



# Study on the relationship between chronic tonsillitis and early stage of kidney failure

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**Abstract:** Objective: to investigate whether chronic tonsillitis is associated with early kidney failure; to analysis the reliability of urine microalbumin as a diagnostic indicator of chronic tonsillitis and early stage of kidney failure; either tonsillectomy is the effective way to prevent complications of chronic tonsillitis and early kidney failure. Methods: 84 patients with chronic tonsillitis who admitted to the department of Otorhinolaryngology, Qinghai University Affiliated Hospital from March 2012 to February 2013 were selected as subjects, 33 males and 51 females who aged between 7-55 years. It was divided into three group according to the course of disease, group A: duration is 1 to 3 years; group B: duration of 3 to 5 years; group C: duration> 5 years; in the immunological laboratory, 12 cases of normal control group were collected, male 7 cases , female 5 cases, aged 7 to 55 years old. The amount of microalbuminuria before and after operation was determined by turbidimetric method. The collected data were analyzed statistically. Results: There was no significant increase in urine microalbumin compared group A and control group,  $P > 0.05$ , the difference was not statistically significant. Group B and group C were significantly higher than those in the control group ( $P < 0.05$ ), the difference was statistically significant. The levels of microalbuminuria in group A pre-operation was significantly higher than that of in group C ( $P < 0.05$ ). The difference was statistically significant. The levels of microalbuminuria in group B were significantly higher than those in group C ( $P < 0.05$ ) during pre-operation. The difference was statistically significant. The levels of microalbuminuria were significantly decreased in group A post-operation compared to the relatively group pre-operation,  $P < 0.05$ , the difference was statistically significant. In group B, pre-operative and postoperative comparison, urine microalbumin was significantly decreased,  $P < 0.05$ , the difference was statistically significant. The levels of microalbuminuria were significantly decreased in post-operative in group C than that of its pre-operation,  $P < 0.05$ , the difference was statistically significant. Conclusion: Patients with chronic tonsillitis can be complicated by early stage of kidney failure. There is a certain clinical value of urine microalbumin used as a diagnostic indicator of chronic tonsillitis and early kidney failure, and its sensitivity gradually increased with the progress of disease. The only way to prevent the chronic tonsillitis complicated by early kidney failure is to do tonsillectomy.

**Key words:** words Urine microalbumin; Early kidney failure; Course of disease; Chronic tonsillitis

## Chapter 1 Preface

The disease incidence rate of 6 to 15-year-old children with chronic tonsillitis (chronic tonsillitis) is 22.04%, in the department of Otorhinolaryngology, chronic tonsillitis is a common and multiple diseases. Inflammation in tonsil relapse for long term, will destroy the balance of immune system and induce complications on multiple organs [1]. Chronic tonsillitis mainly expresses as the proliferative hypertrophic of palatine tonsil and relapse of inflammation response. Proliferative hypertrophy in palatine tonsil is common in children, this is due to the compensatory response of pharyngeal lymph ring to resist the foreign infection, whereas the relapse of inflammation response is more common in adult[2]. Palatine tonsils are easy to expose and easy to be infected by bacterial and other pathogenic microorganisms. Bacterial infection, viral infection, allergy, autoimmune can cause chronic tonsillitis. The study found that reduced immunity, internal secretion, metabolic diseases and nervous system abnormalities may become the cause of tonsillitis. Among it the bacterial infection is the most dominant cause, this is due to the repeated stimulation of aerobic bacteria and anaerobic bacteria, resulting in tonsil crypt obstruction caused by poor drainage, and also causes the accumulation of bacteria and inflammatory exudate, which eventually formed a chronic tonsil inflammation [3].

