Factors Affecting Urinary Fluoride Concentrations Among Patients With Renal Dysfunction

Hsien-Wen Kuo, Chuan-Juan Lin[2], Li-Li Chen[1]

Institute of Environmental Health, and [1]Department of Nursing, China Medical College; [2]Department of Nursing, Hung-Kuang Technology College, Taichung, Taiwan, R.O.C.

Objective. Our objective was to determine the factors that affect urinary fluoride concentrations and to measure fluoride concentrations among subjects with renal function abnormalities.

Methods. Ninety subjects were divided into three groups based on creatinine clearance (Ccr). The control group consisted of 31 hospital personnel with normal renal functions and a Ccr > 50 mL/min. The chronic renal failure (CRF) group consisted of 32 subjects with a Ccr < 50 mL/min. The continuous ambulance peritoneal dialysis (CAPD) group included 27 subjects with a Ccr < 10 mL/min. Subjects' basic demographic information and history of fluoride exposure were obtained by questionnaire. Urine samples were collected from the three groups using different procedures. Urine samples were taken over 24-hours and morning urine samples were also collected. Urinary fluoride concentrations were measured using the ion selective electrode method. Creatinine levels, specific gravity levels, and pH values were also measured.

Results. Several significant factors affected urinary fluoride concentrations, including renal function, tea consumption, exercise habits, and vegetarianism. After adjusting for age and gender using multiple regression analysis, urinary fluoride concentrations among the control group were found to be 2.25 times higher than the CRF group and 5.5 times higher than the CAPD group. This result suggests that patients in the CRF and CAPD groups display poor fluoride excretion efficiencies which may have lead to fluoride accumulation in the kidney and deterioration of their conditions.

Conclusions. It is vital that patients in both the CRF and CAPD groups control their dietary intake of fluoride in order to prevent further deterioration of their conditions. Further research is needed to establish the relationship between fluoride intake and renal abnormalities. **(Mid Taiwan J Med 2001;6:74-81)**

Key words

affecting factors, renal dysfunction, urinary fluoride concentrations

INTRODUCTION

In order to determine optimum levels of systemic fluoride therapy and to help prevent fluoride-related diseases, fluoride intake levels need to be measured. Although frequent consumption of fluoride can help prevent dental caries, excessive intake may be harmful to people with renal abnormalities. Since one important function of the kidneys is to filter fluids in the body, they are exposed to relatively high fluoride concentrations. Thus, when fluoride concentrations become too high, acute fluoride toxicity may occur. Whitford and Taves reported that fluoride, like sodium and chloride, shows a progressive

Received : August 11, 2000. Revised : January 5, 2001.
Accepted : March 16, 2001.
Address reprint requests to : Hsien-Wen Kuo, Institute of Environmental Health, China Medical College, No 91, Hsueh-Shih Road, Taichung 404, Taiwan, R.O.C.

cortex-to-medulla concentration ratio of between three and four [1]. Those portions of the nephron which are responsible for the kidney's ability to concentrate urine and conserve water in the loops of Henle, collecting ducts, and vasa recta are exposed to the highest fluoride concentrations. Based on a study of renal concentrating functions with prolonged sevoflurane or enflurane anesthesia, Frink et al found a higher peak plasma fluoride ion concentration and greater total inorganic renal exposure with sevoflurane anesthesia [2]. The mitochondria in renal collecting duct cells are targets of fluoride ion toxicity and alterations are partly responsible for the sodium and water disturbances observed in patients [3]. In addition, halogenated agents (methoxyflurane, enflurane) have been found to induce fluoride dose-related renal dysfunction.

For patients with renal dysfunction, excessive fluoride intake can hinder excretion of fluoride, leading to its accumulation and further breakdown by the kidneys. According to a report by the Department of Health (DOH) in Taiwan, the number of patients suffering from renal dysfunction has increased [4]. Thus, it is important to limit fluoride intake levels by controlling consumption of high-fluoride items such as seafood, tea, and underground water. Because the kidneys are the major route for fluoride excretion (approximately 50% of fluoride absorbed from the GI tract in adults each day is excreted in the urine), total fluoride intake can best be determined by measuring urine-fluoride concentrations. Although less convenient, the collection of urine samples over a 24-hour period is a more accurate indicator of total fluoride intake than spot samples due to the fluctuation of urinary fluoride levels over time. Ding et al reported that the highest fluoride levels were found at 10:00 pm and the lowest at 2:00 pm. In addition, differences in the urinary fluoride concentrations based on samples collected in the morning, on the spot, and over 24-hours were not significant [5]. In the current study, our objective was to determine the factors affecting urinary fluoride concentrations and to compare urinary-fluoride concentrations among healthy subjects and those with kidney abnormalities.

