Pakistan J. Zool., vol. 55(2), pp 905-911, 2023 DOI: https://dx.doi.org/10.17582/journal.pjz/20210430140411

Effects of Alpha Ketoacid Combined with Hybrid Blood Purification Treatment on Nutritional Status, Renal Function and Expressions of Serum Sclerostin, BMP-7, Irisin in Maintenance Hemodialysis Patients

Cuiping Liu

Nephrology, Beijing Geriatric Hospital, Beijing, 100095, China

ABSTRACT

This study aimed to explore the effect of alpha keto acid combined with hybrid blood purification treatment in patients with maintenance hemodialysis (MHD). 106 patients with MHD were treated in our hospital from February 2017 to January 2020. They were divided into observation group (n=53) and control group (n=53) using a random number table. The control group was given heterozygous blood purification, and the observation group was given alpha keto acid combined with heterozygous blood purification for 6 months. Compared with the renal function indexes before treatment, the levels of SCr and BUN in the 2 groups decreased after 3 and 6 months of treatment, and the reduction in the observation group was higher; After 3 and 6 months of treatment, the levels of TP, PA and Alb in the observation group were higher than those in the control group; Compared with before treatment, after 3 months and 6 months of treatment, the mineral metabolism indexes such as iPTH, P, Ca×P and the levels of Sclerostin, BMP-7 and Irisin in the observation group were significantly improved. Serum levels of TNF-α, IL-6, and CRP in the observation group were lower than those in the control group after 3 and 6 months of treatment; Compared with the situation before treatment, KDTA scores in the two groups increased after 3 and 6 months of treatment, and the increase in the observation group was higher. The application of compound alpha keto acid tablets combined with hybrid blood purification therapy in MHD patients has a positive effect on improving renal function, nutritional status, and quality of life. It can effectively reduce the body's micro-inflammatory state, while regulating mineral metabolism and the expression of Sclerostin, BMP-7 and Irisin, and inhibiting vascular calcification.

Article Information
Received 10 April 2021
Revised 21 May 2021
Accepted 25 May 2021
Available online 09 May 2022
(early access)
Published 06 January 2023

Key words
Maintenance hemodialysis, Compound alpha keto acid tablets, Hybrid blood purification, Renal function, Nutritional status.

INTRODUCTION

Maintenance hemodialysis (MHD) is a commonly used renal replacement therapy in the clinical treatment of end-stage renal disease (ESRD), which can effectively delay the progression of renal failure and prolong the patient's survival (Yang *et al*., 2017; Marsen *et al*., 2017). However, clinical studies have found that long-term MHD treatment can cause a certain degree of chronic micro inflammation and malnutrition in the body, thus increasing the risk of cardiovascular diseases in patients (Zhang *et al*., 2017; Zhang, 2017). Hybrid blood purification treatment is a new kind of blood purification method combining the characteristics of a variety of technologies, which can effectively make up for the deficiency of the conventional hemodialysis model, remove macromolecular toxins in the body, and then relieve the body's micro-inflammation to some extent. However, it cannot play a significant role in the nutritional status, so it should be applied along with other treatment schemes (Luo *et al*., 2017; Shah *et al*., 2016). Compound alpha ketoic acid tablets can effectively regulate protein metabolism in patients with chronic renal insufficiency and prevent the body from being damaged due to protein metabolism disorder (Zhang *et al*., 2017). In this study, the effects of compound alpha ketoic acid tablets combined with hybrid blood purification on nutritional status, renal function and expressions of vascular calcification related factors in MHD patients were analyzed, in order to provide multi-directional data reference for the selection of clinical treatment.

MATERIALS AND METHODS

General data

A total of 106 MHD patients in our hospital from

* Corresponding author: 15011382998@163.com
0030-9923/2023/0002-905 $ 9.00/0

Copyright 2023 by the authors. Licensee Zoological Societ of Pakistan.
This article is an open access ∂ article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

February 2017 to January 2020 were selected as research objects for a prospective randomized controlled study. The patients were divide into the observation group (n=53) and the control group (n=53) using the random number table. There were no significant differences in gender, age, history of dialysis treatment, vascular access, primary kidney disease, body mass index (BMI) and other basic data between two groups before treatment (P>0.05). The study was examined and approved by the Ethics Committee of our hospital (Table I).

