

Original Article

Correlation between salt intake and early kidney damage in hypertensive patients

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Received March 1, 2018; Accepted April 25, 2018; Epub July 15, 2018; Published July 30, 2018

Abstract: Objective: To study the correlation between salt intake and early kidney damage in patients with hypertension. Methods: A total of 2,964 primary hypertension patients admitted in Fujian Provincial Hospital of Fujian Medical University from January 2015 to December 2017 who met the inclusion criteria were selected as research objects, including 1,382 males and 1,582 females. The patients were divided into low intake group, medium intake group, middle high intake group and high intake group according to the quartiles of salt intake. Relevant information was collected including age, gender, course of disease, smoking history, drinking disease, and past medical history. Blood samples were collected and tested involving blood potassium, sodium, creatinine, blood urea nitrogen, blood glucose, blood uric acid, serum cystatin C, triglyceride, total cholesterol, low density lipoprotein, and high density lipoprotein. Patients' 24-hour urine sodium and urine microalbumin were also checked for correlation analysis. Results: There was no statistical difference between the four groups of general data (all $P > 0.05$). Salt intake of male patients 11.4 (7.4-15.4) g/d was higher than that of female patients 9.2 (6.5-12.5) g/d, the difference was statistically significant ($P < 0.05$). The 24-hour microalbuminuria in different salt intake groups were (2.31±0.12), (2.62±0.14), (2.75±0.13), (3.09±0.15), respectively. The 24-hour microalbumin in the middle high intake group and the high intake group were significantly higher than those in the low intake and middle intake groups, and furthermore the high intake group was higher than that in the middle high intake group (all $P < 0.05$). Kidney damage was detected in 525 patients with the proportion of 17.71% among those 2,964 patients enrolled. The detection rates of kidney damage in different salt intake groups were 11.46% (88 cases), 11.38% (91 cases), 20.16% (155 cases) and 30.46% (191 cases), respectively. Kidney damage in the middle high intake and high intake groups were significantly higher than those in the low intake and middle intake groups (all $P < 0.05$). The detection rate of kidney damage in the high intake group was higher than that in the middle high intake group ($P < 0.05$). There was no statistical difference between the proportions of male and female of the four groups ($P > 0.05$). There was a correlation between salt intake and 24-hour urine microalbumin ($r = 0.15$, $t = 4.69$, $P < 0.001$) in patients with hypertension. Multiple linear regression analysis showed that the dependent variables 24-hour urine microalbumin in enrolled patients had significant correlation with patients' independent variable salt intake (OR=16.54, 95% CI 2.49-25.36, $P < 0.001$), systolic blood pressure (OR=10.58, 95% CI 1.05-12.69, $P = 0.04$), blood glucose (OR=10.65, 95% CI 1.12-15.36, $P = 0.02$), and blood uric acid (OR=10.26, 95% CI 3.46-24.24, $P < 0.001$); but there was no significant correlation with course of disease, gender, diastolic blood pressure, serum creatinine, blood urea nitrogen, cystatin C, triglyceride, total cholesterol, low density lipoprotein, high density lipoprotein, blood sodium, blood potassium, and blood chlorine (all $P > 0.05$). Conclusion: Long-term high salt intake is an independent risk factor for early kidney damage. The more daily intake of salt, the heavier the degree of kidney damage. At the same time, related factors such as systolic blood pressure, blood uric acid, and blood glucose are closely related to the occurrence of 24-hour urine microalbumin.

Keywords: Salt intake, hypertension, kidney damage, correlation research

Introduction

Among many chronic diseases, hypertension is one of the more prevalent diseases affecting 25% of adults in the world. By 2010, there were

about 35.538 million hypertensive patients in China [1]. Some studies have shown that hypertension has a significant damage to the target organ of heart, brain and kidney [2, 3]. The reasons for the rise of blood pressure involve many

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factors, such as gene, environment, society, diet, etc. Of dietary factors, intake of sodium and potassium has the greatest impact on blood pressure levels [4]. Natural food consumed in our living environment contains less sodium, so the intake of sodium is mainly from salt. The World Health Organization recommends daily sodium intake should be controlled within 5 g. A survey in China found that the daily intake of sodium in China is about 12 g [5]. Currently, sodium intake is recognized as an important risk factor for cardiovascular disease [6]. There are about 1.65 million people who have died of cardiovascular disease every year, with the most obvious in East Asia [7].

