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A Systematic Review and Meta-analysis of Panaxosides in the Treatment of Glomerulonephritis

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Abstract

Objective Systematic evaluation of the efficacy of panaxoside in the treatment of glomerulonephritis.

Method The retrieve database includes China National Knowledge Infrastructure (CNKI), VIP Chinese sci-tech journal database (VIP), Wanfang database (Wanfang Data), and China Biology Medicine disc (CBM), with the keywords of "ginsenoside", "panaxoside", "glomerulonephritis", "nephritis" and "chronic glomerulonephritis". The retrieved time is limited from January 2000 to June 2020, and the language is limited to Chinese. Review Manager 5.3 was used to deal with the data, the 24 h urine protein, serum creatinine, blood glucose, body weight, serum glucose, total cholesterol and triglyceride were used as the evaluation indexes.

Results A total of 8 articles and 246 patients were included. The results of meta-analysis showed that panaxoside could effectively reduce the content of 24-hour urinary protein [MD = -31.81, 95%CI (-38.74, -24.88), P<0.00001], serum creatinine [MD = -21.89, 95%CI (-30.95, -12.840, P<0.00001], blood glucose [MD = -4.97, 95%CI (-8.66, -1.28), P=0.008], serum glucose [MD = -3.19, 95%CI (-3.66, -2.710, P<0.00001], and triglyceride [MD = -0.72, 95%CI (-0.82, -0.620, P<0.00001]. Conclusion Panaxoside has a good curative effect in the treatment of glomerulonephritis, which provides some reference for the clinical application.

Key words: Panaxoside; Glomerulonephritis; Meta; Curative effect

1. Introduction

Glomerulonephritis was a common kidney disease. According to the survey, the incidence of glomerulonephritis in China was 11% [1]. From the perspective of clinical manifestations, the main symptoms of glomerulonephritis were long-term persistent proteinuria and hematuria, hypertension, renal function damage, which has the characteristics of high incidence, long course of the disease, palindromia, and may develop into renal failure in the late stage of the disease [2].

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Clinical treatment was mainly symptomatic treatment [3]. Ginseng was a valuable traditional Chinese medicine, which has the functions of reinforcing vital energy, help produce saliva and slake thirst, tranquilizing and reinforcing the mind. Panaxoside was one of the main components of Ginseng, at least 40 kinds of panaxoside monomers have been isolated from the Ginseng, among which the most studied Panaxosides were Rg1, Rg3, Rb1, Rd, Re, and Rh1. Panaxosides have attracted much attention in the treatment of anti-fibrosis, angiogenesis, and diabetic nephropathy. A large number of studies have pointed out that Panaxosides have a certain protective effect on the kidney, which can improve the function of glomerular filtration membrane and inhibit the

production of inflammatory factors in renal tubular epithelial cells to improve the occurrence and development of chronic glomerulonephritis [4-8]. Panaxosides have good efficacy in the treatment of glomerulonephritis and other related diseases, but due to the selection of samples and other related factors, the conclusions of the study were not consistent. Therefore, in this study, meta-analysis was used to further explore the effect of Panaxosides in the treatment of glomerulonephritis, to provide a reference for the clinical treatment of glomerulonephritis.

2. Materials and Method

Inclusion and exclusion criteria

Inclusion criteria

(1) The subjects were the patients diagnosed with chronic glomerulonephritis.
(2) Clinical randomized controlled trials
(3) The patients were divided into the experimental group and control group, panaxoside was used as the treatment interventions (unlimited dosage, usage and course of treatment), and the basic treatment including diet control, blood pressure reduction.
(4) The 24 h urine protein, serum creatinine, blood glucose, body weight, serum glucose, total cholesterol (TC) and triglyceride (TG) were used as the evaluation indexes.

Exclusion criteria

(1) The random grouping was not mentioned in the literature or the The random grouping was not used after consultation with the original author.
(2) The test process of the literature was not clear or the design was not rigorous.
(3) Repeated publication and poor quality of literature.
(4) In addition to the basic treatment, other treatment methods were used.
(5) The curative effect index was unreasonable or the treatment results were not published in detail.