Criteria

Inclusion criteria: All the enrolled patients were ESRD patients receiving regular MHD treatment: dialysis ≥3 times per week, 4h each time, single-chamber urea clearance index (spKt/V) ≥1.2, vascular access blood flow velocity ≥200ml/min, urine volume < 400ml at 24h;Regular MHD treatment time ≥3 months; stable condition, no volume overload or significant fluctuation of blood pressure; no history of blood transfusion in recent 3 months; no history of acute infection, hormone or immunosuppressive drugs in the past 1 month; the patients and their families had the right to known and signed informed consent form.

Exclusion criteria: Severe complications; diseases of the endocrine and blood systems; malignant tumor; severe ion disorder; motor dysfunction or lack of autonomous living ability; poor awareness, cognition, communication, mental illness or poor compliance, unable to effectively cooperate with the relevant treatment and examination; a history of surgery or trauma in the last 1 month; medical history of previous acute cardiovascular and cerebrovascular events; complicated with organic lesions of heart, lung, liver and other important organs; having contraindications in the use of multiple treatment regimens in this study; history of drug and alcohol dependence in the last 6 months.

Patients in both groups were given a low-phosphorus, low-protein diet to maintain stable blood sugar and blood pressure. Subcutaneous injection of erythrogenin (North China Pharmaceutical Jintan Biotechnology Co., Ltd., SFDA approval number S20043056) was given at dose of 10000 U/ time, 1 time/week, and oral administration of folic acid (Tianjin Liueng Pharmaceutical Co., Ltd., SFDA approval number H12020215) was given at dose of 5mg/ time, 3 times/day, with hemoglobin (Hb) maintained within 60 - 90g/L.

The control group was given hybrid blood purification: (1) regular hemodialysis twice a week: intravenous injection of low molecular heparin sodium (Jilin Huakang Pharmaceutical Co., Ltd., SFDA approval number H20010233) at dose of 2000-6000IU. The treatment was performed with a hollow fiber hemodialyzer (Fresenius, Type F7), a polysulfone membrane and a standard bicarbonate dialysate. The dialysate flow rate was 500ml/min, the temperature was 36.5°C, the blood flow was 220-250ml/min, and the replacement fluid volume was 30 - 40L. (2) hemodiafiltration was performed once a week between two hemodialysis times: 2000-6000IU of low molecular heparin sodium was injected intravenously before dialysis. A hollow fiber hemodialyzer (FX600 type, Fresenius, Germany) was used for post-replacement,

Table I.- Comparison of general information about the two experimental groups.

Data	Control group (n=53)	Observation group (n=53)	t/χ^2	P
Gender (case)				
Male	32(60.38)	29(54.72)	0.348	0.556
Female	21(39.62)	24(45.28)		
Age (years)	35～73 (53.92±9.16)	35～73 (54.66±9.12)	0.417	0.678
Dialysis treatment history (months)	3～18 (10.70±3.63)	3～18 (10.26±3.57)	0.629	0.531
Vascular access (cases)				
Internal fistula	40 (60.38)	38 (71.70)	0.194	0.660
Long term deep venous catheter	13 (39.62)	15 (28.30)		
Primary kidney disease (cases)				
Chronic glomerulonephritis	15 (75.47)	17 (32.08)	0.919	0.969
Diabetic nephropathy	13(24.53)	12(22.64)		
Chronic interstitial nephritis	14(26.42)	12(22.64)		
Hypertensive renal arteriosclerosis	7(13.21)	8(15.09)		
Polycystic kidney	3(5.66)	2(3.77)		
Other	1(1.89)	2(3.77)		
BMI (kg/m^2)	17.9～24.6 (21.20±1.65)	18.0～24.8 (21.49±1.63)	0.910	0.365

with a replacement volume of 20-45L. (3) Hemodialysis tandem blood perfusion should be performed once every 4 weeks: after 2h hemodialysis, the resin perfusion device (Zhuhai Jianfan, HA130) soaked in heparin salt water was connected in tandem in front of the dialyzer to continue hemodialysis treatment.