Since hypertension causes severe damage to the target organ of the heart, whether it also has the same damage to kidney at the early stage was a goal of this study. In a previous study, high sodium intake led to vascular endothelial dysfunction and vascular damage, which in turn resulted in collagen deposition, interstitial fibrosis, and endothelial dysfunction in renal tubules [8]. A high sodium diet causes changes in the hemodynamics of the kidney through neurohumoral reactions [6]. In animal studies, a high sodium diet leads to high blood pressure, which causes abnormal changes of kidney tubular atrophy and glomerulosclerosis [9]. However, there is lack of studies on early kidney damage in clinical hypertension. Therefore, this research analyzed the correlation of early kidney damage in hypertensive patients with different sodium intake, and investigated the related risk factors of early kidney damage in hypertensive patients.

Materials and methods

Research objects

This research was approved by the Ethics Committee of Fujian Provincial Hospital of Fujian Medical University. A total of 2,964 primary hypertension patients admitted in the hospital from January 2015 to December 2017 who met the inclusion criteria were selected as research objects. There were 1,382 males and 1,582 females with the average age of 50.98 ± 14.32 years old. Patients were divided into four groups according to the quartiles of salt intake: low intake group (≤ 7.1 g), medium intake group (7.2-10.2 g), middle high intake group (10.3-13.8 g), and high intake group

(≥ 13.9 g). There are many ways to calculate the daily salt intake. The most recognized calculation method is based on 24-hour urinary sodium excretion, and the specific formula is: daily salt intake (g) = $10/9 * 24\text{-hour urinary sodium excretion (mmol/24 h)} * 58.5/1,000$ [10, 11].

Inclusion and exclusion criteria

Inclusion criteria: (1) In line with the diagnostic criteria for hypertension, with reference to the America Joint National Committee hypertension guideline: blood pressure was measured 3 times on different days without consumption of anti-hypertensive medication. Systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or hypertension had been clearly diagnosed in the past. (2) Aged between 18-79 years old. (3) Patients signed the informed consent [12].

Exclusion criteria: (1) Secondary hypertension: such as renal hypertension, pheochromocytoma, hypercortisolism and so on. (2) Combined serious cardiovascular complications: such as myocardial infarction, malignant arrhythmia, cardiac function III-IV, etc. (3) Patients with severe infection; (4) Patients with confirmed kidney damage or renal insufficiency. (5) Patients with electrolyte disorders. (6) Patients who were pregnant. (7) Patients who took kidney damage drugs. (8) Patients with serious mental illness, unable to cooperate with the investigation.

Research methods

The collection of medical history and related information included age, gender, course of disease, smoking history, drinking disease, and past medical history.

Collection of blood samples: Research subjects were fasted 8-10 hours before the day of blood collection. The next morning, upper limb elbow venous blood was taken and sent to laboratory for serological index determination by Beckman automatic biochemical analyzer. The detection indicators included: blood potassium, blood sodium, creatinine, blood urea nitrogen, blood glucose, serum uric acid, serum cystatin C, triglyceride, total cholesterol, low density lipoprotein, and high density lipoprotein.

