Efficacy of Bailing Capsule (Traditional Chinese Medicine) in the Treatment of Nephrotic Syndrome: A Meta-analysis

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Cheng *et al.*: Eficacy of Bailing Capsule in the Treatment of Nephrotic Syndrome

Meta-analysis of the existing literature on the treatment of nephrotic syndrome with Bailing capsule in adult patients was carried out to provide evidences for clinical practice. Relevant articles describing the effect were included. A total of 5 documents were selected. The meta-analysis showed that Bailing capsule reduced 24 h urine protein in patients with nephrotic syndrome (standardized mean difference=2.35 (3.72, 0.97), p<0.01), increased the level of serum albumin (standardized mean difference=0.94 (0.37, 1.52), p=0.01), but had no improvement on serum creatinine (standardized mean difference=0.50 (1.25, 0.26), p=0.20) as well as blood urea nitrogen (standardized mean difference=0.10 (0.36,0.17), p=0.48). The adjuvant treatment of nephrotic syndrome with Bailing capsule could reduce proteinuria, enhance plasma albumin and decrease blood lipids in patients. However, these conclusions need to be confirmed by further clinical trials.

Key words: Bailing capsule, nephrotic syndrome, proteinuria, urea nitrogen, meta-analysis

Clinical nephrotic syndrome (NS) is manifested as proteinuria, hypoalbuminemia and hyperlipidemia, which, in the long run, will promote glomerular sclerosis during the progress of NS and gradually develop into end-stage renal failure[1]. In traditional Chinese medicine (TCM), NS belongs to the category of edema and essence and vital energy collapse. The disease is characterized by edema and TCM postulates that the pathological mechanism is mainly spleen and kidney dysfunction, deficiency of as well as *qi* and blood, especially the deficiency of *yang qi* is Ben and water-dampness, damp and hot as well as stagnation of blood stasis is *Biao*, represented as both of deficiency and excess; and it is susceptible to exogenous evils during the course of the disease and the condition is likely to be aggravated due to infections caused by exogenous pathogenic factors[2,3]. The pathogenesis of NS is complicated, closely related to lung, spleen and kidney. At present western medicine mainly uses glucocorticoids treatment and cytotoxic drugs, which pose many problems such as recurrence, hormone dependence and toxic side effects despite

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density lipoprotein (LDL) and one report showed that Bailing capsule can increase the level of high density lipoprotein (HDL, Tables 2-5).

Q heterogeneity test and I_2 test showed that except the effect size index of blood urea nitrogen (p=0.86, I_2=0 %), there was significant heterogeneity in the combination of other indicators. The funnel plot indicated a possibility of publication bias, as shown in fig. 2.

In summary a total of 5 documents were included in the meta-analysis, which showed that Bailing capsule reduced 24 h protein urine in patients with NS, increased the level of serum albumin, did not cause any improvement in serum creatinine and blood urea nitrogen levels. However, 2 of the selected articles reported that Nailing capsules can reduce total blood cholesterol, triglycerides and LDL. These results suggested that the adjuvant treatment of NS with Bailing capsule can further reduce proteinuria, enhance plasma albumin and decrease blood lipids in patients, all of which, however, need to be confirmed by further clinical trials.

NS results from a variety of causes. If a large amount of urine protein is lost from the body, the content of plasma albumin would be reduced and then it will lead to the decrease of blood volume. The excretion of some fibrinogen or anticoagulant factors increases the viscosity of blood, giving rise to the disorders of

TABLE 2: EFFECT OF THE BAILING CAPSULE ON THE URINE PROTEIN IN PATIENTS

	Bailing capsule group			Bailing capsule group				Std. Mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95 % CI
Ying Liu	0.97	0.08	34	3.45	0.29	34	14.70 %	-11.53 [-13.58, -9.47]
Sha Li	0.9	0.42	42	0.91	0.041	40	21.40 %	-0.03 [0.47, 0.41]
Wenqi Zhong	3.1	0.97	20	3.83	1.33	66	21.20 %	-0.58 [-1.08, 0.07]
Cheng Chen	1.21	0.32	45	2.11	0.69	40	21.20 %	-1.69 [-2.19, -1.19]
Hongmi Cao	1.67	1.42	48	2.53	0.73	48	21.40 %	-0.76 [-1.16, -0.35]
Total (95 % CI)			189			228	100.00 %	-2.35 [-3.72, 0.97]

Heterogeneity: Tau_2=2.26; Chi_2=129.61; df=4 (<0.00001); I_2=97 %, test for overall effect: Z=3.34 (p=0.0008)

TABLE 3: ANALYSIS OF THE EFFECT OF BAILING CAPSULE ON SERUM CREATININE

	Bailing capsule group			Control group				Std. mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95 % CI
Ying Liu	34.16	5.47	34	29.48	3.58	34	32.60 %	1.00 [0.49, 1.51]
Wenqi Zhong	33.66	10.86	20	30.28	7.45	66	32.60 %	0.40 [-0.10, 091]
Hongmin Cao	35.72	3.21	50	28.51	6.51	50	34.8	1.39 [0.96, 1.83]
Total (95 % CI)			104			150	100.00 %	0.94 [0.37, 1.52]

