTICAL ANALYSIS

Data analysis was performed using SPSS17.0 statistical software, measurement data was expressed by ($\bar{x} \pm s$), group measurement data was analyzed by one-way variance, further comparison was used by LSD - t, enumeration data was expressed by rate, group enumeration data was tested by X^2 , Pearson's correlation analysis was used, All results were considered statistically differences as $P < 0.05$.

RESULTS

Clinical data, biochemical indicators analysis of each group

The results of detecting and analyzing adequate hemodialysis group, inadequate hemodialysis group, healthy physical examination clinical data and biochemical indicators showed that creatinine, hsCRP, PTH, TSAT, IL-2, IL-6, IL-8, TNF- α , GST levels of

inadequate hemodialysis group were significantly higher than adequate hemodialysis group and the control group, especially the health control group; compared with three groups of hemoglobin level, inadequate hemodialysis group was significantly lower than the rest two groups; the specific numerical value is as shown in table 1

Correlation analysis of GST and hemodialysis degree and the inflammation factor

Correlation analysis of GST and hemodialysis degree and the inflammation factor by Pearson's single factor showed that P value of spKt/V, IL-2, IL-6, IL-8 and TNF-a was lower than 0.05, which had positive correlation, but had no correlation with creatinine, hsCRP, TSAT ($P > 0.05$). The specific numerical value is as shown in table 2.

Adjusted hemodialysis index analysis

The results of detection and analysis of SpKt and GST before and after adjustment of hemodialysis group and inadequate hemodialysis group showed that before and after the adjustment of adequate hemodialysis group of 33 cases patient's SpKt value was 1.3 or higher, but GST value slightly decreased after the adjustment. After the adjustment of inadequate hemodialysis group of 51 cases patient's SpKt value < 1.3 down to 28 cases, $SpKt \geq 1.3$ instead of 0 patients up to 23 cases, and GST numerical presented a downward trend. Compared two groups of patients, we found that, no matter before and after adjustment, the GST value of inadequate hemodialysis group was higher than adequate hemodialysis group. The specific numerical value is as shown in table 3

DISCUSSION

Maintenance hemodialysis became integrated therapy treatment for end-stage renal failure patients with renal replacement therapy; now a large number of studies showed that the prognosis effect of patients with maintenance hemodialysis had intimate relationship with the degree of the dialysis, adequate dialysis had vital

Table 1: Each clinical data, biochemical indicators analysis ($\bar{x} \pm s$)

Index	Adequate hemodialysis group (n=33)	Inadequate hemodialysis group (27/24)	Control group (n=50)	x^2 / p	P value
Gender (male/female)	19/14	27/24	26/24	0.396	> 0.05
Age (g)	52.96 \pm 1.29	52.34 \pm 1.39	49.26 \pm 2.1	0.985	> 0.05
Creatinine (mg/dL)	11.26 \pm 2.36a	12.45 \pm 2.85a	0.98 \pm 0.46	4.985	> 0.05
Hemoglobin (r/DI)	11.98 \pm 1.62a	10.61 \pm 1.74a	14.98 \pm 2.62	5.885	< 0.05
HsCRP (mg/L)	7.02 \pm 1.63a	9.26 \pm 2.32a	0.38 \pm 0.06	12.984	< 0.05
PTH (pg/mL)	192.32 \pm 16.87a	210.32 \pm 20.69a	0.19 \pm 0.06	38.692	< 0.05
TSAT (%)	18.69 \pm 3.45a	20.12 \pm 7.32a	0.69 \pm 0.06	11.002	< 0.05
IL-2 (mmol/L)	24.69 \pm 10.39a	35.36 \pm 11.36ab	7.19 \pm 2.03	10.362	< 0.05
IL-6 (mmol/L)	7.96 \pm 1.06a	9.36 \pm 2.58b	2.03 \pm 1.05	9.742	< 0.05
IL-8 (mmol/L)	12.21 \pm 2.89a	18.63 \pm 3.05a	3.29 \pm 1.03	9.326	< 0.05
TNF- α (mmol/L)	21.36 \pm 8.25a	27.33 \pm 4.98a	4.26 \pm 1.08	8.669	< 0.05
GST (U/L)	20.32 \pm 3.78a	38.19 \pm 4.52ab	10.32 \pm 1.26	6.785	< 0.05

