Universe Scientific Publishing

ORIGINAL ARTICLE

Intervention Effect of Compatibility of Salvianolic Acid A & B on PDGF-C/PDGFR-α Signaling Pathway in Renal Fibrosis

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ABSTRACT **Objective:** To explore the effect of salvianolic acid A & B component molecules of drug compatibility on PDGF-c/PDGFR-α signaling pathway in renal fibrosis of rats. **Methods:** 40 male SPF SD rats were randomly divided into four groups: control group, salvianolic acid A group, salvianolic acid B group and salvianolic acid A + B group, with 10 rats in each group. Each group was treated for two weeks. After the intervention, samples were collected. And scores of HE and Masson was compared. The expression of PDGF-c/PDGFR-α in rental tissue in them was also tested and compared. **Results:** Compared with the control group, the score of HE and Masson in intervention groups was markedly decreased, and scores in salvianolic acid B group and salvianolic acid A + B group were reduced significantly ($p < 0.05$); Compared with the control group, the expression of PDGF-c/PDGFR-α in rental tissue in intervention groups was lower($p < 0.05$), especially in salvianolic acid B group and salvianolic acid A + B group ($p < 0.05$).**Conclusion:** salvianolic acid A & B component molecules of drug compatibility could significantly improve the pathological changes in the kidney tissue of rats, suppress the expression of PDGF-c/PDGFR-α in renal tissue, and improve the renal function, renal tubular function and renal pathology.

KEYWORDS
Salvianolic acid A
Salvianolic acid B
PDGF-C/PDGFR-α
Signaling pathway
Interstitial fibrosis

1. Introduction

Renal fibrosis is not only in the development of a variety of chronic kidney disease (CKD) is an important pathological change, but also through this pathway will lead to advanced kidney disease (ESRD). It is considered to be an irreversible disease, which will result in irreversible damage to renal function, which is mainly manifested in the progressive development of renal tubular interstitial fibrosis and tubular atrophy, which determines the prognosis of renal disease. For kidney disease patients, the dialysis treatment and renal transplantation that they have undergo will consume a lot of financial and material resources which has brought considerably burden to these family, medical institutions and the community. The treatment method that can directly prevent and reverse renal fibrosis has not yet been found. The treatment to delay the development of chronic kidney disease to kidney failure still has a long way to go. Literature studies have shown that A & B has a strong anti-renal fibrosis effect, which can alleviate the renal tubular epithelial cell damage and inhibit renal interstitial fibrosis [1–3]. In this paper, 40 male SD SPF rats were selected to observe the effects of A, B and molecular medicine on the renal fibrosis in rats.

2. Materials and methods

2.1. General information

A total of 40 male SD SPF rats were selected, where the rats aged is 45–60 d and body weight of rats is 210–250 g and were raised in the SPF animal room which free access to food and water with adaptive feeding 3 d after entering the experiment. The 40 rats were divided into 4 groups: control group, A group, B group and A + B group, 10 rats in each group. The four groups of rats on the age, body

doi: 10.18686/aem.v4i2.5
Received: March 2, 2015; Accepted: May 10, 2015; Published online: June 20, 2015

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weight, feeding methods and other general information are not statistical significance ($p > 0.05$), with comparable.

2.2. Method

The purity of Salvianolic Acid A and B were more than 98%. After entering the experiment, all the rats with unilateral ureteral obstruction (UUO) was used to establish a model of renal interstitial fibrosis. After two days of modeling, salvianolic acid A, B, A + B groups was given three intervention for 2 weeks. After the end of treatment collected 24 h urine, abdominal aortic blood taken, picking the right renal tissue, and opened along the longitudinal axis, with 4% paraformaldehyde fixed and were usually placed in liquid nitrogen preservation. The HE score and Masson score and PDGF-c/PDGFR-α expression of were compared among the groups.

2.3. Statistical analysis

All the statistical analysis of the data was statistically analyzed by SPSS 12.0 software. Continuous data were expressed as mean ± standard deviation ($\bar{x} \pm s$). Student t test analyses for comparison between groups, all were done as 2-sided tests, when $p < 0.05$ was considered statistically significant.

3. Results

3.1. Pathological score of four groups of rats

The pathological score of kidney tissue was significantly higher than that in the control group ($p < 0.05$), the HE and Masson scores in the model group were significantly higher than those in the control group (UUO < 1). Compared with the model group, the HE and Masson scores in the treatment group were significantly decreased ($p < 0.05$), the B and HE scores of the rats in the treatment group were significantly lower than those in the Masson group ($p < 0.05$), and the difference was not statistically significant ($p > 0.05$) in the A + B group. It is showed that the compatibility of A, B and its molecular medicine can improve the renal pathological damage and reduce the deposition of collagen.

