Received: 12 August 2024 | Revised: 16 September 2024 | Accepted: 1 October 2024 | Published online: 11 October 2024

International Journal of Advance in Clinical Science Research, Volume 3, 2024
https://h-tsp.com/

# Meta Analysis of Efficacy and Safety of Traditional Chinese Medicine Combined with Immunosuppressive Agents in the Treatment of IgA Nephropathy

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**Abstract:** *Objective: To systematically evaluate the efficacy and safety of traditional Chinese medicine combined with immunosuppressive agents in the treatment of IgA nephropathy. Methods: the randomized controlled trial (RCT) of traditional Chinese medicine combined with immunosuppressive agents in the treatment of IgA nephropathy published in the databases of CNKI, VIP, Wanfang Data knowledge service platform, CBM and PubMed were comprehensively searched by computer. The retrieval time was from the establishment of each database to August 2023. Two researchers independently screened the literature and extracted the original data. The bias risk assessment tool in the Cochrane systematic review manual was used to evaluate the quality methodology, and Revman manager 5.4 software was used for meta-analysis of the included studies. Results: a total of 248 articles were retrieved, and 17 articles were finally included after screening according to the nanodischarge criteria. The total sample size was 1 456, including 730 cases in the experimental group and 726 cases in the control group. The results of meta-analysis showed that traditional Chinese medicine combined with immunosuppressive agents in the treatment of IgA nephropathy could improve the clinical effective rate [OR=3.80, 95% CI (2.79, 5.17), Z=8.51, P<0.00001]; The 24-hour urinary protein quantitation (24hUPQ) was reduced [MD=-0.51, 95% CI (-0.68, -0.34), Z=5.93, P<0.00001]; Reduce the number of urinary red blood cells (U-RBC) [SMD=-1.88, 95% CI (-2.83, -0.93), z=3.87, P<0.0001]; Delay the deterioration of renal function and reduce the level of serum creatinine (SCR) [MD=-10.61, 95% CI (-13.98, -7.25), Z=6.18, P<0.00001]; It was helpful to restore glomerular filtration rate (GFR) [MD=7.79, 95% CI (3.42, 12.53), Z=3.34, P=0.0006], and the above differences were statistically significant (P<0.05). However, there was no significant difference between the two groups in reducing the level of urea nitrogen (BUN) (P=0.15). Conclusion: Traditional Chinese medicine combined with immunosuppressive agents in the treatment of IgA nephropathy is superior to western medicine alone in improving clinical efficacy, with less side effects and high safety. Because the quality of the included literatures is generally low, the number is small, and there is a certain degree of publication bias, high-quality, large sample, multi center clinical randomized controlled trials are needed to verify the above conclusions in the future.*

**Keywords:** IgA nephropathy; Traditional Chinese medicine; Immunosuppressive agents; Meta analysis; Randomized controlled trial.

## 1. Introduction

IgA nephropathy (IgAN) is a kidney disease caused by the deposition of IgA immune complexes in the glomeruli, which is the main cause of chronic kidney disease [1]. In the initial stage, IgAN usually presents with asymptomatic urine abnormalities (e.g., microscopic hematuria with or without proteinuria). With the development of the disease, obvious renal abnormalities (such as gross hematuria, nephrotic syndrome) can evolve into progressive renal failure at the end stage [2]. According to epidemiological surveys, about 50% of IgAN patients will develop into end-stage renal disease within 20 years after diagnosis [3]. The incidence of IgAN shows regional and ethnic differences, with East Asian population having the highest incidence, followed by European population and African population [4]. So far, the pathogenesis of IgAN has not been fully elucidated. Studies have shown that factors such as genes, immunity and environment interact to lead to the variability of clinical manifestations of IgAN [5]. At present, the treatment of IgAN with western medicine is mainly based on systemic medication recommended by domestic and foreign guidelines, including renin-angiotensin system inhibitors and glucocorticoids. However, some IgAN patients with higher Lee grade diagnosed by renal biopsy are not sensitive to glucocorticoid treatment, and the use of immunosuppressants is inevitable at this time [6]. Although immunosuppressants have been widely used in clinical practice, adverse reactions caused by long-term use of immunosuppressants and repeated complications after drug withdrawal have become new problems [7]. In recent years, a number of randomized controlled trials have shown that traditional Chinese medicine combined with immunosuppressants can not only effectively improve the clinical symptoms of IgAN patients, but also delay the deterioration of renal function and reduce adverse reactions [8]. However, there is still a lack of systematic reviews of this combination to evaluate its efficacy and safety in clinical practice. This study intends to systematically review and analyze the effect of traditional Chinese medicine combined with immunosuppressants on the clinical efficacy and safety of IgAN, in order to provide scientific evidence for clinical research.

