A Meta-Analysis of the Treatment of Diabetic Nephropathy using Astragalus Injection combined with Captopril

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Abstract. To observe the effectiveness and safety of using astragalus injection combined with captopril for diabetic nephropathy. The method is using computer database searches and manual retrieval of relevant journals. Astragalus injection combined with captopril was the test drug group. The data was analyzed using Review Manager 5.1 according to the evaluation criteria of RCT recommended by Cochrane 4.2.2. 11RCT and total 641 cases of early and clinical diabetic nephropathy were included. Astragalus injection combined with captopril was more excellent than the control group in the lower of 24hUAER [MD=-21.09, (-37.21,-4.96), P<0.01], 24h urinary protein [MD =- 0.38, (- 47, -0.28), P <0.01], the efficient [RR=1.29, (1.06,1.57), P=0.01], BUN [MD=-0.36, (- 0.62,-0.11), P=0.004], SCr [MD=-4.13, (-7.94,-0.33), P=0.03], FPG [MD=-0.96, (-1.67,-0.24), P=0.009], TC [MD=-1.42, (-1.66,-1.18), P<0.01], and TG [MD=-0.45, (-0.59,-0.32), P<0.01]. There was no significance in 2h PG [MD=-0.07, (-0.65,0.51), P=0.81], and blood pressure ( \sigma^2 =0.15, P=0.69). Astragalus injection combined with captopril was effect and safe in the lower of 24hUAER and the efficient for the patients with diabetic nephropathy. It also needs more randomized controlled trials for high-quality evaluation.

1. Introduction

Diabetic nephropathy (DN) is one of the most common and serious microangiopathy in diabetic patients. Its incidence was 13.55% [1]. The main component of astragalus injection is astragalus membranaceus. Astragalus membranaceus could effectively strengthen cardiac contraction, expand coronary and renal blood vessels and peripheral blood vessels of the whole body, and make skin blood circulation vigorous. It was reported that astragalus membranaceus had the functions of lowering blood sugar and regulating blood lipid [2]. It was rich in the trace elements of selenium that could protect the charge barrier and mechanical barrier of glomerular basement membrane [3].

At present, it is clear that angiotensin-converting enzyme inhibitor (ACEI) can inhibit renin-angiotensin system, reduce the formation of angiotensin II, and reduce the internal pressure of glomerular capillaries, thereby reducing the rate of overpressure, while protecting the kidney. Captopril is the first ACEI used in clinical practice. Literature showed that captopril could effectively improve the prognosis of diabetic nephropathy patients [4, 5]. Its adverse reactions are mainly cough (1%-22%), rash (1%-5%), hypotension (10%), taste changes (1.6-7.3%) and fetal malformation [6]. At present, most doctors use captopril in combination with captopril in clinic, and think that its curative effect is better than that of captopril alone or astragalus injection alone. At present, there is no systematic evaluation of its specific efficacy. The main purpose of this paper is to study the systematic evaluation of astragalus injection combined with captopril in the treatment of diabetic nephropathy, in order to determine its efficacy, and give better direction for clinical doctors.
2. Materials and Methods

2.1. Selection and Exclusion Criteria

Selection criteria (1) Diagnostic criteria for diabetes mellitus were in line with WHO diagnostic criteria in 1985, 1990 or 1999, DN was in line with Mogensen stage III (early diabetic nephropathy) and IV clinical patients (clinical diabetic nephropathy). (2) Gender and age (> 18 years old). (3) A randomized controlled, single-blind or double-blind clinical trial was conducted. The drug in the experimental group was astragalus injection combined with captopril, while the drug in the control group was unlimited. (4) Literature types and languages are not limited.

Exclusion criteria (1) Patients with stage V diabetic nephropathy (end-stage diabetic nephropathy). (2) Primary kidney disease. (3) Pregnant and lactating women. (4) < 18 years old. And allergic patients to test or control drugs.

2.2. Interventions

On the basis of routine treatment, the experimental group: astragalus injection (dosage form, dosage, usage and course of treatment are not limited) +captopril (dosage form, dosage, usage and course of treatment are not limited). The control group: western medicine / traditional Chinese medicine.