3.2. Expression of PDGF-C and PDGFR-α protein in renal tissue of rats

The results showed that: compared with control group, PDGF-C mRNA and PDGFR-α mRNA expression in model group were significantly higher than that in model group ($p < 0.05$), and A + B and PDGFR-α mRNA expression were significantly lower than that in A group ($p < 0.05$), and the effect was better than that in A group ($p < 0.05$), and the difference was statistically significant ($p < 0.05$). The expression of PDGF-C/PDGFR-α, A and B in the kidney tissue of rats were treated with, and the effect of A + B group was better than that of A and B group.

4. Discussion

In our country, there is a deep research in the field of clinical treatment of kidney disease. It is proved that the effect of A and B has a strong anti-renal fibrosis, which can relieve the damage of renal tubular epithelial cells and inhibit renal interstitial fibrosis. Research by Li Qun et al. [4] on salvianolic acid B in improving mechanism of aristolochic acid nephropathy study showed that salvianolic acid B has powerful antioxidant function which can inhibit thrombosis. In the field of clinical treatment of renal fibrosis has remarkable curative effect. Foreign scholars Chen YT [5] considered that the Platelet-Derived Growth Factor (PDGF) and PDGFR-α enhanced the migration of fibroblasts in the kidney, and increased the activity of PDGF and PDGFR-α in the process of fibrosis leading to severe collagen deposition. In this study, the collagen deposition was significantly decreased in the A and B treated rats. Among salvianolic acid A, B, A + B of the three groups,

Table 1. Pathological score of renal tissue in four groups ($\bar{x} \pm s$).

Group	Cases	Dose/mg·Kg^{-1}	HE Score	Masson Score
Control group	10	-	2.96 ± 0.08	2.93 ± 0.04
salvianolic acid A	10	12.5	1.80 ± 0.07	1.76 ± 0.08
salvianolic acid B	10	12.5	1.16 ± 0.06	1.28 ± 0.05
salvianolic acid A+B	10	6.25 + 6.25	1.02 ± 0.12	0.90 ± 0.05
p Value	-	-	< 0.05	< 0.05

Table 2. Expression of PDGF-C and PDGFR- protein in renal tissue of rats ($\bar{x} \pm s$).

Group	Cases	Dose/mg·Kg^{-1}	PDGF-C mRNA	PDGFR-α mRNA
Control group	10	-	1.43 ± 0.16	11.22 ± 0.71
salvianolic acid A	10	12.5	1.07 ± 0.17	8.61 ± 0.37
salvianolic acid B	10	12.5	0.75 ± 0.07	7.36 ± 1.21
salvianolic acid A + B	10	6.25+6.25	0.62 ± 0.08	5.21 ± 1.72
p Value	-	-	< 0.05	< 0.05

salvianolic acid A + B group on HE score and Masson score was significantly lower than that of salvianolic acid A group ($p < 0.05$). It was suggested that the compatibility of A, B and A + B could effectively improve the renal tissue function and alleviate renal interstitial fibrosis. In comparison with the control group, the PDGF-c of A, B, A + B and PDGFR-α were significantly decreased ($p < 0.05$) in the control group. Salvianolic acid A, B, A + B of the three groups showed that salvianolic acid A + B dose group rat renal tissue relative expression of PDGF-c protein was significantly lower than that of salvianolic acid A group and salvianolic acid B group. Thus, the intervention of A, B and PDGF-c/PDGFR-α in the process of renal fibrosis was significant, and the effect of PDGF-c/PDGFR-α in the A + B group was significantly stronger than that of A, B.

Salvionalic B and CTGF group can significantly improve rat kidney tissue pathological changes and its effect is better than that of A group. The group can significantly reduce the collagen deposition in rats. The effect is better than that of A. The effect of Par-3 was significantly decreased in rats. The component compatibility group can significantly reduce the relative expression of PDGF-c mRNA renal tissue in rat where the effect is better than in salvianolic acids in group A. In addition, the component compatibility group can significantly reduce the rat kidney PDGFR alpha relative mRNA and PDGF-c protein expression. The effect was better than in salvionalic acids A and group B. There was no significant difference in the improvement of renal function and renal tubular function in rats with the combination of molecular and molecular medicine. A, B and its molecular agents can improve renal function, renal tubular function and renal pathology in UUO rats. The mechanism may be related to the expression of Par-3 and PDGF-c/PDGFR-α in renal tissues of UUO rats. The mechanism may be related to the expression of PDGF-c and PDGFR-α in renal tissue.

In summary, the compatibility of A, B and PDGF-c can significantly improve the pathological changes of renal tissue fibrosis in rats. The expression of A, B and PDGFR can significantly reduce the renal function, renal tubular function and renal pathology.

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