MATERIALS AND METHODS

Study Population

All 90 subjects were selected from a teaching hospital in central Taiwan. The healthy group consisted of 31 hospital personnel with normal kidney functions [creatinine clearance (Ccr) > 50 mL/min]. The chronic renal failure (CRF) group included 32 patients with Ccr in urine < 50 mL/min and 27 patients in the continuous ambulance peritoneal dialysis (CAPD) group with Ccr in urine < 10 mL/min. All subjects participated on a volunteer basis and the CRF and CAPD groups signed forms of consent.

METHODS

All subjects were interviewed using a questionnaire administered by a formally trained nurse. The data collected included the frequency of use of fluoride-containing toothpaste and vitamins, as well as the frequency of consumption of various foods and drinks containing fluoride, such as tea and seafood. For reasons of convenience and practicality, different procedures and schedules were used to collect urine samples from all subjects during a 24-hour period. One spot urine sample was collected from each subject in the three groups, usually in the morning. Those in the healthy and CRF groups also provided samples, which represented total urinary output during a 24-hour period. In addition, subjects in the healthy group provided four consecutive samples at approximately 6-hour intervals and patients in the CRF group provided one sample. EDTA was added to all samples in order to prevent contamination by other metals. Samples were stored at 4°C for less than 72 hours before urine-fluoride concentrations were measured by the ion selective electrode method.

Fluoride measurements were conducted according to the methods described previously [6,7]. Creatinine concentrations in the urine were measured by Jaffe's Method and specific gravity levels were measured by a hand refractometer. A microprocessor pH meter (Suntex) measured the pH values.

For quality control, a calibration curve was set up for each batch. All correlation coefficients were > 0.999 and relative prediction deviations were < 5%. A total of seven tests were performed on both a high (1.25 ppm) and low (0.3125 ppm) urine-fluoride sample in order to determine reproducibility (CV < 1%). The SAS/PC+6.04 package was used for all statistical analyses, including frequency analysis, univariate analysis, one-way ANOVA, and multiple regression [8].

RESULTS

The three groups were compared based on demographic information and personal habits (Table 1). Factors that significantly affected kidney function included age, education, vegetarianism, vitamin consumption, use of fluoride toothpaste, and the frequency of seafood consumption. Among the healthy group, education levels and the number of unmarried subjects were high (over 77% completed college, 45% unmarried) and their ages were low (< 35 years old = 54.8%). Among the CRF group, the percentage of patients who were vegetarian was high (34%) and vitamin consumption and use of

Table 1. Basic demographic information and fluoride sources for the three groups

Variables	Healthy group (N = 31) n (%)	CRF group (N = 32) n (%)	CAPD group (N = 32) n (%)	*p* value
Gender				
Male	16 (51.6)	14 (43.8)	14 (51.9)	NS
Female	15 (48.4)	13 (56.3)	18 (48.1)	
Age (years)				
< 35	17 (54.8)	4 (12.5)	1 (3.7)	< 0.01
36–50	9 (29.0)	7 (21.8)	5 (18.5)	
51–64	2 (6.5)	7 (21.8)	14 (51.9)	
> 65	3 (9.68)	7 (25.9)	7 (25.9)	
Vegetarian				
No	28 (90.3)	14 (43.8)	22 (81.5)	0.05
Yes	3 (9.7)	21 (65.6)	5 (18.5)	
Regular activity				
No	19 (61.3)	16 (50.0)	16 (59.3)	NS
Yes	12 (38.7)	16 (50.0)	11 (40.7)	
Vitamin consumed				
No	20 (64.5)	30 (93.8)	8 (29.6)	< 0.001
Yes	11 (35.5)	2 (93.8)	19 (70.4)	
Fluoride toothpaste				
Yes	27 (87.1)	22 (68.8)	24 (88.9)	0.03
No	2 (6.5)	2 (6.3)	3 (11.1)	
Unknown	2 (6.5)	8 (25.0)	0 (0.0)	
Frequency of brewed tea				
Usually	11 (35.5)	7 (21.9)	3 (11.1)	NS
Occasional	11 (35.5)	8 (25.0)	4 (14.8)	
Seldom	2 (6.5)	4 (12.5)	5 (18.5)	
No	7 (22.5)	13 (40.6)	15 (55.6)	
Frequency of tea beverage*				
Usually	6 (19.4)	12 (37.5)	17 (62.9)	0.011
Occasional	14 (45.2)	13 (40.6)	9 (33.3)	
Seldom	8 (25.8)	3 (9.4)	1 (3.7)	
No	3 (9.7)	4 (12.5)	0 (0.0)	