Collection of 24 h urine sample: The urine was collected in the conditions of normal rest, diet,

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Table 1. Comparison of general information of hypertension patients in different salt intake groups

Item	Low intake group	Medium intake group	Middle high intake group	High intake group	X ² /F	P
Salt intake (g/d)	5.5 (4.3-6.2)	8.5 (7.8-9.3)	12 (11.1-12.7)	18.5 (16.1-21.5)	10.13	<0.001
Case					0.42	0.82
Male	360	386	367	269		
Female	408	414	402	358		
Age (year)	51.52±15.21	53.75±14.25	50.85±14.26	49.56±13.28	0.36	0.71
Course of disease (year)	3.2 (0.7-8.1)	3.2 (0.9-9.7)	3.1 (1.1-7.9)	3.4 (1.1-8.2)	0.11	0.87
Systolic pressure (mmHg)	152.82±25.31	151.25±20.74	151.36±25.84	150.74±22.69	0.25	0.79
Diastolic pressure (mmHg)	92.45±16.47	89.05±13.26	93.41±15.98	94.58±14.62	1.15	0.70
Blood glucose (mmol/L)	4.92±0.71	4.62±0.64	4.86±0.74	4.81±0.62	1.14	0.62
Serum creatinine (μmol/L)	75.36±18.92	70.58±17.31	72.16±16.25	73.84±18.12	1.45	0.45
Blood uric acid (μmol/L)	339.15±94.26	322.51±88.16	336.12±82.64	339.14±80.32	2.41	0.09
Blood urea nitrogen (mmol/L)	4.5 (3.7-5.4)	4.4 (3.7-5.5)	4.6 (3.7-5.4)	4.9 (4.1-5.9)	0.62	0.32
Cystatin C (mg/L)	0.8 (0.7-1.1)	0.9 (0.8-1.0)	1.1 (0.9-1.3)	0.8 (0.6-1.2)	0.65	0.36
Triglyceride (mmol/L)	1.3 (1.0-1.7)	1.1 (0.8-1.9)	1.3 (1.1-2.0)	1.4 (1.1-2.1)	2.12	0.09
Total cholesterol (mmol/L)	4.53±0.85	4.62±0.86	4.82±0.95	4.76±0.89	0.61	0.31
HDL (mmol/L)	1.25±0.31	1.31±0.29	1.18±0.32	1.21±0.34	0.52	0.42
LDL (mmol/L)	2.52±0.62	2.49±0.69	2.57±0.59	2.47±0.63	1.12	0.60
Serum sodium (mmol/L)	140.21±2.59	140.85±3.26	140.58±3.59	140.82±2.58	1.42	0.43
Serum potassium (mmol/L)	3.81±0.45	3.84±0.47	3.86±0.36	3.91±0.42	1.32	0.64
Serum chlorine (mmol/L)	104.25±3.21	104.23±3.35	104.62±3.51	105.23±5.31	2.35	0.06

Note: HDL, high-density lipoprotein; LDL, low density lipoprotein.

Table 2. Comparison of salt intake between patients in different gender

Item	Female	Male	t	P
Salt intake	9.2 (6.5-12.5)	11.4 (7.4-15.4)	2.65	<0.001

and proper exercise. Normal urination was started at about 7 o'clock on the first day morning and was disposed. Thereafter the urine during the day was collected in a clean container and preservatives were added into it and stirred well. The urine was kept in the container until the last urination in the morning of the second day around 7 o'clock.

The 24 hour retained urine was fully stirred, and the volume of urine was calculated with a measuring cup. Then 100 mL of well-mixed urine was stored at a 2-8°C environment, which would be used to detect the 24 hour urine microalbuminuria [11].

Observation index

Main outcome measures: Daily sodium intake and 24-hour urine microalbumin were calculated from 24-hour urinary sodium excretion, and

the relationship between sodium intake and renal damage was observed.

Secondary outcome measures: Patients' the clinical data, blood pressure, clinical blood monitoring indicators, and 24-hour urine microalbumin were analyzed by multiple linear regression analysis to explore the risk factors of the disease.