The observation group was given compound alpha ketoic acid tablets (Beijing Fresenius Karbi Pharmaceutical Co., Ltd., SFDA approval number H20041442) combined with hybrid blood purification treatment. Heterozygous blood purification was the same as the control group.Oral administration of compound alpha ketoacid tablets was carried out with meal, at dose of tablets/time, 3 times/d.

Observational index

(1) For deermining renal function about 10ml peripheral venous blood of the patient was collected under fasting state after getting up in the morning, centrifuged at 3000R /min for 10min, and the upper serum was collected and stored at -80°C for testing. Meanwhile, urine specimens of the patient were collected and sent to the laboratory department of our hospital for testing. Blood serum was collected and determined by colorimetric method using automatic biochemical analyzer (Hitachi, Type 7600). The blood serum creatinine (SCr) level and the urine urea nitrogen (BUN) level were determined.

(2) For nutritional status: serum total protein (TP) level was determined by biuret method, serum prealbumin (PA) level was determined by immunoturbidimetry, and serum albumin (Alb) level was determined by bromocresol green method. (3) Mineral metabolism before treatment, 3 months after treatment, and 6 months after treatment for the 2 groups: The contents of blood calcium and phosphorus (P) in the blood samples were determined, the product of calcium and phosphorus (Ca×P) was calculated, and the serum iPTH level was determined by chemiluminescence immunoassay. (4) Inflammatory factors before treatment, 3 months after treatment and 6 months after treatment for the 2 groups: Serum levels of tumor necrosis factor (TNF-α) and interleukin-6 (IL-6) were determined by enzyme-linked immunosorbent assay (ELISA) and c-reactive protein (CRP) were determined by immunoturbidimetry. (5) Serum levels of sclerostin, bone morphogenetic protein 7 (BMP-7) and Irisin before treatment, 3 months and 6 months after treatment for the 2 groups: The assay was carried out by ELISA. (6) Kidney disease and dialysis-related quality of life (KDTA) score was used to evaluate the quality of life of the 2 groups before, 3 months and 6 months after treatment, including symptoms, effects of kidney disease, work status, cognitive function, quality of social relations and sleep, with a total score of 0-100, the higher the score, the better the quality of life.

Statistical process

SPSS22.0 software was used for data processing. Measurement data were expressed as ($\bar{x}\pm s$), and t-test was performed. The difference was considered statistically significant when $P < 0.05$.

RESULTS AND DISCUSSION

Table II shows the effect of α-ketoacid combined with hybrid blood purification treatment on renal function, nutritional status, mineral metabolism indicators, inflammatory factor indicators, sclerostin, BMP-7, Irisin and KDTA scores in maintenance hemodialysis patients.

There was no statistically significant difference in serum SCr, BUN, TP, PA, Alb, iPTH, Ca×P, TNF-α, IL-6, CRP, Sclerostin, BMP-7, Irisin levels and KDTA score between the two groups before treatment ($P > 0.05$). Serum SCr, BUN, iPTH, Ca×P, TNF-α, IL-6, CRP, Sclerostinlevels of 2 groups 3 months and 6 months after treatment were lower than those before treatment, and the observation group was lower than the control group ($P < 0.05$). The levels of TP, PA, Alb, BMP-7 and Irisin levels in the observation group at 3 months and 6 months after treatment were higher than those before treatment, and higher than those in the control group ($P < 0.05$).

There was no significant difference in KDTA scores between the two groups before treatment, 3 months after treatment and 6 months after treatment ($P > 0.05$). 3 months and 6 months after treatment, the KDTA scores of the 2 groups were higher than those before treatment, and the observation group was higher than the control group ($P < 0.05$, Table II).

Most MHD patients have malnutrition, inflammation, atherosclerosis syndrome. Medium and macromolecular toxin, microinflammatory state and long term calcium and phosphorus metabolism disorder are independent risk factors leading to cardiovascular events (Ren *et al*., 2016; Liu *et al*., 2017), which can significantly increase the incidence of heart failure, arrhythmia, ischemic heart disease and other diseases and increase the risk of death (Wu *et al*., 2019). Therefore, it has become the main objective of clinical treatment at this stage to correct chronic microinflammation and disorder of calcium and phosphorus metabolism while ensuring effective clearance rate of mesomolecular toxin.