*Tea beverages: commercially prepared drinks available in bottles or cartons, usually with a low amount of tea with added ingredients. CRF = chronic renal failure; CAPD = continous ambulance peritoneal dialysis; NS = not significant.

Table 2. Comparison of urinary fluoride concentrations, creatinine levels, and pH values from spot urine samples

	Healthy group (N = 31)	CRF group (N = 27)	CAPD group (N = 32)	*p* value
Urinary fluoride concentration				
Unadjusted (ppm)	0.38 ± 0.26	0.20 ± 0.17	0.08 ± 0.05	< 0.0115
Adjusted by cre. (mg/g cre.)	0.52 ± 0.37	0.34 ± 0.27	0.18 ± 0.19	< 0.01
Creantine in urine	81.70 ± 43.96	69.84 ± 44.30	69.09 ± 49.51	NS
Specific gravity	1.014 ± 0.007	1.014 ± 0.008	1.013 ± 0.006	NS
pH value	5.48 ± 1.21	4.73 ± 1.04	4.90 ± 1.26	NS

NS = not significant.

Table 3. Comparison of urinary fluoride concentrations, creatinine levels, and pH values from 24-hr samples between healthy and CRF groups

	Healthy group (N = 31)	CRF group (N = 27)	*p* value
Urinary fluoride concentration			
Unadjusted (ppm)	0.33 ± 0.19	0.20 ± 0.19	< 0.01
Adjusted by cre. (mg/g cre.)	0.47 ± 0.29	0.47 ± 0.38	NS
Creantine in urine	76.92 ± 35.86	50.87 ± 32.67	< 0.01
Specific gravity	1.014 ± 0.005	1.014 ± 0.007	NS
pH value	5.00 ± 0.91	5.26 ± 0.96	NS

NS = not significant.

Table 4. Comparison of urinary fluoride concentrations and creatinine levels from spot urine and 24-hr samples between healthy and CRF groups

	24-hour urine	Morning urine	*p* value
Urinary fluoride concentration (unadjusted, ppm)			
Healthy group	0.33 ± 0.19	0.38 ± 0.26	NS
CRF group	0.20 ± 0.19*	0.20 ± 0.17*	NS
Urinary fluoride concentration (adjusted by creatinine, mg/g cre.)			
Healthy group	0.47 ± 0.29	0.52 ± 0.37	NS
CRF group	0.47 ± 0.38	0.34 ± 0.27†	0.04

*$p < 0.01$ and †$p = 0.03$ as compared with the healthy group; NS = not significant.

Table 5. Factors that affect urinary fluoride concentrations based on a multiple regression model

Variables	Beta (S.E.)	*p* value
Group of Kidney function		
CRF (Healthy = 1)	–0.13 (0.09)	NS
CAPD (Healthy = 1)	–0.28 (0.10)	< 0.01
Gender (male = 1)	0.09 (0.06)	NS
Age (< 35 = 1)	–0.001 (0.002)	NS
Use of fluoride toothpaste (no = 1)	0.02 (0.05)	NS
Freguency of brewed tea (no = 1)	0.08 (0.03)	< 0.01
Freguency of sea food consumed (no = 1)	0.04 (0.04)	NS
Habit of vitamin consumed (no = 1)	0.09 (0.07)	NS
Habit of physical activity (no = 1)	–0.14 (0.06)	0.03
Vegetarian (no = 1)	0.18 (0.08)	0.02

F = 4.78 ($p < 0.01$); R^2 = 38.2%; NS = not significant.