Statistical analysis

SPSS 17.0 software was used to analyze the data. The normal distribution measurement data are expressed as mean ± standard deviation ($\bar{x} \pm sd$). The abnormal distribution measurement data were expressed by median M (P_{25} - P_{75}), and analyzed after the natural logarithm transformed into normal distribution data. Different salt intake between groups was compared using single factor analysis of variance, expressed by F. Multiple sets of counting data were compared with chi-square test and expressed by Chi-square. The linear correlation between the two variables was analyzed by Pearson product distance correlation. The multiple linear regression analysis was used to

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Table 3. Detection rate of kidney damage in the different salt intake groups

Item	Low intake group	Medium intake group	Middle high intake group	High intake group
Case	768	800	769	627
24-hour microalbumin	25.36±10.54 ^{a,b}	27.54±11.65 ^{a,b}	32.54±12.62 ^{a,c,d}	37.95±14.56 ^{b,c,d}
Detection rate of kidney damage (%)	88 (11.46) ^{a,b}	91 (11.38) ^{a,b}	155 (20.16) ^{a,c,d}	191 (30.46) ^{b,c,d}
Male (%)	46 (52.27)	47 (51.65)	78 (50.32)	97 (50.79)
Female (%)	42 (47.73)	44 (48.35)	77 (49.68)	94 (49.21)

Note: Compared with the high intake group ^aP<0.05; compared with the middle high intake group ^bP<0.05; compared with the medium intake group ^cP<0.05; compared with the low intake group ^dP<0.05.

Table 4. Pairwise comparison of 24-hour urine microalbuminuria between the four groups

Comparison	t	P
Low intake group and medium intake group	1.21	0.12
Low intake group and middle high intake group	3.12	<0.001
Low intake group and high intake group	5.12	<0.001
Medium intake group and middle high intake group	2.75	<0.001
Medium intake group and high intake group	4.59	<0.001
Middle high intake group and high intake group	2.24	0.01

analyze the risk factors that affecting early kidney damage. The difference was considered statistically significant with P<0.05.

Results

General information

The general information of patients in different salt intake groups was compared, and the salt intake of each group was significantly different (P<0.05). There were no statistical differences in age, gender, course of disease, systolic blood pressure, diastolic blood pressure, blood glucose, serum creatinine, blood uric acid, urea nitrogen, cystatin C, triglyceride, total cholesterol, low density lipoprotein, high density lipoprotein, blood sodium, serum potassium, and blood chlorine of four groups (all P>0.05), and the baseline of four groups were comparable. See **Table 1**.

Comparison of salt intake between patients in different gender

All patients were compared for salt intake by gender, of which 1,582 were females and 1,382 were males. The salt intakes of these two groups were 9.2 (6.5-12.5) g/d and 11.4 (7.4-15.4) g/d, respectively. The difference

between the two groups was statistically significant (P<0.05). See **Table 2**.

Comparison of 24-hour microalbumin and kidney damage detection rate in different salt intake groups

The 24-hour microalbumin in different salt intake groups was (2.31±0.12), (2.62±0.14), (2.75±0.13), (3.09±0.15), respectively. Among them, the 24-hour microalbumin in the middle high intake group was significantly higher than that in the low intake and medium intake group (t=3.12, P<0.001; t=2.75, P<0.001). The 24-hour microalbumin level in the high intake group was significantly higher than that in the low and medium intake groups (t=5.12, P<0.001; t=4.59, P<0.001). The high intake group 24-hour microalbuminuria was higher than that in the middle high intake group (t=2.24, P=0.01). Of the 2,964 patients enrolled, kidney damage was detected in 525 patients with the proportion of 17.71%. The detection rates of kidney damage in different salt intake groups were 11.46% (88 cases), 11.38% (91 cases), 20.16% (155 cases) and 30.46% (191 cases), respectively. The kidney damage in the middle high intake group was significantly higher than that in the low intake and medium intake groups ($\chi^2=4.69$, P<0.001; $\chi^2=3.21$, P=0.01). The incidence of kidney damage in high intake group was significantly higher than that in the low and medium intake groups ($\chi^2=5.43$, P<0.001; $\chi^2=4.85$, P<0.001). The kidney damage detection rate in the high intake group was higher than that in the middle high intake group ($\chi^2=3.54$, P=0.03). There was no statistical difference in male-to-female ratios among the four groups (P>0.05). See **Tables 3-5**.