## 2. Materials and Methods

### 2.1 Inclusion and Exclusion Criteria

2.1.1 Inclusion criteria

(1) Study type: the RCT literature on the treatment of IgAN with traditional Chinese medicine combined with immunosuppressive agents published at home and abroad; (2) Subjects: IgAN patients diagnosed by renal biopsy; (3) Intervention measures: the control group was treated with immunosuppressive therapy, and the experimental group was treated with traditional Chinese medicine on the basis of the control group (there was no limit to the form, dosage, usage of traditional Chinese medicine, etc.). Both groups could be treated by antihypertensive, calcium supplementation, anti-infection, etc. (4) Outcome indicators: ① Total effective rate; ② 24-hour urinary protein quantification (24hUPQ); ③ Urine red blood cell count (U-RBC); ④ Serum creatinine (Scr); ⑤ blood urea nitrogen (BUN); ⑥ glomerular filtration rate (GFR), at least one of the above outcome measures should be included in the included studies. Total effective rate =(cured + markedly effective + effective) number of cases/total number of cases ×100%.

2.1.2 Exclusion criteria

(1) Non-RCT literature; (2) Systematic reviews, conference guidelines, animal experiments, dissertations, etc.; (3) duplicate publications, incomplete data and the full text could not be obtained; (4) literature with inconsistent experimental content, intervention measures and control measures;

**2.2 Data Sources and Retrieval Strategy:**

China National Knowledge Infrastructure (CNKI), VIP, Wanfang Data Knowledge Service Platform, China Biology Medicine Disc (CBM), PubMed and other databases were searched from the establishment of each database to August 2023. Chinese search terms included "IgA nephropathy" "Chinese medicine/Chinese patent medicine/Chinese medicine preparation" "immunosuppressant" "tripterygium wilfordii polyglycoside tablets" "mycophenolate mofetil" "Leflunomide" "randomized controlled trial", etc. English search terms included "IgA nephropathy" "Traditional Chinese medicine" "Immunosuppressive Agents" "Mycophenolate mofetil" "randomized" controlled trial ", etc. All searches were performed using a combination of subject words and free words.

**2.3 Literature Screening and Data Extraction**

Endnote X9 software was used to manually eliminate repeated published literature. Titles and abstracts were preliminarily read to exclude literature that did not meet the inclusion and exclusion criteria, and the full text was further read for screening.

Data extraction included: the basic information of the included studies, course of disease, sample size, intervention measures, control measures, course of treatment, outcome indicators, adverse reactions, etc. Two researchers independently screened literature and extracted data, and cross-checked them. If there was any disagreement, a third researcher was consulted to solve the problem.

**2.4 Included in Research Quality Evaluation**

Quality assessment of included studies was independently performed using the RCT bias risk assessment tool recommended by the Cochrane handbook, including: random allocation method, allocation concealment, blinding, withdrawal and withdrawal of samples, selective result reporting, and other biases. The quality of bias risk of the included literature was assessed from 7 aspects through 3 risk levels. In order to avoid subjective bias, the quality evaluation of the included literature was completed by two researchers independently, and the results were cross-checked.

**2.5 Statistical Methods**

Review Manager 5.4 software was used to perform a meta-analysis of the included studies. Relative risk OR was used as the effect indicator for binary variables, and mean difference (MD) or standardized mean difference (SMD) was used as the effect indicator for continuous variables. The effect size was expressed with 95% confidence interval (CI), and $P < 0.05$ was considered statistically significant. The Q test and I2 test were used to test the heterogeneity. If $P > 0.1$ and $I2 < 50\%$, the heterogeneity was small, and the fixed effect model was used. If $P \leq 0.1$ and $I2 \geq 50\%$ suggested heterogeneity among the studies, the random effect model was used, and further sensitivity analysis or subgroup analysis was used to find the source of heterogeneity. Funnel plot was used to analyze the potential publication bias of the included studies.

## 3. Results

**3.1 Number of Included Literatures**

248 relevant literatures were obtained through preliminary search, 192 duplicate literatures were excluded, 19 reviews, animal experiments and other literatures were excluded, 153 literatures that did not meet the inclusion and exclusion criteria were excluded after reading the abstract, and 17

literatures that met the inclusion and exclusion criteria were obtained after reading the full text of the remaining 20 literatures [9-25]. The literature screening flow chart is shown in Figure 1.