Based on previous clinical treatment experience, it can be found that MHD treatment can remove some nutrients from the body while removing toxins, thus resulting in malnutrition of the patients. Moreover, routine hemodialysis can hardly improve the patients' microinflammation state, easily causing dysfunction of the oxidative stress system and immune disorder, etc, so that the

overall effect is not ideal. In addition, although low-protein and low-phosphorus diets can reduce the serum level of patients to a certain extent, they are prone to aggravate protein-thermal malnutrition (Guo *et al*., 2019; Vaziri *et al*., 2016). Therefore, it is of great importance to improve the blood purification program and adjuvant drug therapy. Based on the above analysis, compound alpha ketoic acid tablets used along with hybrid blood purification regimen to treat MHD patients. Hybrid blood purification has the advantages of intermittent hemodialysis, continuous blood purification and blood perfusion, which can clear toxins out of the body by means of dispersion, convection and adsorption, and significantly improve the state of micro-inflammation (Xing *et al*., 2017). Macroporous polymer with good biocompatibility can form huge surface area with numerous micropores, which has little influence on hemodynamics (Xiao and Ji, 2019). Moreover, it has advantages such as high strength, large adsorption capacity and fast speed. Hybrid blood purification has low requirements on equipment and professional technology, small nursing workload, and low treatment cost. It is the most ideal blood purification method with the most ideal treatment effect at the present stage (Chen *et al*., 2016). Compound is alpha keto acid compound preparations, containing 5 kinds of amino acids, 1 kind of hydroxyl AnJiSuanGai and 4 kinds of ketone AnJiSuanGai. It can provide the human body with essential amino acids such as leucine and valine through amino acid transamination and amination. It can also combine part of urea nitrogen to produce essential amino acids, reduce nitrogen intake, inhibit the protein decomposition process of the body, and improve the nutritional state of the body by regulating amino acid metabolism and metabolic acidosis (Zou *et al*., 2017; Ding *et al*., 2019). Zhang *et al*. (2018) pointed out that the application of compound ketoacid tablets on the basis of high-throughput dialysis could effectively improve the nutritional status of MHD patients and promote lipid, calcium and phosphorus metabolism in the body.

Table II.- Effect of ketotic acid combined with hybrid blood purification treatment on renal function, nutritional status, mineral metabolism indicators, inflammatory factor indicators, sclerostin, BMP-7, Irisin and KDTA scores in maintenance hemodialysis patients.

Group	Observation group (n=53)			Control group (n=53)		
Time	Before treatment	3 months after treatment	6 months after treatment	Before treatment	3 months after treatment	6 months after treatment
Renal function						
SCr (μmol/L)	257.60±92.68	116.24±52.71[a]	97.30±19.35[a]	264.37±90.84	149.02±67.58[a]	108.18±21.02[a]
BUN (mmol/L)	36.69±14.27	21.42±6.07[a]	16.49±3.73[a]	38.02±13.58	25.06±7.85[a]	18.51±4.69[a]
Nutritional status indicators						
TP (g/L)	60.58±5.83	65.03±6.59[a]	68.24±7.82[a]	59.72±6.09	60.50±6.28	61.06±6.53
PA (g/L)	34.86±3.97	39.58±4.40[a]	42.75±5.36[a]	35.14±3.72	35.49±4.13	36.09±4.58
Alb (g/L)	31.72±3.49	36.09±4.37[a]	38.26±4.84[a]	32.35±3.28	32.84±4.05[a]	33.19±4.46
Mineral metabolism indicators						
iPTH (ng/L)	412.07±69.48	357.41±48.35[a]	248.54±22.29[a]	409.15±71.42	384.06±52.39[a]	317.98±25.36[a]
P (mmol/L)	2.14±0.23	1.67±0.18[a]	1.54±0.12[a]	2.07±0.26	1.86±0.20[a]	1.78±0.16[a]
Ca×P ($mmol^2/L^2$)	4.36±0.34	3.57±0.26[a]	3.28±0.23[a]	4.25±0.38	3.80±0.32[a]	3.69±0.28[a]
Inflammatory factors						
TNF-α (ng/L)	80.47±12.83	68.52±8.49[a]	57.04±5.32[a]	79.53±11.90	75.14±9.65[a]	71.29±7.41[a]
IL-6 (ng/L)	77.43±11.21	59.02±7.86[a]	54.93±7.05[a]	76.82±12.06	69.48±9.29[a]	63.05±8.12[a]
CRP (mg/L)	10.45±2.51	6.03±1.79[a]	4.75±1.28[a]	10.20±2.73	8.71±2.06[a]	7.68±1.74[a]
Sclerostin (ng/ml)	4.83±1.02	3.68±0.52[a]	2.83±0.37[a]	4.95±0.87	4.79±0.82	4.67±0.69
BMP-7 (pg/ml)	1187.91±94.58	1260.49±108.63[a]	1294.62±116.39[a]	1198.24±97.09	1207.86±102.25	1225.80±104.53
Irisin (ng/ml)	54.36±8.41	102.14±19.34[a]	147.29±35.26[a]	55.48±9.27	56.38±9.64	57.03±10.31
KDTA scores	57.41±10.27	68.54±12.52[a]	72.26±14.04[a]	56.28±11.02	62.67±11.38[a]	65.84±12.79[a]