2.3. Literature Retrieval

The Cochrane Library database (deadline 2017.1), Wiley Online Library (1999-2017), China Journal Full Text Database (1980-2017.1), China Doctoral Dissertation Full Text Database (1999-2017.1), China Excellent Master's Dissertation Full Text Database (1999-2017.1), China Important Conference Dissertation Full Text Database (2000-2017.1) (2000-2017.1), and searched the international academic literature database: German Springer Journal Title Database (1840-2017.1), British Taylor & Francis Journal Title Database (1789-2017.1), Earthscan Journal Title Database (1990-2017.1), and foreign standard database (1919-2017.1). EBSCO (1984-2016), Chinese key words: Astragalus membranaceus, Astragalus injection, Diabetes mellitus, Diabetic nephropathy, Captopril. English search terms: milkvetch, milkvetch injection, astragalus, astragalus injection, diabetic, diabetic nephropathy, Captopril. In recent 10 years, Chinese Journal of Diabetes and Journal of Cardiocerebrovascular Disease with Integrated Traditional Chinese and Western Medicine were manually searched.

2.4. Observation Indicators

The main observation indicators were 24-hour urinary protein quantification, 24-hour urinary albumin excretion rate (24h UAER), urinary albumin (Alb), effective rate, blood urea nitrogen (BUN), and serum creatinine (Scr). The secondary efficacy indicators were fasting blood glucose (FPG), total cholesterol (TC), and triglyceride (TG). The markedly effective standard was 24 hours urinary microalbumin < 19 mg. The effective standard was 24 hours urinary microalbumin 30-35 mg. The ineffective standard was 24 hours urinary microalbumin value did no significantly decrease or increase.

2.5. Data Extraction and Quality Evaluation

Data extraction and quality evaluation was based on the RCT quality evaluation criteria recommended by Cochrane 4.2.2 manual: (1) whether or not the group was concealed. (2) whether the random method was correct. (3) the use of blind method. (4) whether or not the descriptions of lost interviews or withdrawal were analyzed by ITT.

2.6. Statistical Analysis

The analysis process was implemented by Meta Analysis Software Review Manager 5.1 provided by Cochrane website. Relative risk (RR) was used as the statistical analysis for the counting data, and Peto algorithm was used as the statistical method. The weighted mean difference (WMD) was used to measure the data. Each effect was expressed in 95% confidence interval. The test level was 0.05.
3. Results

3.1. Research Description

This study described the search strategy developed by the Cochrane Collaborative Network Kidney Disease Unit. After searching Chinese and English literature, 19 relevant documents were finally found, and none of them were selected in English. 11 randomized controlled trials were selected, 333 cases in the experimental group and 308 cases in the control group. 641 patients with early and clinical diabetic nephropathy were enrolled.

3.2. Comparisons of Observational Indicators

Four clinical trials reported 24-hour UAER indicators. Meta-analysis showed that MD=-21.09, (-37.21, -4.96) was better than the control group in reducing 24-hour UAER indicators (P=0.01) (Figure 1. The left side is advantageous for the experimental groups, and the right side is advantageous for the control groups. The same follows).

![Figure 1. Comparison of the efficacy of UAER at 124h](image1)

Only one clinical trial reported the urinary microalbumin index. For Dong Shaogui 2005, the effect of reducing urinary microalbumin was significantly better than that of the control group (P <0.01) (Figure 2).

![Figure 2. Comparison of the efficacy of 24h urinary protein quantification](image2)

Four clinical trials reported 24-hour urinary protein quantitative indicators. MD=-0.38, (-0.47, -0.28), 24-hour urinary protein quantitative indicators were better than the control group (P < 0.01). Two clinical trials reported an effective rate of RR = 1.29 (1.06, 1.57), which was better than that of the control group (P = 0.01) (Figure 3).

![Figure 3. Efficiency comparison](image3)

Four clinical trials reported BUN indicators, MD=-0.36, (-0.62, -0.11), which were better than the control group in reducing BUN indicators (P=0.004) (Figure 4).
Four clinical trials reported SCr indicators, MD=-4.13, (-7.94, -0.33), which were better than the control group in reducing SCr indicators (P=0.03) (Figure 5).

Five clinical trials reported FPG indicators, MD=-0.96, (-1.67, -0.24), which were better than the control group in reducing FPG indicators (P=0.009) (Figure 6).

Three clinical trials reported 2hPG, MD=-0.07, (-0.65, 0.51). There was no significant difference in FPG reduction between the two groups (P=0.81) (Figure 7).

Four clinical trials published records of blood pressure, and there was no significant difference between the two groups (P > 0.50) (Figure 8: 1.systolic pressure, 2.diastolic pressure).
Figure 8. Comparison of the efficacy of blood pressure
Four clinical trials reported TC indicators, MD=-1.42, (-1.66, -1.18), and TC indicators were better than those of the control group (P<0.01) (Figure 9: 1. The course of treatment is less than 6 weeks. 2. The course of treatment is 12 weeks).