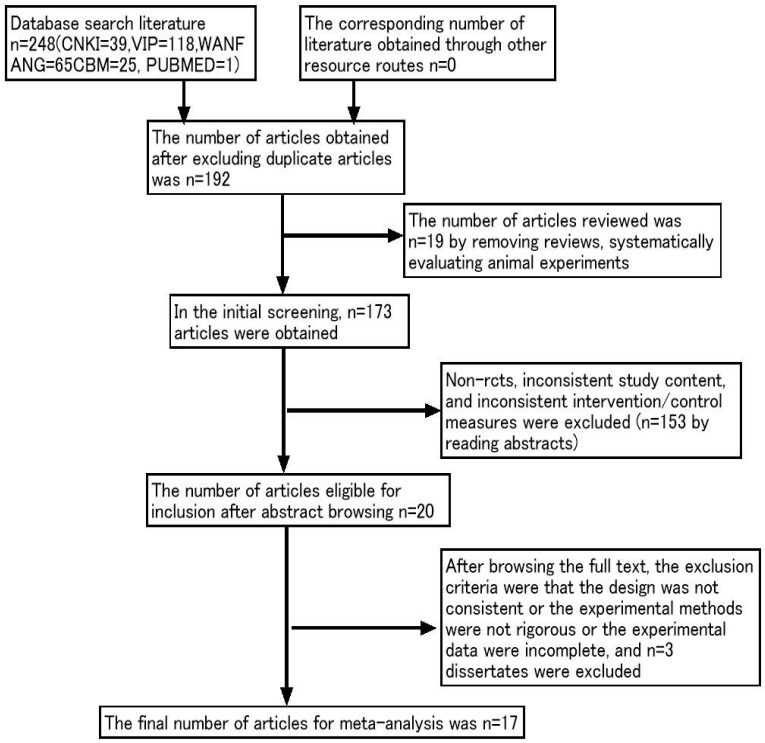



**Figure 1:** Flow chart of literature screening

### 3.2 Basic Information of the Included Literature

This study finally included 17 literatures, with a total sample size of 1 456 cases, including 730 cases in the experimental group (1 case dropped off, and 729 cases were actually included) and 726 cases in the control group. There was no significant difference in the baseline level between the experimental group and the control group, and the two groups were comparable. The basic information of the included studies can be found in Table 1.

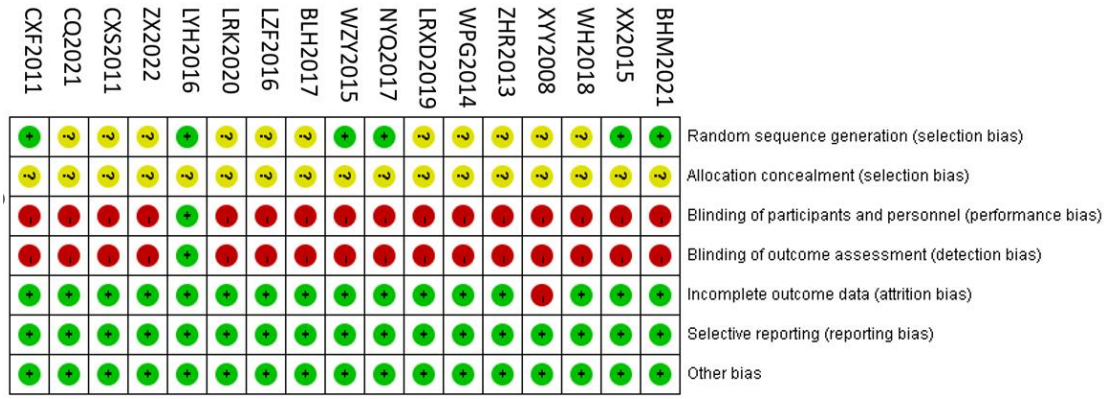
**Table 1:** Basic information of the included studies

| Included literature The First Author | Year | Sample capacity (T/C) | course of treatment | intervening measure | | outcome indicator |
|---|---|---|---|---|---|---|
| | | | | T | C | |
| ChenQiang(CQ)[11] | 2021 | (44/44) | 1months | QFYS+LEF | LEF | ① |
| BaoHongMei(BHM)[12] | 2021 | (50/50) | 8 weeks | ZY+TAC | TAC | ① |
| XiaYuanYu(XYY)[13] | 2008 | (45/45) | 6 months | SYKF+LEF | LEF | ①②③ |
| ZhangHuiRu(ZHR)[14] | 2013 | (22/20) | 6 months | LGT+MMF | MMF | ①②④ |
| WangPeiGui(WPG)[15] | 2014 | (30/30) | 1 months | LGT+MMF | MMF | ① |
| XiangXu(XX)[16] | 2015 | (47/47) | 6 months | HK+MMF | MMF | ①②④ |
| WangZhanYun(WZY)[17] | 2015 | (75/75) | 84 days | ZY+CsA | CsA | ①②③④⑤⑥ |
| LuYIingHua(LYH)[18] | 2016 | (30/30) | 6 months | LGT+MMF | MMF | ① |
| LuoZhiFeng(LZF)[19] | 2016 | (42/42) | 6 months | YSHS+LEF | LEF | ①②③ |
| BaiLiHua(BLH)[20] | 2017 | (45/45) | 6 months | HK+LEF | LEF | ①②④ |
| ChenXiSheng(CXS)[9] | 2011 | (20/19) | 24 weeks | LGT+MMF | MMF | ①②④ |
| ChenXiangFu(CXF)[10] | 2011 | (22/21) | 4 months | BYHW+LEF | LEF | ②③ |
| NiuYuQin(NYQ)[21] | 2017 | (80/80) | 6 months | HXHY+MMF | MMF | ①④⑤ |
| WuHao(WH)[22] | 2018 | (45/45) | 6 months | YQYY+MMF | MMF | ①③④⑤ |
| LuoRuXiDe(LRXD)[23] | 2019 | (41/40) | 12 weeks | HK+MMF | MMF | ①②③④⑥ |
| LanRenKui(LRK)[24] | 2020 | (46/47) | — | HK+MMF | MMF | ① |
| ZhengXin(ZX)[25] | 2022 | (46/46) | 6 months | HK+MMF | MMF | ①②③④⑤⑥ |

Note :T: experimental group C: control group; HK: Huangkui capsule; YQYY: Yiqi Yangyin decoction; HXHY: traditional Chinese medicine for promoting blood circulation and removing blood stasis; YSHS: Yishen Huashi granules; LGT: Tripterygium wilfordii polyglycosides; ZY: traditional Chinese medicine; SYKF: Shenyan Kangfu tablet; QFYS: Qufengyusheng decoction; BYHW: Buyang Huanwu soup; MMF: mycophenolate mofetil; LEF: leflunomide; CsA: cyclosporin A; ① effective rate; ②24hUPQ; ③U-RBC; ④Scr; ⑤BUN; ⑥GFR.