With the rapid development of immunology in recent years, in the study of chronic tonsillitis, there is research restriction on the local physiological changes and pathogenesis of inflammation in tonsil, it is well known that tonsil has important effect in maintaining and regulating the immune system[4-5]. Due to the effects of virus, bacteria and inflammatory factors, and reduced autoimmune function, function of tonsil in immune balance was broken, leading to long-term suffering from chronic tonsillitis, and also distant organs will produce a corresponding immune response. Due to the role of blood circulation,

tonsil immune cells and immune cell chemokines are transmitted to the body organs, and cause significant functional damage to the distant organs, especially in the heart, kidney, limb joint damage is most significant [ 6]. However, in recent years, chronic tonsillitis damage to the kidney has receives more concern.

Through recent years of research and reports we can see that chronic tonsillitis and IgA nephropathy (IgA nephropathy, IgAN) is closely related. The most common chronic progressive renal lesion is IgA nephropathy which characterized by deposition of glomerular mesangial area immunoglobulin A (IgA). In some cases, in IgAN, the IgA of glomerular mesangial deposition and IgA produced by tonsil B cell mostly are the poly-IgA from J chain-positive, and both can also be effectively combined [7]. Studies have shown that patients with IgA nephropathy of focal chronic tonsillitis, creatinine and urea nitrogen was significantly increased, urinary sediment erythrocyte and urinary protein will appear obviously, and the pathological point of view, the kidney will also be irreversible damage [8].

When the immunity in body decreased or being infected, pathogens that hide in the deep part of tonsil can cause acute attack of tonsillitis, and simple antibiotic treatment can only eliminate the pathogens at the tonsils, and tonsillectomy is the only way to remove the lesions at deep part of tonsil[9]. Therefore, to prevent chronic tonsillitis complicated with early kidney damage, the only effective way is tonsillectomy and this has important clinical application value.

In recent years, domestic and foreign experts have used the scattering rate turbidimetric method, enzyme-linked immunosorbent assay (ELISA) to determine the urine albumin content, study found that it is difficult to control the intra-and inter-assay variability of the ELISA system at about 10% due to the urine sample dilution process, the standard washing method of enzyme and the error when loading sample when using ELISA to measure urinary microalbumin. In this case, the rate of turbidimetric method is more accurate and reliable

[10]. Therefore, this article is about by detecting the microalbuminuria content, to explore the relationship of chronic tonsillitis and early kidney failure; to analyze that either content of urine albumin as a diagnostic indicator of chronic tonsillitis early renal damage diagnosis is reliable or not; to determine the tonsillectomy is the effective way to prevent chronic tonsillitis complicated with early kidney failure.

## Chapter 2 Materials and Methods

### 2.1 screening of experimental specimens

12 healthy volunteers from Qinghai University Affiliated Hospital and 84 patients with bilateral tonsillitis surgery from the department of Otorhinolaryngology (ear, nose and throat /ENT), Qinghai University Affiliated Hospital from March 2012 to February 2013 were selected as subjects. The urine albumin content from 12 cases healthy volunteers, the pre-operative and postoperative urine microalbumin content from 84 patients were evaluated. 12 healthy and 84 patients aged 7-55 years, 39 males and 57 females with an average age of  $(27.03 \pm 1.01)$  years. The selection criteria of 12 healthy subjects and 84 patients: without hematuria, urine protein was in the normal range, erythrocyte sedimentation rate (esr) no decrease, anti-O test negative; renal function test was in the normal range; ECG, X chest radiograph were normal; excluded hypertension, diabetes and cardiovascular disease. 84 patients also had to meet the criteria of record of chronic tonsillitis history, clinical symptoms and tonsillectomy

### 2.2 Experimental equipment and methods

The main equipment and the source:

BN II automatic special protein analyzer (SIEMENS, Germany)

Major reagents and source:

?Albumin determination kit (SIEMENS, Germany)

#### Experimental method

##### Urine collected

12 healthy subjects were collected their morning urine, 84 patients were collected their morning urine before surgery and within 1 week after surgery, collected samples were kept in clean urine cup, and sent to the department of Immunology, Qinghai University Affiliated Hospital within 2 hrs for sample testing.

##### Urine microalbumin determination

5 ml of urine samples were taken within 4 hrs and the supernatant was separated after centrifugation. According to the BN II automatic special protein analyzer program requirements, sample was tested and the data was obtained (normal reference: ALBU: 0 - 30mg / L).