Heterogeneity: Tau_2=0.20; Chi_2=8.49; df=2 (=0.01); I_2=76 %, test for overall effect: Z=3.22 (p=0.001)

TABLE 4: ANALYSIS OF THE EFFECT OF BAILING CAPSULE ON SERUM CREATININE

	Bailing capsule group			Control group				Std. mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95 % CI
Ying Liu	125.88	11.06	34	126.59	13.24	34	25.00 %	-0.06 [-0.53, 0.42]
Wenqi Zhong	43.48	11.75	20	71.5	15.56	66	23.80 %	-1.88 [-2.46, -1.30]
Cheng Chen	90.53	20.01	45	90.11	19.87	40	25.40 %	0.02 [-0.41, 0.45]
Sha Li	88.67	18.58	42	91.44	15.75	40	25.80 %	-0.16 [-0.55, 0.23]
Total (95 % CI)			141			180	100 %	-0.50 [-1.25, 0.26]

Heterogeneity: Tau_2=0.53; Chi_2=32.22; df=3 (<0.00001); I_2=91 %, test for overall effect: Z=1.29 (p=0.20)

TABLE 5: ANALYSIS OF THE BAILING CAPSULE AFFECTING BLOOD UREA NITROGEN

	Bailing capsule group			Control group				Std. mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95 % CI
Ying Liu	125.88	11.06	34	129.26	23.15	34	31.7 %	-0.18 [-0.06, 0.29]
Wenqi Zhong	6.1	1.2	20	6.25	1.31	66	28.7 %	-0.12 [-0.62, 0.38]
Cheng Chen	5.83	1.8	45	5.85	1.72	40	39.6 %	-0.01 [-0.44, 0.41]
Total (95 % C)			99			140	100.0 %	-0.10 [-0.36, 0.17]

Heterogeneity: Tau_2=0.00; Chi_2=0.29; df=2 (=0.86); I_2=0 %, test for overall effect: Z=0.70 (p=0.48)

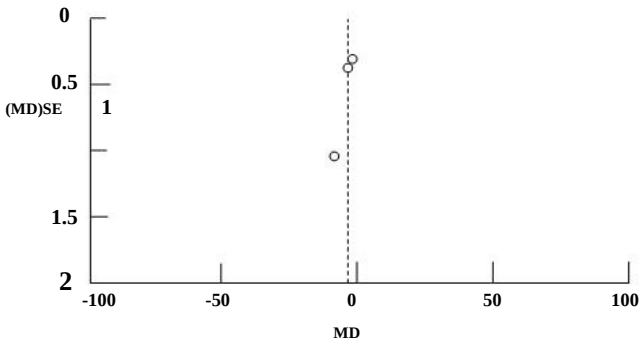

Fig. 2: Funnel plot of the effect of Bailing capsule on proteinuria

anticoagulation, coagulation, and fibrinolysis systems in human body and ending up in hyperlipidemia, ultimately leading to the dysfunction of glomeruli with disordered structure[11]. Studies have shown that[12-13] proteinuria can cause damages to glomerular intrinsic cells such as mesangial cells and podocytes as well as to tubulointerstitium. Persistent proteinuria can lead to the progression of renal injury and the level of proteinuria is closely related to the development of chronic renal failure. Therefore, the reduction of proteinuria is an important target for the treatment of NS[14]. The results of this study revealed that Bailing capsule can effectively reduce proteinuria in patients with NS with a mechanism probably related to inhibition of the formation of glomerular sub epithelial immune complex, lowering the loss of anionic charge in glomerular basement membrane and alleviating glomerular high filtration. Furthermore, it has been reported that[15] Bailing capsule can inhibit the activation of aldose reductase, thus reducing the permeability of glomerular basement membrane and reducing urinary protein.

Patients with NS are also characterized by hyperlipidemia. The deposed lipid can stimulate the proliferation of glomerular mesangial cells, increase extracellular matrix synthesis, promote tubulointerstitial fibrosis and glomerular sclerosis and thus aggravate renal injury[16-17]. Additionally, hyperlipidemia will exacerbate the risk of cardiovascular disease, so it is also an independent risk factor for the progression of NS[18]. The 2 studies included in this paper showed that Bailing capsule can reduce total cholesterol, triglyceride and LDL with the mechanism may associated with reduced lipid peroxide as well as enhanced superoxide dismutase and lecithin cholesterol acyl transferase (LCAT) activity.

It was also revealed in this study that Bailing capsule can improve the level of serum albumin in patients, which may be related to proteinuria reduction and that meanwhile Bailing capsule enables to promote protein synthesis with an adrenocorticoid like effect.

However it is necessary to draw attention to the following limitations of the study, such as there was obvious inter-study heterogeneity among the trials, differing in basic treatment program, drug dose and duration of therapy as well as patient's pathological type and clinical manifestations; there was publication bias; there was limited number of studies of low quality and the cited documents all were Chinese version; the long-term efficacy of Bailing capsule failed to be observed.

To sum up, this analysis shows that Bailing capsule can effectively reduce proteinuria and increase plasma albumin and may reduce blood lipids in patients with NS. But these need to be confirmed by further large-scale trials of high quality.

Conflict of interest:

No conflict of interest between any of the authors.

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