### 3.3 Quality Evaluation of Included Studies

Among the 17 included literatures, 5 studies [10, 12, 16, 18, 21] adopted the random number table method, 1 study [17] adopted the random drawing method, and the remaining studies were described as "random". None of the studies mentioned allocation concealment. One study [18] was double-blind, and the other studies did not mention blinding. One study [13] mentioned loss of follow-up, discontinuation and dropout, and mentioned the reasons. All the studies had described outcome measures, complete data, and no other apparent bias. There were no significant differences in the basic characteristics (gender, age, course of disease, etc.) of the patients in the included studies, and the baseline data were comparable. See Figures 2 and 3 for specific quality assessments.




Note: "+" meets the standard; "-" did not meet the standard; "?" I don't know.

**Figure 2:** Risk of literature bias

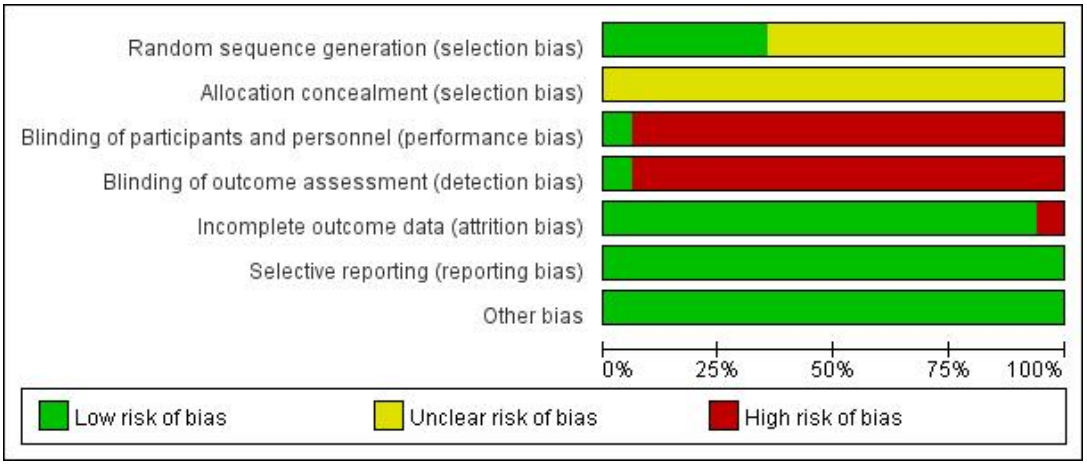



**Figure 3:** Proportion of items at risk of bias

### 3.4 Results of Meta-analysis

3.4.1 Effective rate

16 articles [9, 11-25] reported the effective rate of the two groups. The heterogeneity test (P=0.22, $I^2$=20%) showed that there was little heterogeneity among the studies, and the fixed effect model was used for Meta-analysis. The results showed that the effective rate of the combined treatment group was significantly higher than that of the control group [OR=3.8, 95%CI (2.79, 5.17), Z=8.51, P<0.00001]. See Figure 4.