##### Case grouping

The patients were divided into three groups according to the course of the disease: Group A is the duration between 1 to 3 years; Group B is the duration of 3 to 5 years; Group C is the duration of more than 5 years; 12 healthy subjects were the control group.

### 2.3 statistical methods

SPSS17.0 software was used to analyze the data of microalbuminuria in urine. The data were expressed as mean  $\pm$  standard deviation. The levels of microalbuminuria in the preoperative of each group and control groups and among all groups and control group were statistically analyzed by variance analysis. The content of microalbumin was analyzed using paired t-test for the data of preoperative and postoperative of each group. Test level  $\alpha = 0.05$ ,  $P < 0.05$  was statistically significant.

## Chapter 3 Results

### Determination of microalbuminuria in urine

Patients group: 84 subjects, male 34 cases, female 50 cases, the average age was  $(16.91 \pm 1.04)$  years old, preoperative urine microalbumin content is  $(22.82 \pm 1.92)$  mg / L, the highest was 26.65 mg / L, the lowest was 19.00 mg / L; postoperative urine microalbumin content was  $(16.22 \pm 0.86)$  mg / L, the highest was 17.94 mg / L, the lowest was 16.22 mg / L.

Group A: course of disease was 1-3 years, 27 cases, male 11 cases, female 16 cases, the average age was  $(21.3 \pm 1.92)$  years old, preoperative urinary microalbumin content  $(14.53 \pm 1.38)$  mg / L, the highest 17.36 mg / L, the lowest was 11.7 mg/L; postoperative urine microalbumin content was  $(11.90 \pm 0.92)$  mg/L, the highest was 13.82 mg/L, the lowest was 10.04 mg/L.

Group B: course of disease was  $>3-5$  years, 32 cases, male 13 cases, female 19 cases, average age was  $27.03 \pm 1.37$  years old, preoperative urine microalbumin content was  $(22.61 \pm 1.86)$  mg/L, the highest was 26.42 mg/L, and the lowest was 18.81 mg/L, postoperative urine microalbumin content was  $(15.80 \pm 1.37)$  mg/L, the highest was 18.66 mg/L and the lowest was 13.06 mg/L.

Group C: course of disease was  $> 5$  years, 25 cases, 10 male, 15 female, average age was  $33.64 \pm 2.00$  years old, preoperative urine microalbumin content was  $(32.06 \pm 5.32)$  mg/L, the highest was 43.03 mg/L, the lowest was 21.80 mg/L, postoperative urine microalbumin content was  $(21.32 \pm 1.60)$  mg/L, the highest was 24.64 mg/L and the lowest was 18.00 mg/L.

Healthy Group: 12 subjects, male 5 cases, female 7 cases, average age was  $26.00 \pm 3.44$  years old, the level of urine microalbumin was  $12.85 \pm 1.54$ , the highest was 16.24 mg/L, the lowest was 7.6 mg/L.

### 3.2 Analysis of urine microalbumin in preoperative and control groups

Each group at preoperative stage was compared with the control group, urine microalbumin was not significantly increased,  $P > 0.05$ , the difference was not statistically significant. Group B and group C were significantly higher than those in the control group ( $P < 0.05$ ). The difference was statistically significant.

### 3.3 Analysis of urine microalbumin between groups in preoperative and control groups

Group A compared with Group C in the preoperative, urine microalbumin was significantly increased,  $P < 0.05$ , the difference was statistically significant. The levels of microalbuminuria in group B were significantly higher than those in group C ( $P < 0.05$ ). The difference was statistically significant. (See Table 1)

### 3.4 Analysis of microalbuminuria in preoperative and postoperative of all groups

In group A, preoperative compared with the postoperative, urine microalbumin was significantly reduced,  $P < 0.05$ , the difference was statistically significant. In group B, preoperative and postoperative comparison, urine microalbumin was significantly decreased too,  $P < 0.05$ , the difference was statistically significant. The levels of microalbuminuria were significantly decreased in postoperative of group C compared to preoperative,  $P < 0.05$ , the difference was statistically significant. (See Table 1)

Table 1: Comparison of preoperative and control groups in each group, the comparison between the two groups before surgery, the two groups before and after surgery.