Table 6. Ratio of predicted to observed values for urinary fluoride concentrations (ppm) based on multiple regression models (adjusted for age and gender from the healthy group)

Variables	N	Observed value (O)	Predicted value (E)	O/E ratio
CRF group	32	0.20 ± 0.17	0.45	2.25
CAPD group	27	0.08 ± 0.05	0.44	5.5

fluoride toothpaste were low (6.3% and 68.8%, respectively). The frequency of tea consumption was highest among the healthy group. The frequency of seafood consumption was highest among the CAPD group (> 3 times/week = 62.9%). Except for the frequency of seafood consumption, both the frequency and number of fluoride sources were highest among the healthy group.

The data found in Table 2 compare urinary fluoride concentrations, creatinine, specific gravity, and pH values from spot urine samples from the three groups. Urinary fluoride concentrations and pH values differed significantly among the three groups. Overall, urinary fluoride concentrations were highest among the healthy group and lowest among the CAPD group. Both unadjusted and adjusted for creatinine and specific gravity, urinary fluoride concentrations were also highest among the healthy group. The pH values (5.48) in urine were highest among the healthy group and lowest among the CRF group (4.73). In the renal dysfunction groups, urine acidity was highest. Creatinine in urine was also highest among the healthy group (81.70 mg/L), but there were no significant differences among the three groups. However, there was a high degree of variation among the three groups for creatinine in urine.

The data found in Table 3 were used to compare urinary fluoride concentrations, creatinine, specific gravity, and pH values based on 24-hour urine samples from the healthy and CRF groups. Urine-fluoride concentrations (ppm) were higher in the healthy group compared with the CRF group. Creatinine concentrations in the healthy group were significantly higher than in the CRF group since patients in the latter group were suffering from renal disorders. However, after adjustment for creatinine, the differences in urinary fluoride concentrations (mg/g crea.) were not significant.

The data shown in Table 4 compare urinary fluoride concentrations based on 24-hour and spot urine samples from the healthy and CRF groups. Unadjusted for urinary fluoride concentrations (ppm), the differences between the two groups for both sets of samples were not significant. However, unadjusted urinary fluoride concentrations for the healthy group were significantly higher than for the CRF group. For urinary fluoride concentrations (mg/g crea.) adjusted for creatinine, there was a significant difference between the 24-hour and spot urine samples among the CRF group.

The data found in Table 5 show the factors affecting urinary fluoride concentrations using multiple regression analysis. Renal function was a significant factor, and urinary fluoride concentrations were higher in the healthy group than in the CRF or CAPD groups. As frequency of tea consumption and excercise increased, especially among vegetarians, urinary floride concentrations also increased. Factors such as gender, age, use of fluoride toothpaste, and consumption of seafood and vitamins were not significant.

The data found in Table 6 show predicted values of urinary fluoride concentrations between patients in the CRF and CAPD groups using a multiple regression model. Adjusted for age and gender (using data from the healthy group), the predicted values (E) for the CRF and CAPD groups were 0.45 and 0.44, respectively, whereas the observed values (O) were 0.2 and 0.08, respectively. Therefore, the urinary fluoride concentrations in the CRF and CAPD groups were 2.25 and 5.5 times (O/E ratio) lower than the healthy group. This

finding suggests that the kidneys of patients in the CRF and CAPD groups display poor fluoride excretion efficiency.

DISCUSSION

The kidneys are the main target of acute fluoride toxicity. Since fluoride concentrations increase from the cortex to the medulla, those portions of the nephron responsible for concentrating urine and conserving water are exposed to the highest fluoride concentrations within the kidneys. Fluoride ions are filtered from the plasma in the glomerular capillaries into the urinary space of the Bowman's capsule following variable degrees of tubular reabsorption. The absorption mechanism may involve diffusion of hydrogen fluoride (HF) molecules [9]. When urine is relatively alkaline, nearly all of the fluoride exists in the ionic form and remains within the tubule to be excreted. However, when urine is relatively acidic, proportionately more of the fluoride exists in the undissociated form which increases the transtubular HF concentration gradient. Factors which alter urinary pH and affect the quantitative features of ion metabolism include: diet, certain metabolic or respiratory diseases, certain drugs, and altitude of the subject's residence. In the current study, the factors affecting urinary fluoride concentrations were vegetarianism, tea consumption and kidney function. These results are consistent with those of previous studies which showed that a vegetarian diet rendered pH values more alkaline, and a meat-rich diet resulted in more acidic pH values [9]. Several metabolic and respiratory disorders (such as diabetes mellitus, renal tubular acidosis, asthma and chronic obstructive pulmonary disorder) cause disturbances in the acid-base balance and changes in urinary pH which may affect the metabolism and biological impact of fluoride.