Literature retrieve

The retrieve database includes China National Knowledge Infrastructure (CNKI), VIP Chinese sci-tech journal database (VIP), Wanfang database (Wanfang Data), and China Biology Medicine disc (CBM), with the keywords of "ginsenoside", "panaxoside", "glomerulonephritis", "nephritis" and "chronic glomerulonephritis". The retrieved time is limited from January 2000 to June 2020, and the language is limited to Chinese.

Literature screening and data extraction

Two researchers independently screen and evaluate the literature, and if there were differences, they can reach an agreement after discussion, or consult relevant statistical professionals to solve them. Cochrane systematic Review Manual 5.1 was used to evaluate the methodological quality of the included clinical trials, including random method, blind method, allocation concealment, data integrity, selective reporting and other sources of bias.

Statistical analysis

In this study, Review Manager 5.3 was used to deal with the data. The data type of the study was measurement data, and the measurement data was expressed by mean difference (MD), and the results were expressed by 95% confidence interval (CI). $\chi 2$ test was used to test the heterogeneity of the included literature. If the $\chi 2$ test results showed that $P>0.05$ or $I2<50\%$, it was considered that there was no heterogeneity among the studies, and the fixed effect model was used. If the $\chi 2$ test results show that $P\leq 0.05$ or $I2\geq 50\%$, it was considered that there was heterogeneity among the studies, and the random effect model was used. The analysis results were given in the form of a forest map, and the funnel chart was used to analyze the potential publication bias.

3. Results

Literature retrieval results

A total of 1252 references were obtained through search. After abstract and full-text reading, 8 references [10-17] were included according to the inclusion and exclusion criteria, with a total of 246 patients. The specific literature retrieval process is shown in Figure 1.

