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Original Article

A control study of the response from chinese patients with minimal change disease and focal segmental glomerulosclerosis to steroid therapy

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Abstract: Objective: This study aimed to evaluate the clinical characteristics and response to steroid therapy of adult Chinese patients with nephrotic syndrome caused by minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS). Methods: 59 patients with MCD and 143 with FSGS were enrolled in this retrospective analysis and they were treated with steroids. The factors we focused are as follows: the prevalence of total remission, steroid responsiveness, progression to chronic renal failure and need of renal replacement therapy due to end-stage renal disease (ESRD). Results: Initial serum creatinine of the MCD group was 1.15 ± 0.49 mg/dL, while the FSGS group was 1.51 ± 0.92 mg/dL (P = 0.03). Patients with MCD seemed to be sensitive to the steroid therapy: 72% have been complete remission and 5% have been partial remission. However, only 56.2% of the patients with FSGS were sensitive to such treatment (P = 0.02). Moreover, the response to corticosteroids was reduced by 81% of the risk of chronic renal failure to patients with FSGS (P<0.001). However, total remission was associated with a reduction by about 85% (P<0.001). Conclusion: The response to steroid therapy was the most significant protective factor for renal function, besides, FSGS was associated with less steroid responsiveness.

Keywords: Minimal change disease, focal segmental glomerulosclerosis, steroid

Introduction

Nephrotic syndrome is characterized with the presence of nephrosis, chiefly proteinuria, hypoalbuminemiaand edema [1]. There are many causes and it may be the result of a glomerular disease that is limited to the kidney, called primary nephrotic syndrome [2, 3]. Minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) are the two most common primary causes of nephrotic syndrome in children and adults respectively. For MCD, nephrons appear normally when viewed with an optical microscope as the lesions are only visible by using an electron microscope. FSGS is characterized by the appearance of tissue scarring in the glomeruli [4, 5].

In terms of the response to steroid therapy, patients were classified as steroid-sensitive, with a prevalence of 15% in children and 40% in adults, or steroid-resistant nephrotic syndrome (SRNS) which usually appeared at end-stage renal disease (ESRD) [6]. Most SRNS patients have focal segmental glomerulosclerosis, but MCD and FSGS may be seen [7]. The treatment of SRNS has been a difficult problem for a long time due to its poor response to immnosupressive drugs. High dose steroids were always used with variable success rates in children and adults with MCD and FSGS [8].

In this study, we evaluated the response to steroid of adult patients who were diagnosed with MCD or FSGS and had the characteristic of proteinuria. We went in for probing into the clinical differences between these two different diseases in adult patients, in order to serve for the treatment in the future.

Materials and methods

Samples

In this longitudinal retrospective study, 202 Chinese patients who were diagnosed with

Table 1. Demographics of patients

Variables	MCD	FSGS	*p*-value
Age (years)	25 [20, 36] years	33 [21, 46]	0.06*
Gender - Male (%)	52%	43%	0.43
Arterial hypertension (%)	14%	28%	0.16
Serum creatinine (mg/dL)	1.15 ± 0.49	1.51 ± 0.92	0.03#
Proteinuria (g/24 hours)	6.89 [4.32, 9.67]	4.12 [2.05; 6.71]	<0.001*

#Student t test. *Mann-Whitney.

MCD or FSGS included. All patients were self-declared ethnic Han. Children more than twelve years old were also followed up in our clinic. Demographic characteristics included age, gender, hypertension at diagnosis, initial levels of proteinuria and serum creatinine. The research was approved by the medical ethics committee in our hospital, and all the patients agreed as well as signed the informed consent.

Drug treatment

All patients were firstly treated with corticosteroids following the clinic's protocol: 1 mg/kg/d of prednisone orally for both MCD and FSGS patients. When it was half reduction in the initial proteinuria level, or level below 2.0 g/24 hours, it was defined as segmental remission; however, complete remission was defined as proteinuria turned negative (The proteinuria level was below 0.15 g/24 hours). If corticosteroid response was absent after about 4 to 6 months of treatment with 1 mg/kg/day of prednisone orally, patients were treated with cyclophosphamide or cyclosporine, but the responses to these treatment modalities were not detected in this study.

After all those procedures, we collected the related data every month and analyzed the prevalence of complete remission, the response to corticosteroids, progression to renal failure and need for renal replacement therapyon account of stage 5 chronic kidney disease (5-CKD). The whole procedure of follow-up lasted about 3 years.