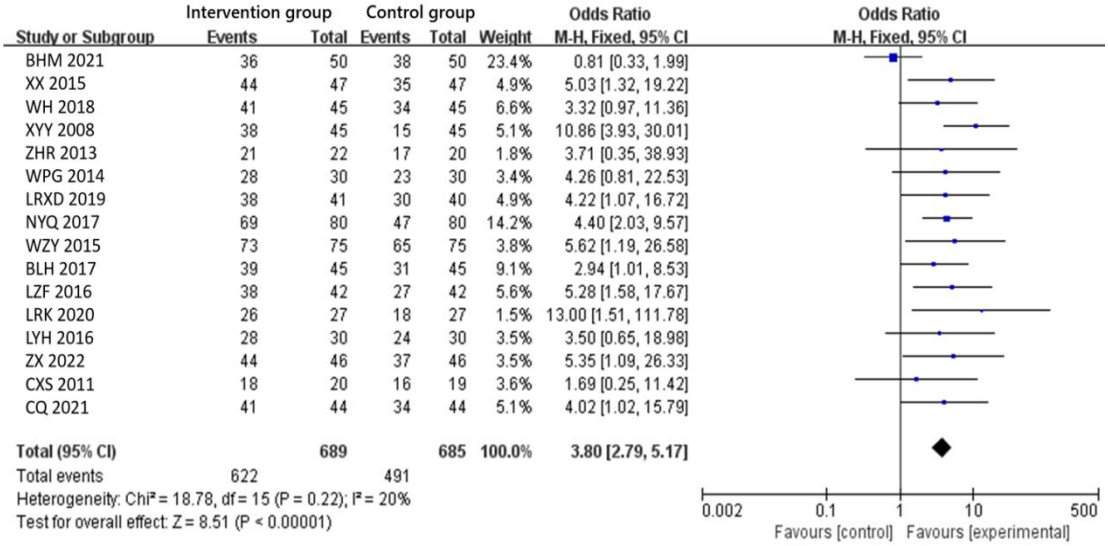



**Figure 4:** Meta-analysis forest plot of clinical response rates

3.4.2 24hUPQ

There were 10 studies [9, 10, 13, 14, 16, 17, 19, 20, 23, 25] on 24hUPQ, which reported the 24-hour urinary protein quantification of the two groups, and the heterogeneity test showed that the heterogeneity between the studies was significant (P<0.00001, $I^2$=93%). After excluding articles by articles, it was found that the main source of heterogeneity was that Xiang Xu [16], Zhang Huiru [14] included cases of elderly IgAN patients, and Chen ChenXisheng [9] included cases of IgAN patients with severe proteinuria, so the random effect model was used for Meta-analysis. The results showed that the combined treatment group was significantly better than the immunosuppressant control group in reducing 24-hour urinary protein [MD=-0.51, 95%CI (-0.68, -0.34), Z=5.93, P < 0.00001]. See Figure 5.

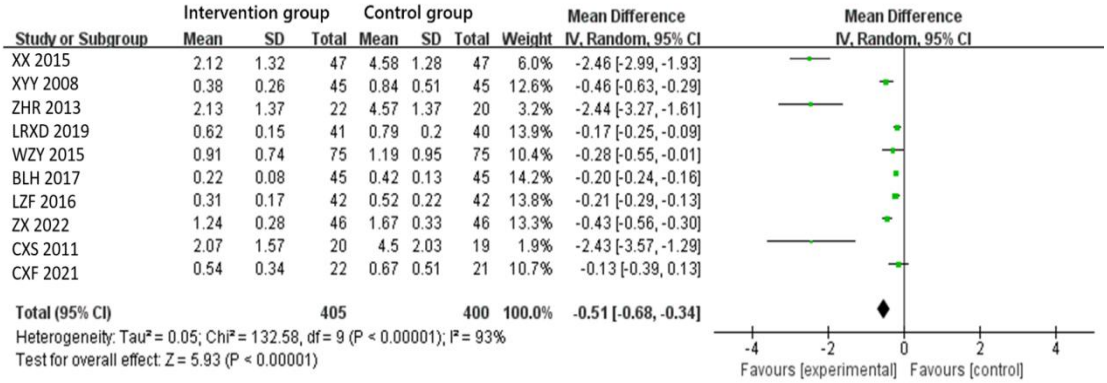



**Figure 5:** Meta-analysis forest plot of 24-hour urinary protein quantification

3.4.3 U-RBC

7 articles [10, 13, 17, 19, 22, 23, 25] reported the urinary red blood cell count indexes of the two groups. Because the counting units of each study were different, the effect size was pooled by SMD. After heterogeneity test, $I^2$=91%>50%, and Q test P < 0.00001. It is suggested that there is great heterogeneity among the studies, which may be related to the severity of the disease, treatment methods, treatment time and other factors of the patients in each study. Therefore, the random effects model was used for Meta-analysis. The results showed that the effect of combined traditional Chinese medicine group on reducing urine red blood cell count was better than that of the control group [SMD=-1.88, 95%CI (-2.83,

-0.93), Z=3.87, P < 0.0001]. See Figure 6.

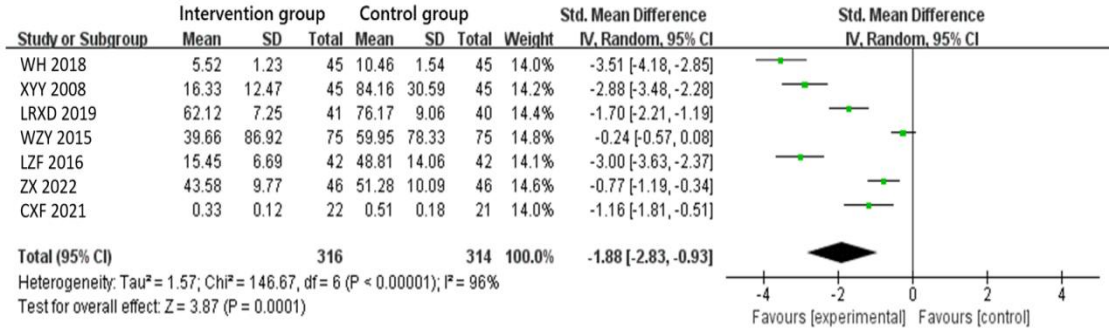



**Figure 6:** Meta-analysis forest plot of urinary red blood cell counts

3.4.4 Renal function

There were 9 studies [9, 14, 16, 17, 20-23, 25] recorded serum creatinine. After the combined effect size, the heterogeneity of each study was $I^2$=95%>50%, and the P value of Q test was <0.0001, indicating that there was large heterogeneity among the studies. The random effect model was used to merge the effect size, and the forest plot (see Figure 7) showed: (MD=-20.13, 95%CI [-35.72, -4.53], Z=2.53, P=0.01). In order to ensure the accuracy and stability of the study, sensitivity analysis was carried out by removing literatures one by one, and it was found that the heterogeneity was significantly reduced ($I^2$=12%<50%) when the study of Niuqin [21] was removed, indicating that the study of niuqin was the main source of heterogeneity of this index. The results showed that the effect of reducing serum creatinine in the combined treatment group was significantly better than that in the control group [MD=-10.61, 95%CI (-13.98, -7.25), Z=6.18, P<0.00001]. See Figure 8.