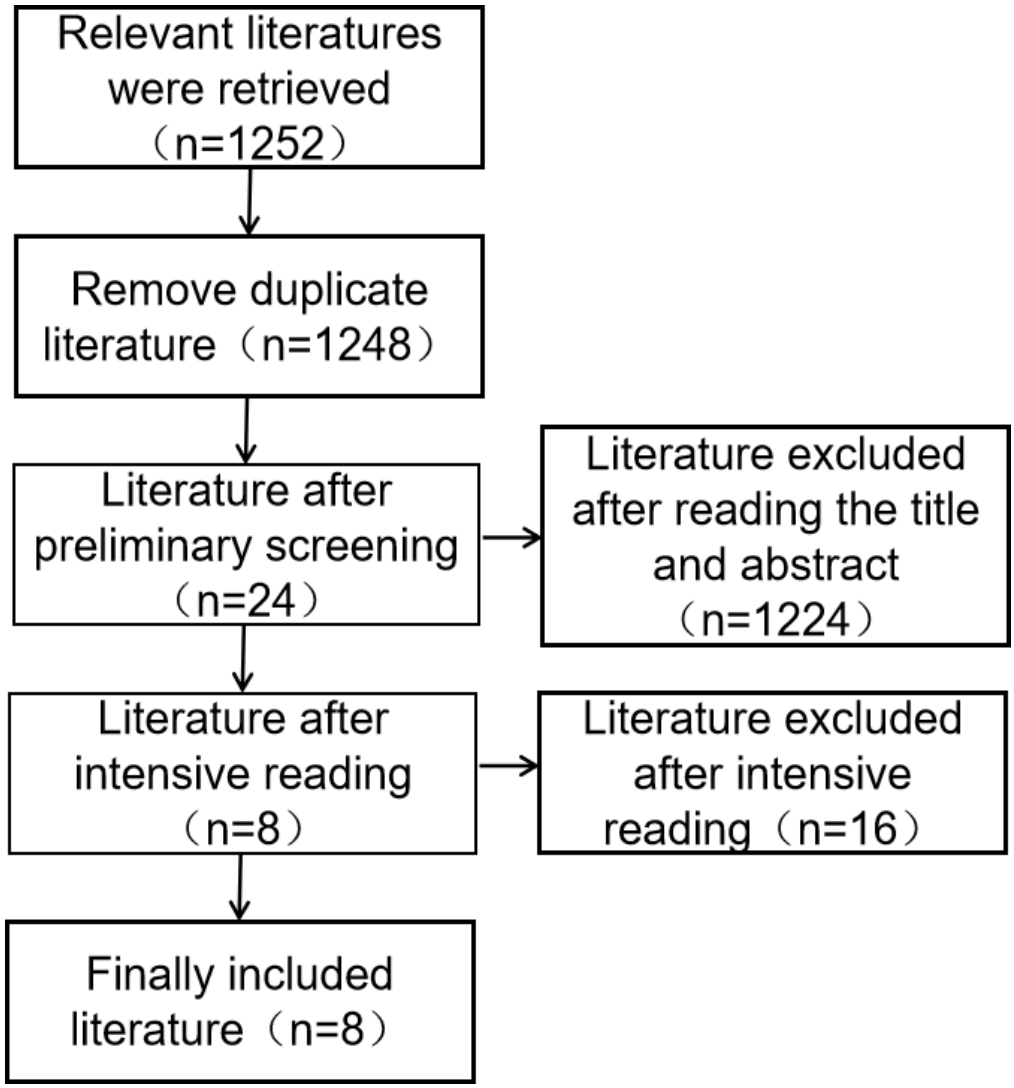

Figure 1 Literature retrieval process

The basic characteristics of the inclusion research

A total of 8 articles [10-17] were included in this study. There were 163 cases in the treatment group and 83 cases in the control group. The main observation indexes were the 24 h urine protein, serum creatinine, blood glucose, body weight, serum glucose, TC, and TG, as shown in Table 1.

Table 1 The basic characteristics of the inclusion research

Inclusion research	Experimental group	Control group	24 h urine protein (mg)		Serum creatinine (μmol/L)		Blood glucose (mmol/L)		Body weight		Serum glucose (mmol/L)		TC (mmol/L)		TG (mmol/L)	
			Experimental group	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group
WangJuan 2014[10]	10	10	5.26±0.49	14.03±0.76	65.42±5.23	96.21±3.52	21.07±0.98	26.53±0.85								
Liu Ni 2019[11]	42	8			112.07±3.56	135.58±5.47	12.35±1.56	26.22±2.15					5.34±2.47	10.56±2.31	1.08±0.08	1.78±0.15
ZhangJie 2012[12]	24	8	105.3 ± 6.8	185.3± 8.9									2.81±0.73	3.01 ± 0.51	2.27±0.70	2.65±0.91
ZhouTong 2016[13]	9	10	2.28±0.90	4.42 ±1.48	107.14 ±14.46	114.57±10.37			363.57 ±22.71	276.86±13.23	21.87±5.59	24.53±6.30	5.59±0.97	6.43 ±1.15	4.01±0.49	4.74 ±1.12
Ni Haixiang 2009[14]	18	18					29.3±5.1	29.7±7.3	197.8±20.5	188.2±40.4						
ZhangXuekai 2008[15]	13	13	82.14±5.74	103.39±8.36	67.87±2.30	76.11 ±3.44			241.67 ±10.59	234.50±7.43	8.78±0.61	11.97±0.63			3.56±0.23	4.49 ±0.44
Ma Xiaofen 2010[16]	36	10	499.88 ±46.80	913.33±59.09	57.65±5.34	87.00 ±2.44	23.49±1.66	25.08 ±0.95								
ZhangLina 2009[17]	9	9	5.00±0.47	9.27 ±0.64	57.65±5.34	87.00 ±2.44	22.23±1.33	25.08 ±0.95								

Detection of the 24 h urine protein

A total of 6 studies were included, and the heterogeneity analysis showed that P<0.00001, I2=100%. There was heterogeneity among the studies, and the random effect model was used. The results showed that there was a statistically significant difference between the panaxoside treatment group and the control group [MD =-31.81, 95% CI (-38.74, -24.88), P<0.00001], indicating that the treatment of glomerulonephritis with panaxoside could significantly reduce the 24 h urine protein level of the patients compared with the control group (Figure 2).