Statistical analysis

The data was analyzed by SPSS version 20. Frequencies and percentages were presented for categorical variables while mean and standard deviation were used for numerical variables. When abnormal distribution occurred, the data was presented by median and interquatile interval (Q1; Q3). Normality was assessed by the Shapiro-Wilk test. Categorical variables were compared by the Fisher exact test or the chi square test. Student t-test was used for numerical variables when there showed normal distribution of the data. Mann-Whitney test was applied in other cases. Multivariate analysis used for regarding the risk factors of developing renal failure was carried out by Cox logistic regression. The level of statistical significance was set at $P<0.05$.

Results

Study characteristics are distributed according to histological types of glomerulopathies (**Table 1**). Among these patients, 59 of them have been diagnosed with MCD and 143 of them have been diagnosed with FSGS. Subsequently, 25 cases of FSGS were excluded because they were classified as secondary FSGS.

In the primary FSGS group, the median age was 33 [21, 46] years, 43% of the patients were males. Although patients in MCD group were younger (25 [20, 36] years), there were no significant differences between mean age compared to FSGS group ($P = 0.06$). Also, there were no differences in the prevalence of gender related to the histological types of glomerulopathies ($P = 0.43$). The difference of the prevalence of hypertension did not reach statistical significance ($P = 0.16$).

Due to the initial serum creatinine, a kind of important clinical characteristic for patients' nephrotic syndrome, we examined this factor in MCD and FSGS groups. In **Figure 1**, it could be seen that the initial serum creatinine of the MCD group was 1.15 ± 0.49 mg/dL, while the group with FSGS was 1.51 ± 0.92 mg/dL ($P = 0.03$). All patients had nephrotic syndrome to some extent in the course of follow-up and initial levels of 24-hour proteinuria were 37% higher among patients with MCD: 6.89 [4.32, 9.67] vs. 4.12 [2.05; 6.71] g ($P<0.001$).

As shown in **Figure 2**, 76% of patients with MCD seemed to be sensitive to the steroid therapy: 72% were complete remission and 5% partial.

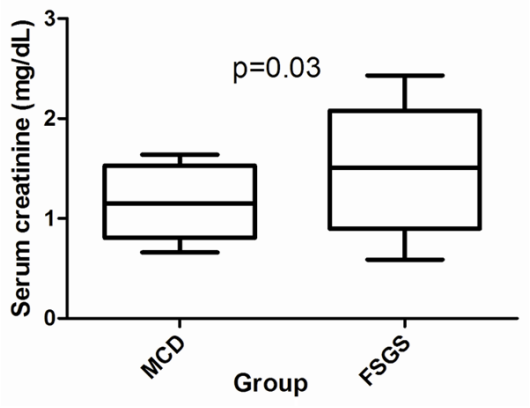

Figure 1. Creatinine serum levels of patients with MCD and FSGS.

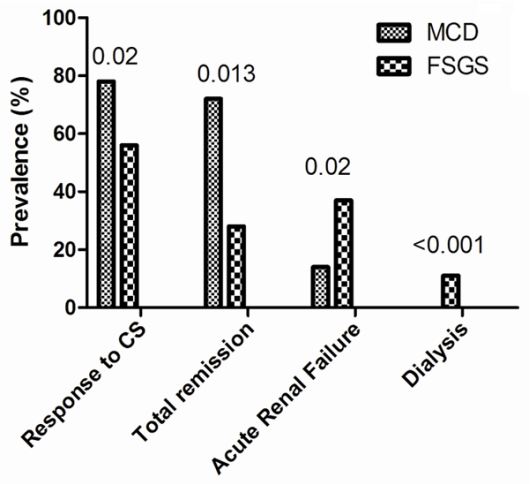

Figure 2. The prevalence of several factors of patients with MCD and FSGS.

What's more, only 56.2% of them with FSGS were sensitive to such treatment (P = 0.02). The total remission between MCD group and FSGS group had a significant difference (P = 0.013). There were fifteen patients relapsing after accepting corticosteroid in the MCD group and sixteen in the FSGS group. Eight patients with MCD (13.6%) had renal failure at diagnosis and all these cases associated to hypovolemia which may lead to pre-renal acute renal failure and acute tubular necrosis. Moreover, the prevalence of renal failure was 37% (P = 0.02) and 11% required dialysis (P<0.001) in FSGS patients.