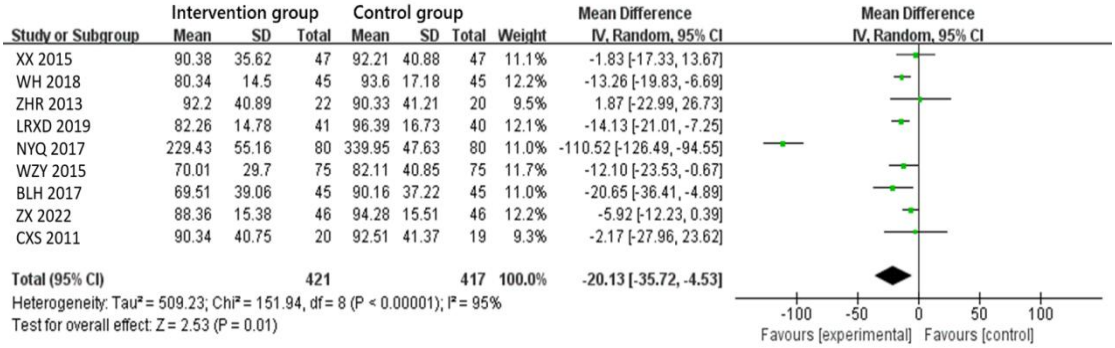



**Figure 7:** Meta-analysis forest plot of serum creatinine

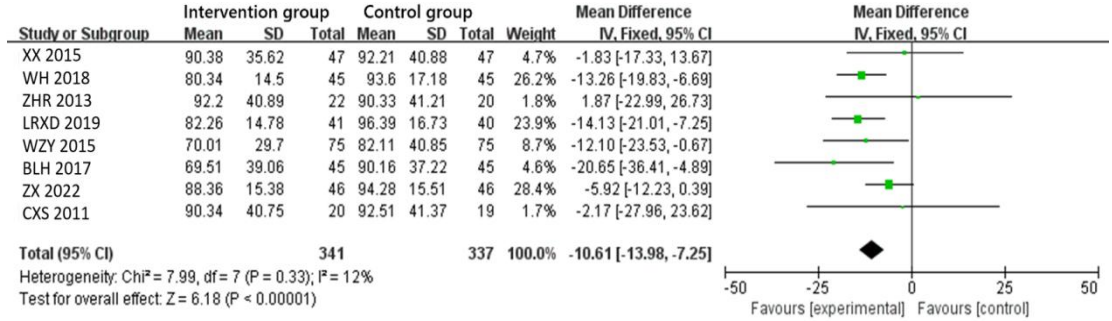



**Figure 8:** Meta-analysis forest plot of serum creatinine

Four studies [17, 21, 22, 25] contained urea nitrogen in the outcome index, which was tested for heterogeneity (P<0.00001, $I^2$=90%), indicating that there was great heterogeneity among the studies.

After excluding each study, it was found that the main reason for bias was Wang Zhan Yun [17] 's study according to the renal function classification of the included cases, Different TCM preparations were used in the experimental groups, so a random-effects model was used for the meta-analysis. The results showed that the effect of some experimental groups on reducing urea nitrogen was better than that of the control group (MD=-0.82, 95%CI [-1.94, -0.29], Z=1.45, P=0.15>0.05), but the difference was not statistically significant, as shown in Figure 9.

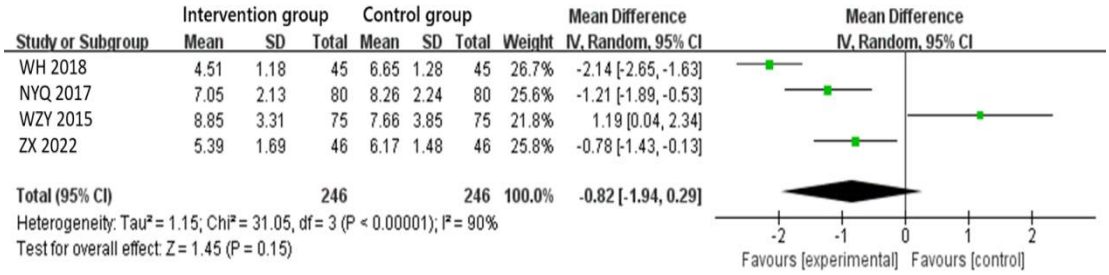



**Figure 9:** Forest plot of urea nitrogen meta-analysis

Three studies [17, 23, 25] recorded the level of glomerular filtration rate in the outcome indicators. After heterogeneity test, ($I^2$=43%<50%, Q test P=0.17), indicating that there was little heterogeneity among the studies, and the fixed effect model was used for Meta-analysis. The results showed that the recovery effect of glomerular filtration rate in the experimental group was better than that in the control group [MD=7.79, 95%CI (3.42, 12.53), Z=3.34, P=0.0006], and the difference was statistically significant, see Figure 10.