Urinary pH values among CRF and CAPD patients in this study were generally acidic. This suggests that the increase in the rate of diffusion from the tubular tube to the interstitial fluid resulted in less fluoride excretion and greater fluoride accumulation in the kidneys and blood. Since many of these patients have had kidney disorders for long periods of time, a considerable amount of fluoride may have accumulated, thus exacerbating their conditions. Schiffl and Binswanger showed that patients suffering from chronic renal disease tended to continue to excrete healthy levels of dietary fluoride until the creatinine clearance fell below 25 ml/min [10]. For the current study, it was assumed that all the patients with renal dysfunction consumed similar fluoride-rich diets. In these patients, the elevation of the serum fluoride concentrations was delayed and was less than might be expected from impairment of the glomerular filtration rate due to diminished tubular reabsorption caused by expansion of the extracellular fluid compartment. Further research is needed to establish the relationship between blood-fluorine concentrations and urinary fluoride concentrations among CRF and CAPD patients. Kono and Spak et al found decreased fluoride clearance levels among both adults and children with impaired renal functions, indicating that patients with impaired kidney functions may have reduced margins of safety for the development of skeletal and dental fluorosis compared to subjects with normal renal functions [11,12]. In Taiwan, a large proportion of the population regularly drinks tea made from fluoride-rich tea leaves. Kuo et al [13] estimated that the maximum daily intake of fluoride in the general Taiwanese population is 6.326 mg/day, of which 43% comes from beverages. Walters and Sherlock reported that among habitual tea drinkers, 1.3 mg (72%) of their total daily intake of fluoride comes from tea consumption [14]. In the current study, approximately 22% of the patients with CRF consume tea three or more times daily compared with 11% of patients among the CAPD group.

Decreased renal clearance may occur among patients with impaired renal functions. In the current study, urinary fluoride concentrations for CRF and CAPD patients

were 2.25 and 5.5 times (O/E ratio) lower than for subjects in the healthy group. It is important to note that this calculation assumes that there was no difference between the subjects with regard to fluoride intake. This result suggests that the kidneys of the patients with CRF and CAPD displayed poor fluoride excretion efficiency, which may have resulted in fluoride accumulation in the kidneys or other organs. As such, it is crucial for CRF and CAPD patients to control dietary intake of fluoride in order to prevent further deterioration of their conditions.

In a study of fluoride metabolism, Spencer et al reported that urine-fluoride excretions ranged from 1.51 to 3.09 mg/day (average 2.26 mg/day) and fecal-fluoride excretions ranged from 0.19 to 0.43 mg (avg. 0.29 mg/day), based on an average daily fluoride intake of 4.4 mg, indicating that urine was the primary source of fluoride excretion [15]. The four main sources of fluoride include diet, toothpaste, dentifrices (mouth rinses), and tablets. It has been reported that the average daily intake of fluoride in the Taiwanese population is 1.57 mg [13] and that the primary source is from tea leaves. Since urinary fluoride excretions for patients with CRF were significantly lower than for patients with healthy kidney functions, a significantly higher retention of fluoride was noted among CRF patients [15,16]. The results of the current study are consistent with this finding. If subjects with renal dysfunction were exposed to high levels of fluoride intake, their conditions could further deteriorate. Whitford et al showed that patients treated with 1.23% APF gel had elevated plasma fluoride concentrations and urinary fluoride concentrations of up to 30 μmol/L or more for several hours, which may have resulted in renal concentrating defects [17]. Although APF gel is not commonly used in Taiwan, it is still necessary to be aware of fluoride intake since there are many sources of fluoride in the environment. The authors recommend that patients with renal dysfunction regulate their intake of fluoride-rich foods and drinks in order to avoid exacerbating their conditions.