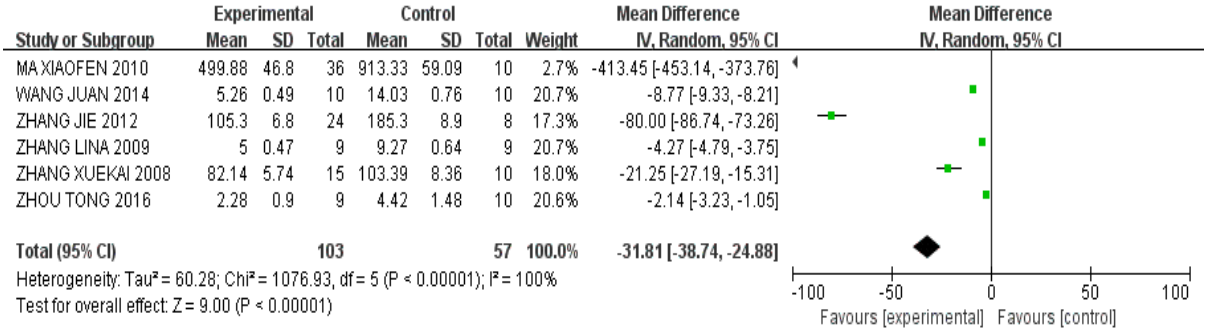

Figure 2 Meta-analysis of the 24 h urine protein levels in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

Serum creatinine

A total of 6 studies were included, and the heterogeneity analysis showed that P<0.00001, I2=98%. There was heterogeneity among the studies, and the random effect model was used. The results showed that there was a statistically significant difference between the panaxoside treatment group and the control group [MD =-21.89, 95%CI (-30.95, -12.84), P<0.00001], indicating that the treatment of glomerulonephritis with panaxoside could significantly reduce the serum creatinine level of the patients compared with the control group (Figure 3).

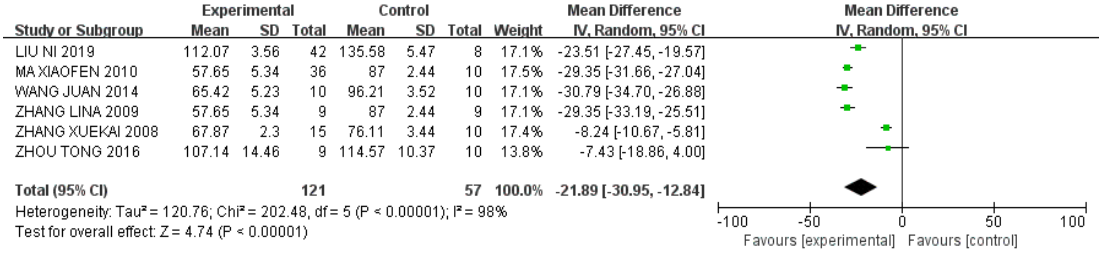

Figure 3 Meta-analysis of the serum creatinine levels in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

Blood glucose

A total of 5 studies were included, and the heterogeneity analysis showed that *P*<0.00001, I^2=98%. There was heterogeneity among the studies, and the random effect model was used. The results showed that there was a statistically significant difference between the panaxoside treatment group and the control group [MD =-4.97, 95%CI (-8.66, -1.28), *P*=0.008], indicating that the treatment of glomerulonephritis with panaxoside could significantly reduce the blood glucose level of the patients compared with the control group (**Figure 4**).

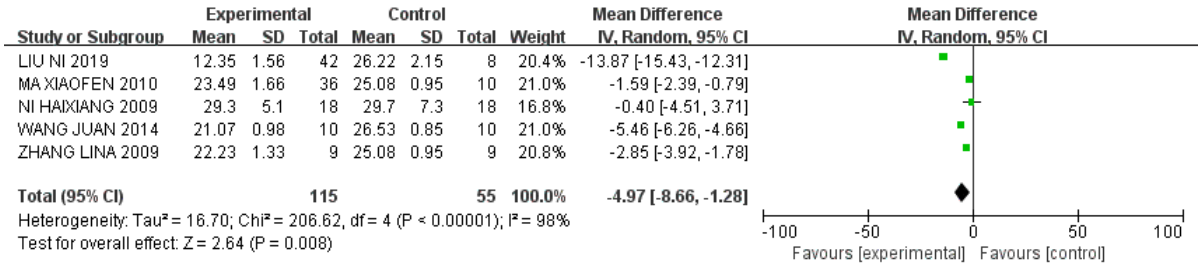

Figure 4 Meta-analysis of the blood glucose levels in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