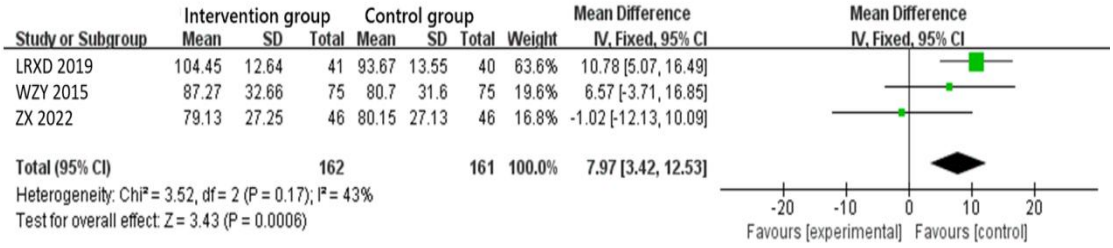



**Figure 10:** Meta-analysis forest plot of glomerular filtration rate

Although the results showed that the reduction of serum creatinine and the recovery of glomerular filtration rate in the traditional Chinese medicine combined with immunosuppressant group was better than that in the immunosuppressant group alone, there was no statistically significant difference in the comparison of serum creatinine within the group after treatment in the trial of Chen Xisheng [9]. In the study by Wang Zhanyun [17], there was no significant difference in the comparison of glomerular filtration rate before and after treatment within the group and between the groups after treatment, P>0.05, which was only used as a safety index. Therefore, the efficacy of traditional Chinese medicine combined with immunosuppressive agents in the treatment of renal function in IgAN patients still needs to be verified by a large number of clinical RCT experiments.

3.4.5 Publication bias assessment

The publication bias of the clinical effective rate of the 16 included articles was evaluated, and the funnel plot was drawn with the pooled OR value as the abscissus and the derivative value as the ordinate. The results showed that the left and right distribution of the funnel plot was asymmetrical, and the funnel plot was concentrated on the right side, suggesting that there was a certain degree of publication bias in the included studies. See Figure 11

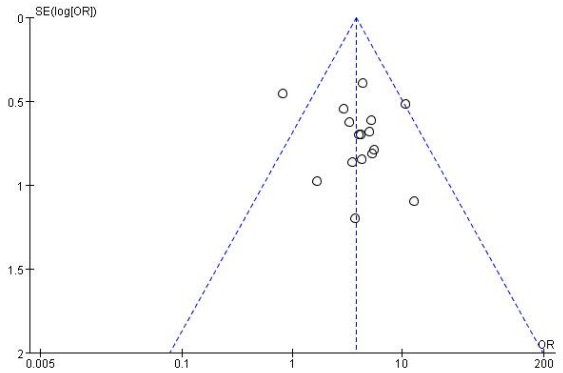



**Figure 11:** Funnel plot of clinical response rate

In this study, a total of 8 studies [9, 13, 14, 16, 19, 20, 23, 25] reported the occurrence of adverse reactions, among which abnormal liver function and digestive tract reactions were more common. Except for 1 study [9], the symptoms disappeared after the symptomatic treatment of stomach protection and diarrhea, the other studies did not describe the outcome of symptoms. Three studies with abnormal liver function [13, 19, 20] showed improvement after reducing the dosage or adding hepatoprotective drugs, as shown in Table 2.

**Table 2:** Adverse effects of the included literature

| Included Literature | Years | Intervening Measure | Sample Size T/C | Adverse Reaction T/C | | | | | Prognosis |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Digestive ract Dymptom | Pruritus | Swirl | Anemia | Abnormal liver function | |
| XZ [25] | 2022 | HK+MMF | 46/46 | 1/3 | 0/1 | 0/1 | | | Not described |
| LRXD [23] | 2019 | HK+MMF | 41/40 | 2/1 | | | 1/1 | | Not described |
| BLH [20] | 2017 | HK+LEF | 45/45 | 0/1 | | | | 0/1 | ① |
| LZF [19] | 2016 | YSHS+LEF | 42/42 | | 1/4 | | | 1/6 | ② |
| XX [16] | 2015 | HK+MMF | 47/47 | 5/6 | | | | | Not described |
| ZHR [14] | 2013 | LGT+MMF | 22/20 | 3/3 | | | | | Not described |
| XYY [13] | 2008 | SYKF+LEF | 45/45 | 0/1 | | | | 0/2 | ① |
| CXS [9] | 2011 | LGT+MMF | 20/19 | 4/4 | | | | | ③ |

Note: HK: Huangkui capsules; LGT: Tripterygium wilfordii polyglycosides; YQYY: Yiqi Yangyin decoction; HXHY: traditional Chinese medicine for promoting blood circulation and removing blood stasis; SYKF: Shenyan Kangfu tablet; ZY: traditional Chinese medicine; QFYS: Qufengyusheng decoction; BYHW: Buyang Huanwu soup; MMF: mycophenolate mofetil; LEF: leflunomide; CsA: cyclosporin A; ① The dosage of LEF was reduced, and the patient was improved after rehydration and liver protection. ② Liver function recovered after liver protective treatment; ③ The symptoms disappeared after stomach protection and antidiarrheal treatment.