Group	N	preoperative(mg/L)		
		postoperative(mg/L)	value t	value P
A	27	14.53±1.38△	11.94±0.92	3.44
		0.02		
B	32	22.61±1.86*△	15.86±1.37	3.95
		0.00		
C	25	32.06±5.32*	21.32±1.61	2.30
		0.03		
Control group	12	12.85±1.54		

Note: \* Compared with the control group  $P < 0.05$ , ☆ compared with the B group  $P < 0.05$ , △ and C group compared to  $P < 0.05$

## Chapter 4 Discussion

### 4.1 Analysis of urine microalbumin in preoperative group and control groups

Urine microalbumin refers to the presence of microalbumin in the urine. Under normal circumstances, the renal proximal tubule through the active way to reabsorb almost all albumin, a small amount of albumin in normal urine, the normal concentration of 0.102-0.120mg / min, that is, microalbuminuria. Urine microalbumin content increased in urine is one of the important pathophysiological changes in the kidney. There are pore barrier and charge barrier on the glomerular filtration membrane, [11] pore barrier is: the membrane has a number of radius of 3 -4nm with a negative charge of microporous, charge barrier refers to: there is a negative charge of heparan sulfate and glycoprotein, both of them limit the plasma medium and macromolecule with negatively charged protein pass through. Because of the albumin diameter is large and contains a large number of negative charge, it is not easy pass through the filtration membrane, thus the current commonly used laboratory indicators are difficult to reflect the early kidney damage [12], but by the scattering rate turbidimetric method can accurately obtain urine microalbumin content.

The pathogenesis of chronic tonsillitis has not yet elucidated, the current research direction has been shifted from the local physiological pathology and inflammation of the tonsils towards to the disagreement in the immune response of each organs of the whole body. Mainly think that the tonsil work as an important immune organ was long term stimulated by relapse inflammation, will loss the function in maintaining the immune balance of body. When chronic tonsillitis develops into immune lesions on various distant organ, tonsil peripheral blood immune cells and chemokines reached each distant immune organ, producing an immune response. Obviously kidney is the most being damaged organ, in which it leads to damage in glomerular filtration membrane, albumin rate filtration increased, renal tubular damage, and reabsorption of albumin capacity became weakened [13-21].

The levels of microalbumin were also measured by using turbidimetric method in this paper. Group A: preoperative urine microalbumin content (14.53 ± 1.38) mg / L; Group B: preoperative urine microalbumin content (22.61 ± 1.86) mg / L; Group C: preoperative urine microalbumin content (32.06 ± 5.32) mg / L; control group: urinary microalbumin content (12.85 ± 1.54) mg / L. The levels of microalbuminuria in group B and C were significantly higher than those in normal group, among which group C was the most significant. Statistical analysis: Group A compared with the control group, urine microalbumin no significant increase,  $P > 0.05$ , the difference was not statistically significant. Group B and group C were significantly higher than those in the control group ( $P < 0.05$ ). The difference was statistically significant. This study shows that the patients with the course of disease > 3 to 5 years of chronic tonsillitis

complicated with early kidney failure has urine microalbumin excretion which is in the normal range but compared to healthy group, it increased significantly. Whereas the urine albumin excretion content is higher than the normal range are generally the patient with more than 5 years of chronic tonsillitis. Thus indicating the presence of chronic tonsillitis is in early kidney damage, which is consistent with the findings of Luo Rong [22]. Ye Changbin [23] found that the urine microalbumin content in hypertension patient is (98.51 ± 12.31) mg / L by using turbidimetric method, Geng Xianghua [24] also used the same method to measure the amount of microalbuminuria in diabetes mellitus patients and the result is (248.3 ± 105.9)mg/L. This paper shows that the preoperative urine microalbumin in Group C is (32.06 ± 5.32) mg / L, thus this indicated that diabetic patients have the highest risk of early kidney damage, followed by hypertension and then is the chronic tonsillitis. At present, the literature on the risk of chronic tonsillitis, diabetes and hypertension on early damage of kidney compared in country and foreign has not been reported, further studies have to be done.