Body weight

A total of 3 studies were included, and the heterogeneity analysis showed that *P*<0.00001, I^2=97%. There was heterogeneity among the studies, and the random effect model was used. The results showed that there was no statistically significant difference between the panaxoside treatment group and the control group [MD = 34.36, 95%CI (-16.14, 84.86), *P*=0.18], indicating that there was no significant difference between the panaxoside treatment glomerulonephritis group and the control group (**Figure 5**).

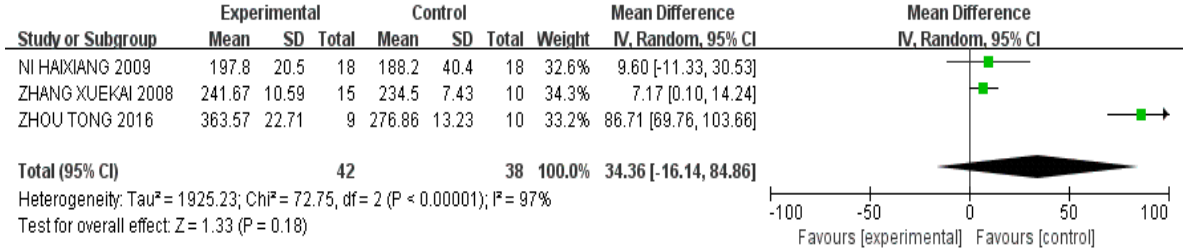

Figure 5 Meta-analysis of the body weight in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

Serum glucose

A total of 2 studies were included, and the heterogeneity analysis showed that *P*=0.85, I^2=0%. There was no heterogeneity among the studies, and fixed-effect model was used. The results showed that there was a statistically significant difference between the panaxoside treatment group and the control group [MD =-3.19, 95%CI (-3.66, -2.71), *P*<0.00001], indicating that the treatment of glomerulonephritis with panaxoside could significantly reduce the serum glucose level of the patients compared with the control group (**Figure 6**).

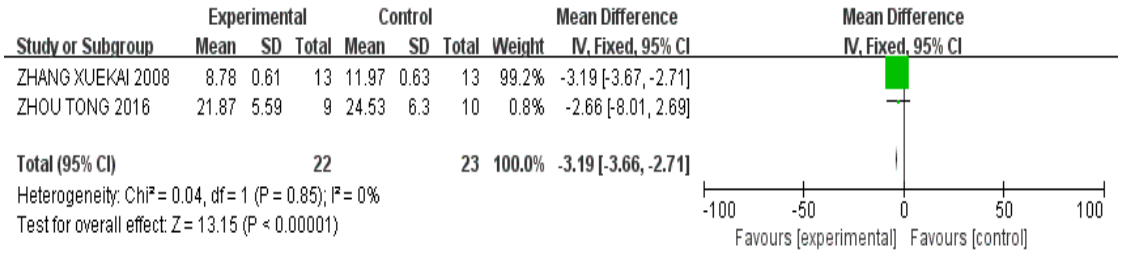

Figure 6 Meta-analysis of the serum glucose levels in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

TC

A total of 3 studies were included, and the heterogeneity analysis showed that *P*<0.00001, I^2=93%. There was heterogeneity among the studies, and the random effect model was used. The results showed that there was no statistically significant difference between the panaxoside treatment group and the control group [MD=-1.89, 95%CI (-3.99, 0.21), *P*=0.08], indicating that the treatment of glomerulonephritis with panaxoside could significantly reduce the TC level of the patients compared with the control group (**Figure 7**).