Figure 9. Comparison of the efficacy of TC
Four clinical trials reported TG indicators, MD=-0.45, (-0.59, -0.32), which were better than those of the control group (P<0.01) (Figure 10).

4. Discussion
In this paper, 11 clinical trials were summarized and evaluated. It was concluded that astragalus injection combined with captopril group was superior to control group in reducing 24-hour UAER index and efficiency (P=0.01). Three clinical trials mentioned adverse reactions, and two clinical trials showed no significant adverse reactions. The remaining one clinical trial showed 9 adverse reactions, manifested as cough. There were 4 cases in the experimental group and 5 cases in the control group, and there was a transient increase in creatinine and blood potassium in the control group.

This evaluation system only evaluates 11 clinical trials that meet the selection criteria. Therefore, although the preliminary efficacy of Astragalus injection combined with captopril on urinary protein can be obtained as a result of controlled trials, the results need to be confirmed by further large sample randomized controlled clinical trials.
References
[1] Wang Zhulan, Feng Genbao, Wang Yanyan, et al. (1995) Investigation and clinical analysis of 642 cases of diabetic nephropathy. Chinese Journal of Diabetes, 3 (1): 7-8.
[2] Liu Daofang. (1998) Research progress of Astragalus membranaceus. Information on Traditional Chinese Medicine, 15 (2): 13-14.
[3] Bai Le. (1998) Clinical Observation on 47 Cases of Renal Proteinuria Treated with Astragalus Injection. Shanghai Medicine, 19(1): 15-16.
[4] Zhao Shuhao. (1996) Advances in the treatment of diabetic nephropathy with angiotensin converting enzyme inhibitors. Foreign Medicine: Endocrinology, 16(3): 138-140.
[5] Zhao Shuhao, Lin Jun, Liu Donghui, Huang Lingning, et al. (2008) Clinical study of captopril in reversing early diabetic nephropathy. Clinical meta-analysis, 23 (19): 1411-12.
[6] Huang Chunyou. (2009) Adverse reactions of captopril. Clinical rational drug use, 2(5): 58-59.
[7] Jin Yishu, Wang Yanqiu. (2000) Observation of curative effect of captopril and Astragalus Injection on 64 cases of diabetic nephropathy. Heilongjiang Medical Science, 23(2): 9-10.
[8] Zhang Shiwei, Ji Yulian. (2000) Observation on the curative effect of Astragalus injection on 18 cases of early diabetic nephropathy. New Medicine, 31(2): 95-96.
[9] Yang Yuwang, Liu Qin, Zhang Ying. (2002) Captopril and Astragalus injection in the treatment of 60 cases of diabetic nephropathy. Medical Selection, 21 (3): 343-344.
[10] Guo Qingyou, Tang Chuanfen, Fang Xiaohong. (2004) Observation of curative effect of Astragalus Injection on early diabetic nephropathy. Chinese Journal of Rural Medicine, 11(3): 10-11.
[11] Liu Dan, Liu Song, Ding Hong. (2004) Observation of curative effect of Astragalus Injection on diabetic nephropathy. China Factory and Mine Medicine, 17(6): 446-447.
[12] Wang Qilan. (2004) Observation on the Therapeutic Effect of Astragalus Injection on 30 Cases of Diabetic Nephropathy, Zhongyuan Medical Journal, 31(23): 6-7.
[13] Dong Shaogui. (2005) Observation on the efficacy of Astragalus injection combined with captopril in the treatment of early diabetic nephropathy. Journal of Modern Integrated Chinese and Western Medicine, 14 (8): 989-990.
[14] Liu Yinhong, Yang Li, Liu Ju, et al. (2005) Clinical observation of Astragalus injection combined with captopril in the treatment of early diabetic nephropathy. Chinese Journal of Integrated Traditional Chinese and Western Medicine, 25 (11): 993-995.
[15] Li Hanjun. (2007) Clinical observation of Astragalus injection combined with captopril in the treatment of early diabetic nephropathy. Chinese medicine emergency, 16(8): 945-979.
[16] Li He, Zhang Ping, Jiao Junqiang. (2008) An analysis of Astragalus injection combined with captopril in the treatment of proteinuria in early diabetic nephropathy. Gansu Traditional Chinese Medicine, 21(8): 21-22.
[17] Cui Baosheng. (2009) Clinical observation of Astragalus injection combined with captopril in the treatment of early diabetic nephropathy. Journal of Clinical and Experimental Medicine, 8(11): 76-77.