## 4. Discussion

IgAN is the most common primary glomerulonephritis in the world, however, its exact cause is still unclear [26]. Studies have shown that immune factors play a key role in the development of IgAN [27]. There are no specific therapies capable of targeting key pathways involved in disease pathogenesis [28]. Traditional IgAN treatment mainly focuses on supportive measures aimed at delaying glomerular disease progression and reducing nonspecific damage to the kidney [29]. In recent years, a deeper understanding of the early inflammatory and immune mechanisms leading to glomerular injury in IgAN has led to the wider use of immunosuppressive agents to treat IgAN. However, there is no conclusive evidence that immunosuppressants have a clear efficacy in the treatment of IgAN, so

according to the KDIGO guidelines, the use of immunosuppressants in the treatment of IgAN is generally not recommended, unless the patient presents with special conditions such as crescentic IgAN or rapidly progressive IgAN [30, 31].

Mycophenolate mofetil (MMF), as an immunosuppressant that inhibits lymphocyte proliferation, has played a great role in the treatment of IgAN. However, there are great controversies in the specific clinical efficacy of MMF. The effects of MMF on end-stage renal disease (ESKD) progression, complete remission, SCr doubling, GFR, proteinuria, infection, and malignancy are still unclear [32]. A meta-analysis showed that the efficacy of mycophenolate mofetil differed between races, and only effective conclusions could be drawn in Asian populations [33]. Studies have shown that immunosuppressants and glucocorticoids can significantly reduce the risk of proteinuria and ESKD in IgAN patients [34]. Previous meta-analyses have shown that immunosuppressive agents reduce proteinuria and delay deterioration of renal function compared with supportive care alone. However, there are still controversies about the regimen of immunosuppressive agents (including combination or monotherapy), dose and duration of administration. More and more studies have shown that TCM intervention has the characteristics of multi-link, multi-pathway and multi-target, which has a significant effect on podocyte injury in IgAN, can protect podocyte and reduce proteinuria, showing a good application prospect [35].

IgAN is usually classified into the categories of "blood in urine", "edema", "deficiency" and "low back pain" in traditional Chinese medicine, and its etiology and pathogenesis mainly involve exogenous pathogenic toxins or internal injury damp-heat. In terms of syndrome differentiation, in the acute attack stage, it is often manifested as pathogenic excess syndrome, while in the chronic persistent stage, it is mainly deficiency syndrome. With the development of clinical research and evidence-based medicine in the treatment of IgAN with traditional Chinese medicine, we have summarized a variety of Chinese medicine prescriptions and Chinese patent medicines for the treatment of IgAN. Modern pharmacological and animal experimental studies have shown that Tripterygium wilfordii polyglycoside tablets may improve the colonic inflammatory response of IgAN mice, affect the expression of serum BAFF, and inhibit the secretion of Gd-IgA1, thereby improving 24-hour urinary protein quantification, reducing serum creatinine and urea nitrogen and other indicators, and reducing renal pathological damage [36]. Huangkui capsule, Yishen Huashi granule, Shenyan Kangfu tablet and other Chinese patent medicines have a variety of effects, such as anti-inflammation, anti-oxidative stress, and immune regulation [37-39]. Different TCM prescriptions or Chinese patent medicines in different stages of IgAN can improve the clinical efficacy and reduce the occurrence of toxic side effects and complications.

Comprehensive studies have shown that Chinese medicine and immunosuppressive agents have their own advantages and disadvantages in the treatment of IgAN. Immunosuppressive agents and hormones alone produce obvious side effects, while the combination of Chinese medicine can make up for the deficiency of western medicine. The meta-analysis included 17 randomized controlled trials involving 1456 patients. The results showed that traditional Chinese medicine combined with immunosuppressant could improve the total effective rate, reduce the urine protein and urine red blood cells, improve the glomerular filtration rate and reduce the serum creatinine level, and there was significant difference compared with the control group ($P<0.05$). There was no significant difference in the improvement of urea nitrogen, indicating that traditional Chinese medicine combined with immunosuppressant had limited improvement in urea nitrogen. Safety evaluation showed that the adverse reaction rate of the traditional Chinese medicine combined with immunosuppressant group was lower, mainly nausea and vomiting, abdominal pain, diarrhea and other gastrointestinal reactions. Some adverse reactions were relieved after reducing the dose of immunosuppressive agents or

symptomatic treatment.

The deficiencies of this study include: (1) the quality of the included studies was generally low, and some literatures did not mention blinding and allocation concealment. (2) The study was a small sample and single-center study, and the test power was insufficient, which may affect the accuracy of the results. (3) All the included studies were from China, with limited applicability and lack of international literature support. (4) The study period of the included randomized controlled trials was too short to evaluate the long-term efficacy and safety of the drugs. (5) There was heterogeneity among the studies, which may be related to the differences in the type of literature study, the course of disease, drug dose, basic treatment medication, and data extraction and processing methods.

In conclusion, traditional Chinese medicine combined with immunosuppressive agents in the treatment of IgAN can improve the clinical efficacy, reduce the amount of urine protein and urine red blood cells, improve the glomerular filtration rate and reduce the serum creatinine level. However, based on the shortcomings of this meta-analysis, large sample and multi-index clinical randomized controlled trials are still needed to evaluate the efficacy and adverse reactions of the drugs in the future.

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