### 4.2 Analysis of microalbuminuria in preoperative urine between groups

Chronic tonsillitis relapsing causing most of the peripheral blood T cells subsets continue to increase, whereas a group of T cell subsets continue to decrease. This group of reduced T cell subsets was negatively correlated with the concentration of Cystatin C which is used to determine the increased glomerular filtration [25-26].

Determination of preoperative urine microalbumin in Group A, B and C. Group A: urine microalbumin content is (14.53 ± 1.38) mg / L; Group B: urinary microalbumin content is (22.61 ± 1.86) mg / L, Group C: urinary microalbumin content is (32.06 ± 5.32) mg / L. Comparison of Group C to Group A and Group B, found that Group C > Group A and Group C > Group B. By statistical analysis: the preoperative urine microalbumin in Group A and Group C, there was a significant increase,  $P < 0.05$ , the difference was statistically significant. There is obviously increased when compared Group B and Group C ( $P < 0.05$ ), the difference was statistically significant. Chronic tonsillitis may pass through peripheral blood immune cells and chemokines and response with kidney immunity, leading to glomerular filtration membrane and renal tubular damage [13-21]. This study shows that urinary albumin as an indicator of chronic tonsillitis complicated with early kidney damage have a certain clinical value and its sensitivity gradually increased with the progress of the disease and these finding is consistent the research finding of Wei Youren [27], Luo Rong [22] and other research.

### 4.3 Analysis of microalbumin in preoperative and posterior urine of each group

When body immunity decreased or infected, pathogens that hide in the deep part of tonsil can cause acute attack of tonsillitis, and simple antibiotic treatment can only eliminate the pathogens at the tonsils, and tonsillectomy is the only way to remove the lesions at deep part of tonsil.

Major factors of incidence in chronic tonsillitis are bacterial infection, viral infection, allergic, autoimmune immune, and current years found that immunity decreased, internal secretion, metabolic diseases and nervous system, etc. may be the cause of tonsillitis. Bacterial infection is the accounted as first cause, due to the aerobic bacteria and anaerobic repeated stimulation, resulting in tonsillar crypt obstruction caused by poor drainage, but also caused the accumulation of bacteria and inflammatory exudate, which eventually formed a chronic tonsil Inflammation [3].

Determination of preoperative and postoperative urine microalbumin in Group A, B and C. Group A: postoperative urine microalbumin content is (11.90 ± 0.92) mg / L; Group B: postoperative

urine microalbumin content is  $(15.86 \pm 1.37)$  mg / L; Group C: postoperative urine microalbumin content is  $(21.32 \pm 1.60)$  mg / L. The difference in content between preoperative and postoperative in Group C is the largest, the difference in content between preoperative and postoperative in Group A is the smallest. The levels of microalbuminuria in group A, B and C were decreased in postoperative compared to preoperative content, respectively. The levels of microalbumin were significantly lower in postoperative compared to preoperative in group A ( $P < 0.05$ ), and the difference was statistically significant. In group B, postoperative content was significantly decreased compared to the preoperative content,  $P < 0.05$ , the difference was statistically significant. The levels of microalbumin were significantly lower in postoperative compared to preoperative in group C ( $P < 0.05$ ), and the difference was statistically significant. This study shows that the prevention of chronic tonsillitis complicated by early kidney damage, the only effective way is tonsillectomy. This is in line with Kielmovitshl's findings.

### Chapter 5 Conclusion

Patients with chronic tonsillitis can be complicated by early renal damage. Urinary albumin is a diagnostic indicator of chronic tonsillitis early kidney failure which has a certain clinical value, and with the progress of the disease gradually increased its sensitivity. Tonsillectomy is the only effective way to prevent chronic tonsillitis complicated by early kidney failure.

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