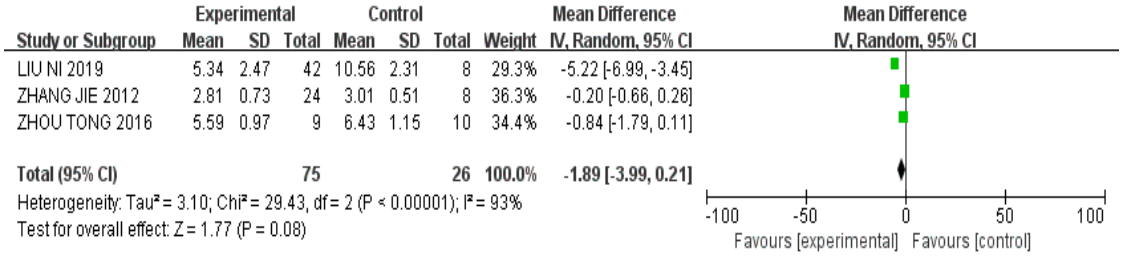

Figure 7 Meta-analysis of the TC levels in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

TG

A total of 4 studies were included, and the heterogeneity analysis showed that *P*=0.39, I^2=0%. There was no heterogeneity among the studies, and the fixed effect model was used. The results showed that there was a statistically significant difference between the panaxoside treatment group and the control group [MD = -0.72, 95%CI (-0.82, -0.62), *P*<0.00001], indicating that the treatment of glomerulonephritis with panaxoside could significantly reduce the TG level of the patients compared with the control group (**Figure 8**).

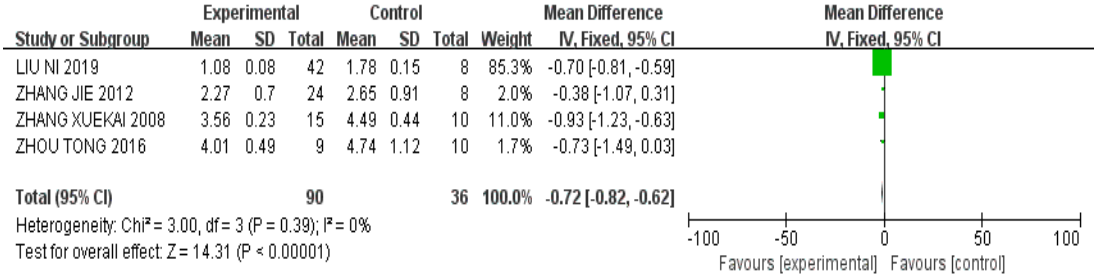

Figure 8 Meta-analysis of the TG levels in the panaxoside treatment group and the control group for the treatment of glomerulonephritis

Publication bias

The funnel chart analysis of the literature with serum creatinine as an index showed that the scattered points were concentrated on both sides of the invalid line, and the funnel diagram was basically symmetrical, indicating that the included literature was less likely to have publication bias (**Figure 9**).