In **Table 2** and **Figure 3**, we evaluated the variables associated with the risk of developing chronic renal failure in patients with FSGS. In a multivariate analysis, the response to corticosteroids was reduced by 81% of the risk of chronic renal failure (P<0.001). However, total remission was associated with a reduced by about 85% of the risk (P<0.001).

Discussion

Nowadays, FSGS and MCD were altogether considered to be the most frequent causes of nephrotic syndrome [9]. Some studies suggested that FSGS was the most frequent primary glomerular disease, whose predominance was in accordance with recent studies all over the world and revealed its frequency was increasing [10]. Lupus nephritis predominated among secondary glomerulopathies in most regions [11]. Previous studies noted that membranous glomerulonephritis was the main cause of nephrotic syndrome in adults [12, 13]. However, nephrotic syndrome was considered as the leading cause only in the elderly population in recent years [14].

In this study, we evaluated the clinical characteristics and response to steroid therapy of patients with FSGS and primary MCD. It was discovered that patients with FSGS were older than those with MCD, but there was no difference in ages as well as gender between these two groups. Actually, MCD in childhood is probably more common in males, but there is apparently no gender difference in adults. Moreover, during follow-up, all patients had nephrotic syndrome, and few in these two groups were submitted to renal biopsy when the proteinuria level was still less than 3.5 g/24 h [15]. What was known to all was that less than 10% of MCD patients did not have nephrotic proteinuria when the disease disappeared, while such percentage could reach to 30% in FSGS patients [16]. In this study, initial levels of proteinuria in patients with MCD (average 7.9 g/24 h) were higher than those with FSGS (average 5.1 g/24 h). A study analyzed mean levels of proteinuria on patients with MCD was at 10 g/24 h and serum creatinine of 1.4 mg/dL, which was similar to the levels detected in the study (7.9 g/24 h and 1.1 mg/dL, respectively) [17]. It also showed an incidence of hypertension in adults with MCD that reaches forty percent. However, 13% of MCD patients had hypertension in the study. This percentage is higher in cases of FSGS.

Table 2. Relative risks of patients of MCD and FSGS groups developing renal failure

Variables	Relative risks	95% Confidence interval	*p*-value
Total remission	0.19	0.05-0.43	<0.001
Response to corticosteroid	0.25	0.13-0.54	<0.001

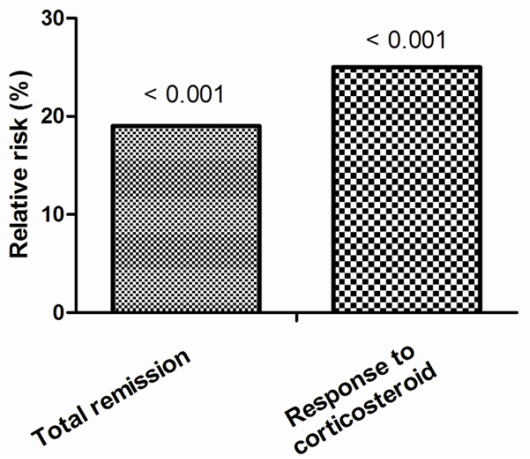

Figure 3. Comparison of relative risks developing renal failure between MCD and FSGS groups.

What's more, it has shown that patients with nephrotic syndrome by MCD or primary FSGS should be treated with corticosteroids because spontaneous remission is uncommon in MCD and FSGS [18]. Without specific treatment, MCD is related to increasing risk of mortality from other diseases and FSGS, with progression to 5-CKD [19-21]. Patients included in this analysis were initially treated with prednisone 1 mg/kg/day orally. Patients with MCD seemed to be sensitive to the steroid therapy: 72% were complete remission and 5% partial, and only 56.2% of them with FSGS were sensitive to such treatment.

Our findings may also have implications for precise drug application and discoveries of newsteroid medications in the future. In some circumstances, our findings will also be helpful for the design of trials that comparing the effect of medications in two clinical groups.

Nevertheless, this study has several limitations. We found that there was no difference in terms of gender or ethnicity in both groups. However, MCD in childhood is more frequent in males instead of the same in both genders [22]. Besides, in the United States, there is an African-American patient with FSGS who has higher prevalence [17]. Thus, the results should be viewed as inferential and referential for children and some other specific conditions.

In conclusion, the paper described the clinical characteristics and the response to steroid of Chinese patients with MCD and FSGS, and demonstrated the protective role of this therapy, which was dissimilar to other results observed in other countries.

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Disclosure of conflict of interest

None.

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