Table 2: Correlation analysis of GST and hemodialysis degree and the inflammation factor

	spKt/V	IL-2	IL-6	IL-8	TNF-a	Creatinine	hsCRP	TSAT	PTH
r	0.478	0.426	0.468	0.433	0.418	0.112	0.164	0.137	0.145
P	0.000	0.004	0.002	0.001	0.005	0.078	0.092	0.084	0.069

Table 3: Hemodialysis index analysis before and after adjustment

Group	Cases	Before adjustment			After adjustment		
		SpKt<1.3	SpKt>1.3	GST	SpKt<1.3	SpKt>1.3	GST
Adequate hemodialysis group	33	0	33	20.32±3.78	0	33	18.62±3.74
Inadequate hemodialysis group	51	51	0	38.19±4.52	28	23	30.12±5.32ab

Note: compared with control group, a P<0.05; Compared with adequate hemodialysis group, b P<0.05.

significance for improving the quality of survival in patients with end-stage renal disease and prolonging survival period (Bin, 2013). Kt/V value was currently one of the important indicators for assessing patients' hemodialysis adequacy. However because Kt/V value could only be used to reflect the clearance of small molecules and cannot effectively reflect the removal of macromolecular material, there were some shortcomings in accuracy and sensitivity, therefore, in the clinical assessment of hemodialysis adequacy should be comprehensive indicators in order to improve the accuracy (Zhanyuan *et al.*, 2012). GST was a kind of enzyme involved in second phase reaction of biological conversion in the liver, which could combine with a variety of halogenated compounds and epoxy compound, its main effect was to catalyze and restore glutathione thiol and combine hydrophobic material, to make the electrophilic compounds can be converted into hydrophilic compounds to excrete from urine or bile, which played the role of detoxification (Xiaojie, 2011; Chang *et al.*, 2013). Besides GST, regulatory substance such as hs-CR, IL-2, 6, 8 and TNF-a, etc. were taken as index for comprehensive exploration, thus to enhance accuracy.

Urine toxin, micro inflammation and nutrition status were the main problems that lead to a variety of complications in dialysis patients and threaten the long-term survival rate and survival quality (Minyan, 2012) Dialysis could clear the retention water generated in dialysis interval (reach to dry weight), remove the toxin generated by decomposition and metabolism of the protein, correct electrolyte and acid-base balance disorder, which made people feel comfortable and to the point of psychological rehabilitation and return to society (Xiaojie, 2011). This study showed that GST level of hemodialysis group was higher than control group, which indicated that GST can be the basis of hemodialysis project adjustment. Through further analysis of adequate dialysis group and inadequate dialysis group, we found inadequate dialysis group GST level before and after the adjustment was also higher than adequate dialysis group, IL-2, IL-6, IL-8 and TNF- α were significantly higher than adequate hemodialysis group,

which may be result from the loss of large amounts of protein caused by patients within adequate hemodialysis, thus appear the symptom of chronic malnutrition, which made the weakened immunity and patients with rising inflammation levels. In addition, the study showed that GST and IL-2, IL-6, IL-8, TNF- α positively correlated, which suggested that GST can be used as a predictor of end-stage renal disease patients' inflammatory level. Essence of micro inflammation is immune inflammation, is the activation inflammation state that the body activates mononuclear macrophage system to cause TNF- α proinflammatory factor in the stimulation of a variety of chemicals, endotoxin, immune complex and alexin (Minyan, 2012). Studies showed that (Tianzuo *et al.*, 2011), inadequate dialysis and micro inflammation of the blood dialysis medium and small molecule toxins may be one of the key factors of patients with malnutrition; high flux hemodialysis could clear the leptin and other toxins molecule in the plasma, to improve the nutritional status of dialysis patients, which accords with the research.

GST could achieve cell protection through a combination of a variety of toxins and active response endotoxin levels in the body (Yang *et al.*, 2014). The above research showed that GST level and spKt/V of patients with maintenance hemodialysis and associated inflammation factors have certain relevance. It effectively reflected the blood dialysis adequacy by detecting GST, which has the guiding significance for adjusting the clinical blood dialysis solution.

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