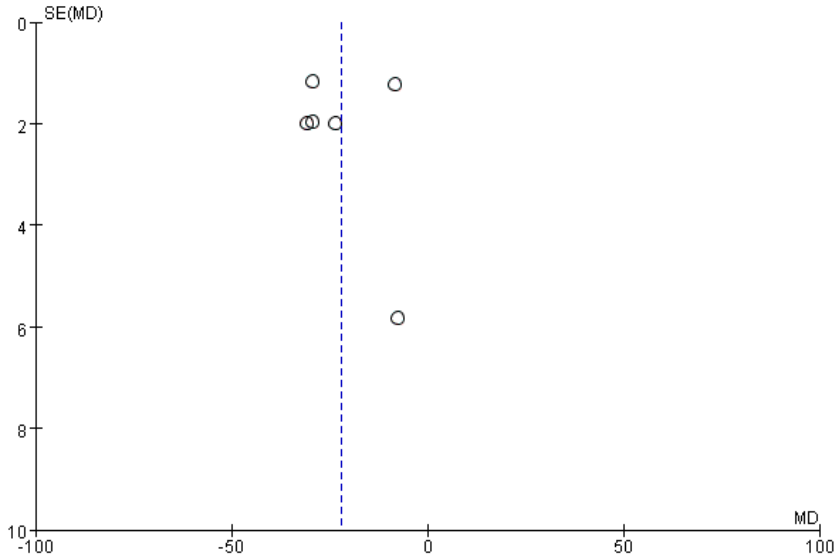

Figure 9 Funnel analysis of serum creatinine

4. Discussion

It was reported that glomerulonephritis was one of the main causes of end-stage renal failure [18]. The pathological changes of glomerulonephritis were mainly characterized by the diffuse or focal inflammation changes of bilateral glomeruli. According to the pathogenesis, glomerulonephritis can be divided into many types, such as focal segmental glomerulosclerosis, mesangial capillary vascular glomerulonephritis, and membranous nephropathy. The final stage of the disease is renal failure, which has a great impact on the physical and mental health of patients [19]. The current treatment mainly takes delaying the renal dysfunction, prevention and treatment of serious complications as the treatment principle [20], the specific measures include reducing the 24-hour urine protein content, serum creatinine, blood pressure, so as to minimize renal damage in patients with glomerulonephritis.

Traditional Chinese medicine Ginseng has been used in China for thousands of years. As one of the main active components of Ginseng, panaxoside Rg1 has certain effects of promoting intelligence, anti-aging, anti-oxidation, and improving immunity. Studies have shown that panaxoside has the effect of anti-glomerulonephritis and protecting renal function [21]. From the perspective of pathology, panaxoside can alleviate the tubulointerstitial damage and mitochondrial swelling in membranous nephropathy. Panaxoside can initiate the DNA replication of proximal convoluted tubular epithelial cells to repair renal tubular tissue necrosis caused by the gentamicin and achieve therapeutic effect [22]. The 24-hour urine protein and serum creatinine were two important indexes to judge renal function. The content of protein in the urine of normal people was relatively small, when the kidney was damaged, the content of protein in urine will increase significantly. Therefore, the content of urinary protein fluctuates greatly in a day, and the 24-hour urine protein was often used as an index to judge the renal function of patients with nephropathy. Serum creatinine was a metabolite secreted into the blood by human muscle tissue, which was mainly filtered by glomeruli. When the glomerular function is normal, the patient's serum creatinine level is relatively constant, once the glomerulus is damaged, the patient's serum creatinine level can be significantly increased, and its concentration is closely related to the severity of the disease. In this study, the results of meta-analysis showed that panaxoside could effectively reduce the 24-hour urinary protein content [MD =-31.81, 95%CI (-38.74, -24.88), P<0.00001] and serum creatinine level [MD =-21.89, 95%CI (-30.95, -12.84), P<0.00001], indicating that panaxoside has a good clinical effect in the treatment of glomerulonephritis. This is basically consistent with the conclusions of previous studies [11-14]. It can be seen that for patients with glomerulonephritis, the occurrence and development of glomerulonephritis can be delayed by controlling urinary protein and serum creatinine. In addition, the results of meta-analysis in this study also showed that panaxoside could reduce the TG level of patients [MD = -0.72, 95%CI (-0.82, -0.62), P<0.00001], serum glucose level [MD = -3.19, 95%CI

(-3.66, -2.71), P<0.00001], and blood glucose level [MD = -4.97, 95%CI (-8.66, -1.28), P=0.008] with diabetic glomerulonephritis. Panaxoside can be used to formulate a reasonable treatment plan for patients with diabetic nephropathy.

From the research results, the conclusions of this study were basically consistent with the results of previous studies. However, there are still the following shortcomings. First of all, the literature included was insufficient. In this paper, the retrieval language was limited to Chinese, although the relevant English literature was less, it was not included in this paper. Secondly, the sample size included in this paper was insufficient. Therefore, the follow-up research should collect the relevant references comprehensively and conduct a large sample survey to support it.

Conclusion

To sum up, compared with the control group, panaxoside treatment can improve the levels of 24-hour urine protein, serum creatinine, TG, serum glucose, and blood glucose, indicating that panaxoside has a better clinical effect in the treatment of glomerulonephritis.

Authors' contributions

Gang Wang conceived and designed the experiments; Guochen Zhao performed the experiments; Xiaojuan Guo analyzed the data and wrote the paper.

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Conflicts of interest

The authors report no conflicts of interest.

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