The results of this study showed that compared with application of hybrid blood purification alone, combined application of alpha ketoacid tablets treatment and hybrid blood purification can significantly improve TP, PA, Alb and other nutritional status indicators of MHD patients, reduced SCr, BUN levels and improved the patient's renal function. Combined application of alpha keto acid tablet and hybrid blood purification can fully eliminate toxins in the body, reduce its adverse influence on organism, protect kidney, speed up the protein synthesis, inhibit the decomposition process, improve the body's nutritional status, and make the patient's physical condition and quality of life were improved significantly.

Microinflammatory reaction and calcium and phosphorus metabolism disorder are common complications in MHD patients, with persistence and relative occidentality, which are key factors affecting the prognosis of patients (Chang *et al*., 2016). In MHD patients, renal function decreases and the ability to clear inflammatory cytokines is low, which further puts the body in a state of persistent inflammation and continuously increases the level of inflammatory cytokines such as TNF-α, IL-6 and CRP, causing local inflammatory damage and increasing the risk of multiple complications (Qiao *et al*., 2018). Pathological studies have found that the disorder of calcium and phosphorus metabolism in the body can cause secondary hyperparathyroidism, which leads to excessive deposition of calcium and phosphorus in the extracellular matrix of the vessel wall, promotes the calcification of coronary arteries, makes them narrow and brittle, and then induces cardiovascular complications (Zhong *et al*., 2017; Shang *et al*., 2017). Serum factors such as Sclerostin, BMP-7 and Irisin are all related to calcium and phosphorus metabolism and the formation of vascular calcification, among which Sclerostin is a glycoprotein secreted specifically by bone cells, which can participate in the regulation of bone-vascular axis. Stimulation of vascular calcification can lead to increased serum Sclerostin level, which is an effective factor reflecting the vascular calcification status of patients (Wu *et al*., 2017). BMP-7 and Irisin can inhibit the formation of vascular calcification. BMP-7 can effectively maintain the phenotype of vascular smooth muscle cells and inhibit the expression of inflammatory factors. Irisin can induce the differentiation and proliferation of osteoblasts, increase cortical bone mass, and promote bone formation. Elevated serum BMP-7 and Irisin levels can effectively reduce the occurrence of vascular calcification, and at the same time reduce calcium deposition, phosphorus metabolism disorder and secondary hyperthyroidism (Li *et al*., 2019; Zhang *et al*., 2018). In this study, 1 month and 3 months after treatment, the levels of iPTH, P, Ca×P and other mineral metabolism indicators as well as the levels of Sclerostin, BMP-7 and Irisin in the observation group were all better than those in the control group, and the serum levels of TNF-α, IL-6 and CRP were all lower than those in the control group ($P<0.05$). Compound alpha ketoic acid tablets contain ketoyl analogens, which can supplement the essential amino acids lacking in MHD patients, and combine with nitrogen-containing toxins in the blood to get out of the body, so as to improve the nutritional status, improve the immune function, and thus significantly alleviate the body's micro-inflammation (Li *et al*., 2020). In addition, calcium in compound ketoic acid tablets can combine with P *in vivo* to reduce the serum P level in body, thus improving the metabolic state of calcium and phosphorus, inhibiting hyperthyroidism, and reducing vascular calcification. Therefore, on the basis of hybrid blood purification, the application of compound alpha ketoacid tablets can significantly improve the micro-inflammation status and calcium and phosphorus metabolism disorder in MHD patients, with a significant treatment effect. Multi-slice spiral CT and electron beam CT are the gold standards for clinical diagnosis of vascular calcification, but their detection costs are expensive and the radiation dose is high (Chen *et al*., 2017). In this study, serum levels of Sclerostin, BMP-7, Irisin and other serum factors before treatment, 3 months and 6 months after treatment are measured, which provide basis for dynamical and quantitative evaluation of the vascular calcification status of MHD patients.