REFERENCES

1. Whitford GM, Taves DR. Fluoride-induced diuresis: renal-tissue solute concentrations, functional, hemodynamic, and histologic correlates in the rat. *Anesthesiology* 1973;39:416-27.
2. Frink EJ Jr, Malan TP Jr, Isner RJ, et al. Renal concentrating function with prolonged sevoflurane or enflurane anesthesia in volunteers. *Anesthesiology* 1994;80:1019-25.
3. Cittanova ML, Lelongt B, Verpont MC, et al. Fluoride ion toxicity in human kidney collecting duct cells. *Anesthesiology* 1996;84:428-35.
4. Taiwan Department of Health of The Executive Yuan. Public Health in Taiwan, Republic of China, Department of Health, The Executive Yuan, R.O.C., 1995.
5. Ding CS, Wang G, Chiang CI. Observation of fluoride excretion in urine. [Abstract] *Chinese Preventive Medicine* 1982:128.
6. Tusl J. Fluoride ion activity electrode as a suitable means for exact direct determination of urinary fluoride. *Anal Chem* 1972;44:1693-4.
7. Kuo HW, Chen LL, Wang RY, et al. Effect of fluoride mouth-rinse program on urinary fluoride concentrations. *Chin Dent J* 1998a;17:59-67.
8. SAS/STAT. User's Guide, Release 6.04 Edition, SAS Institute Inc., Cary, N.C., U.S.A., 1986.
9. Whitford GM. The physiological and toxicological characteristics of fluoride. [Review] *J Dent Res* 1990;69:539-49.
10. Schiffl HH, Binswanger U. Human urinary fluoride excretion as influenced by renal function impairment. *Nephron* 1980;26:69-72.
11. Kono K. Health effects of fluorine and its compounds. [Review] *Nippon Eiseigaku Zasshi* 1994;49:852-60.
12. Spak CJ, Berg U, Ekstrand J. Renal clearance of fluoride in children and adolescents. *Pediatrics* 1985;75:575-9.
13. Kuo HW, Chang WG, Chang SK, et al. Factors associated with bone quality in central Taiwan communities. *J China Medical College* 1998b;7:45-54.
14. Walters CB, Sherlock JC, Evans WH, et al. Dietary intake of fluoride in the United Kingdom and fluoride content of some foodstuffs. *J Sci Food Agric* 1983;34:523-8.
15. Spencer H, Lewin I, Wistrowski E, et al. Fluoride metabolism in man. *Am J Med* 1970;49:807-13.
16. Malan TP Jr, Kadata Y, Mata H, et al. Renal function after sevoflurane or enflurane anesthesia in the Fisher 344 rat. *Anesth Analg* 1993;77:817-21.
17. Whitford GM, Allmann DW, Shahed AR. Topical fluoride effects on physiologic and biochemical processes. *J Dent Res* 1987;66:1072-8.

影響腎臟異常患者尿中氟濃度之相關因素

郭憲文 林靜娟[2] 陳麗麗[1]

中國醫藥學院 環境醫學研究所 中國醫藥學院 護理系[1] 弘光技術學院 護理系[2]

目的 由於氟化物是一種毒性物質，因此對患有腎臟病者更應注意氟化物之攝取總量，本研究之目的探討影響尿中氟濃度之相關因素及腎功能異常者尿中氟濃度。

方法 依肌酐酸清除率(Ccr)將90位對象分成三組，31名健康組之腎功能正常且Ccr大於50 ml/min，32名慢性腎衰竭(CRF)患者，其Ccr小於50 ml/min，而27名連續腹膜透析(CAPD)患者，其Ccr小於10 ml/min。利用問卷收集研究對象之基本資料及其氟化物暴露量資料，尿液之收集包括24小時(每六小時一次)及晨尿，並以氟電極測定氟濃度，並測定尿肌酐酸、尿比重及pH值。

結果 經多變項迴歸分析得知影響尿中氟濃度之因素包括人體腎功能、茶攝取量、運動習慣及素食者；並經多變項迴歸分析調整個人年齡及性別後，健康組尿中氟濃度較CRF組高出2.25倍及CAPD組高出5.5倍，此是否顯示腎臟病患可能無法排除過多氟化物貯存於體內，而更加重對腎臟之正常功能。

結論 建議腎臟功能異常者應特別注意氟化物之攝取量，以避免過多氟化物累積在腎臟。未來研究宜進一步探討氟攝取量與腎病變之相關性。（中台灣醫誌 **2001;6:74-81**）

關鍵詞

影響因子，腎臟異常，尿中氟濃度

聯絡作者：郭憲文

地　址：404台中市北區學士路9號

中國醫藥學院 環境醫學研究所

收文日期：8/11/2000　　修改日期：1/5/2001

接受日期：3/16/2001