CONCLUSION

In conclusion, compared with hybrid blood purification, the combined application of ketoic alpha acid tablets and hybrid blood purification is better, which can significantly improve the renal function, nutritional status, micro-inflammation status, calcium and phosphorus metabolism of MHD patients, and further improve the quality of life of patients. It is an ideal treatment plan for MHD patients, and is worthy of clinical application.

Statement of conflict of interest

The authors have declared no conflict of interests.

REFERENCES

Chang, C.T., Wang, G.J., Kuo, C.C., Hsieh, J.Y., Lee, A.S., Chang, C.M., Wang, C.C., Shen, M.Y., Huang, C.C., Sawamura, T. and Yang, C.Y., 2016. Electronegative low-density lipoprotein increases coronary artery disease risk in uremia patients on maintenance hemodialysis. *Medicine*, **95**: e2265.

https://doi.org/10.1097/MD.0000000000002265

Chen, P.L., Gong, D.H. and Xu, B., 2017. Analysis of factors influencing the progression of cardiovascular calcification in maintenance hemodialysis patients. *Chinese J. Nephrol. Dialy. Transplant*., **26**: 403-407.

Chen, H., Wang, D.G., Yuan, L., Liu, G.L., He, H.J., Wang, J., Zhang, S. and Hao, L., 2016. Clinical characteristics of patients with diabetic nephropathy on maintenance hemodialysis: a multicenter cross-sectional survey in Anhui Province, Eastern China. *Chinese med. J.*, **129**: 1291. https://doi.org/10.4103/0366-6999.182832

Ding, H., Han, Y.Y. and Zhang, Y., 2019. Clinical study of Haikun Shenxi Capsule combined with compound α-ketoic acid tablets in the treatment of chronic renal failure. *Drugs Clinic*, **34**: 3050-3054.

Guo, H.B., Xin, B. and Zhang, Q., 2019. Progress in TCM prevention and treatment of protein and energy consumption in maintenance hemodialysis patients. *Med. Recapitul*., **25**: 3677-3681.

Li, D.Y., Yuan, X.K. and Liu, G.L., 2019. Correlation study of serum Irisin and BMP-7 levels with vascular calcification and calcium and phosphorus metabolism in maintenance hemodialysis patients. *China J. Modern Med*., **29**: 41-46.

Li, H.L., Li, H., Cao, Y.F., Qi, Y., Wang, W.Q., Liu, S.Q., Yang, C.D., Yu, X.Y., Xu, T., Zhu, Y. and Chen, W., 2020. Effects of keto acid supplements on Chinese patients receiving maintenance hemodialysis: A prospective, randomized, controlled, single-center clinical study. *Chinese med. J.*, **133**: 9-16. https://doi.org/10.1097/CM9.0000000000000578

Liu, Z.G. and Shi-Ren S., 2017. Study on the clearance effect of serum parathyroid hormone in maintenance hemodialysis patients by common blood purification method. *China Med. Pharm*., **7**: 246-248.

Luo, J., Hu, H. and Li, Y., 2017. Effects of Hybrid blood purification on β2 microglobulin levels and microinflammatory status in maintenance hemodialysis patients. *Chongqing Med*., **46**: 4070-4071.

Marsen, T.A., Beer, J., Mann, H. and German IDPN-Trial Group, 2017. Intradialytic parenteral nutrition in maintenance hemodialysis patients suffering from protein-energy wasting. Results of a multicenter, open, prospective, randomized trial. *Clin. Nutr.,* **36**: 107-117. https://doi.org/10.1016/j.clnu.2015.11.016

Qiao, D.L., Shan, L. and Wu, H.Y., 2018. Correlation analysis of serum 25-hydroxyvitamin D3 levels with inflammation and nutritional status in maintenance hemodialysis patients. *J. Bengbu med. Coll*., **43**: 191-194.

Ren, H., Gong, D., Jia, F., Xu, B. and Liu, Z., 2016. Sarcopenia in patients undergoing maintenance hemodialysis: Incidence rate, risk factors and its effect on survival risk. *Renal Failure*, **38**: 364-371. https://doi.org/10.3109/0886022X.2015.1132173

Shah, A., Bross, R., Shapiro, B.B., Morrison, G. and Kopple, J.D., 2016. Dietary energy requirements in relatively healthy maintenance hemodialysis patients estimated from long-term metabolic studies. *Am. J. clin. Nutr.*, **103**: 757-765. https://doi.org/10.3945/ajcn.115.112995

Shang, H.P., Song, X.P. and Li, X.L., 2017. Correlation between hemoglobin variation and cardiovascular and cerebrovascular events in maintenance hemodialysis patients. *Chinese J. Blood Purificat*., **16**: 322-325.

Vaziri, N.D., Kalantar-Zadeh, K. and Wish, J.B., 2016. New options for iron supplementation in maintenance hemodialysis patients. *Am. J. Kidney Dis.*, **67**: 367-375. https://doi.org/10.1053/j.ajkd.2015.09.031

Wu, X.Y., Zhang, Z. and Xu, T.H., 2017. Correlation analysis of serum Sclerostin and vascular calcification in maintenance hemodialysis patients. *Chinese J. Blood Purificat*., **16**: 793-797.

Wu, L.H., Zhang, M. and Chen, X.Q., 2019. Correlation of serum parathyroid hormone levels with cardiac function and quality of life in maintenance hemodialysis patients. *China J. Modern Med*., **29**: 112-117.

Xiao, L.J. and Ji, D.X., 2019. Progress in clinical application of hybrid blood purification technology. *Chinese J. Blood Purificat*., **18**: 550-552.

Xing, L., Gao, Z.H. and Wang, N., 2017. Effect of hybrid blood purification on quality of life of maintenance hemodialysis patients. *Int. J. Transplant. Hemopurificat*., **15**: 40-42.

Yang, J., Jiang, W.Y. and Wu, X., 2017. Comparison of effects of intravenous injection of iron sucrose and oral administration of iron agent on renal anemia and oxidative stress in maintenance hemodialysis patients. *Guizhou med. J*., **41**: 1075-1077.

Zhang, K., Wang, S.T. and Hu, X.Z., 2017. Risk factors of cardiovascular disease in maintenance hemodialysis patients. *Shandong med. J*., **57**: 82-84.

Zhang, X.H., 2017. The correlation between serum 25-hydroxyvitamin D level and nutritional status, lipid level and inflammatory factors in maintenance

hemodialysis patients. *Anhui med. Pharmaceut. J.*, **18**: 653-655.

Zhang, H.R., Lv, H.X. and Zhang, J.M., 2017. Effect of compound alpha ketoacid tablets combined with Niaoduqing granules on renal function and serum levels of TNF-α and IL-18 in diabetic nephropathy patients. *Hebei med. J.*, **39**: 1011-1013.

Zhang, W., Zheng, Y.Y. and Wang, X.L., 2018. Effect of compound alpha ketoacid tablets combined with high-throughput dialysis on nutritional status, lipid profile and cardiovascular calcification in maintenance hemodialysis patients. *J. Guangxi med. Univ.*, **35**: 1289-1293.

Zhang, Z., Wu, X.Y. and Xu, T.H., 2018. Correlation between serum bone morphogenetic protein 7 and abdominal aortic calcification in 30 patients undergoing maintenance hemodialysis. *Chinese J. Pract. Intern. Med.*, **38**: 1165-1168.

Zhong, X.J., Wu, Q. and Zhang, L.H., 2017. Correlation between hemoglobin variation and cardiovascular and cerebrovascular events in maintenance hemodialysis patients. *Chinese J. Nephrol. Dialy. Transpl.*, **26**: 212-216.

Zou, S., Ban, L.L. and Feng, L.M., 2017. Clinical observation of compound α-ketoacid tablets in the treatment of type 2 diabetes with early diabetic nephropathy. *China Pharmacy*, **28**: 4981-4983.