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Table 5. Pairwise comparison of early detection rate of kidney damage between the four groups

Comparison	χ^2	P
Low intake group and medium intake group	1.10	0.21
Low intake group and middle high intake group	4.69	<0.001
Low intake group and high intake group	5.43	<0.001
Medium intake group and middle high intake group	3.21	0.01
Medium intake group and high intake group	4.85	<0.001
Middle high intake group and high intake group	3.54	0.03

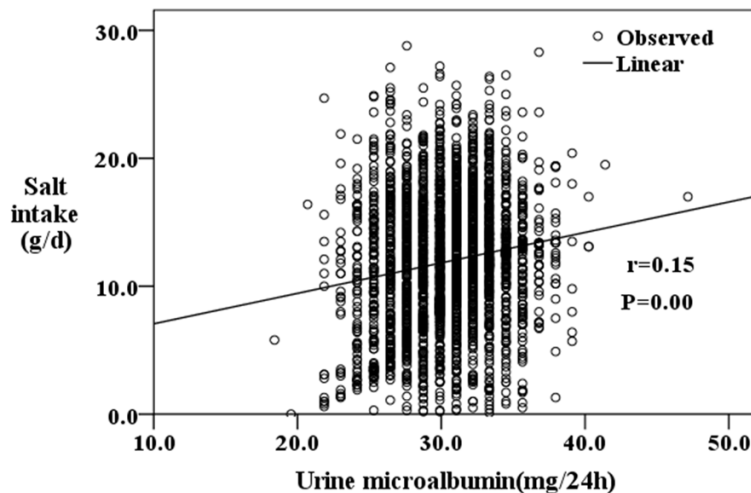


Figure 1. Relationship between 24-hour urine microalbuminuria and salt intake.

Relationship between 24-hour urine microalbuminuria and salt intake

There was a correlation between salt intake and 24-hour urine microalbumin in hypertensive patients ($r=0.15$, $t=4.69$, $P<0.001$). See **Figure 1**.

Analysis of risk factors of 24-hour urine microalbuminuria

The data of 525 patients with kidney damage was analyzed. With 24-hour microalbumin as dependent variable, relevant factors included salt intake, course of disease, gender, systolic blood pressure, diastolic blood pressure, blood glucose, serum creatinine, blood uric acid, urea nitrogen, serum cystatin C, triglyceride, total cholesterol, low density lipoprotein, high density lipoprotein, blood sodium, blood potassium, and blood chlorine as independent variables. The dependent variables and independent variables were analyzed by multiple linear regres-

sion analysis and it showed that the dependent variables of 24-hour urine microalbumin in enrolled patients had significant correlation with independent variables of patients' salt intake (OR=16.54, 95% CI=2.49-25.36, $P<0.001$), systolic blood pressure (OR=10.58, 95% CI=1.05-12.69, $P=0.04$), blood glucose (OR=10.65, 95% CI=1.12-15.36, $P=0.02$), and blood uric acid (OR=10.26, 95% CI=3.46-24.24, $P<0.001$). However, there was no significant correlation with course of disease, gender, diastolic blood pressure, serum creatinine, blood urea nitrogen, cystatin C, triglyceride, total cholesterol, low density lipoprotein, high density lipoprotein, blood sodium, blood potassium, and blood chlorine (all $P>0.05$). See **Table 6**.

Discussion

In previous studies, salt intake in China was about 12 g [5]. The recent survey found that the daily average salt intake in China is 9.1 g [11]. Both are higher than the international recommended daily salt intake level of less than 5 g. At the same time, the study also found that the salt intake in the Northern China is higher than the South; it might be related to climate, diet and cooking method [13]. In this research, only partial inclusion cases of lower intake group with salt intake less than 7.1 g met the international standards. In terms of gender differences in salt intake, study has also found that male salt intake was significantly higher than female [14]. Our research also found that salt intake of male was higher than that of female, with statistical difference ($P<0.05$), which was consistent with the above research result.

The damage of kidney caused by hypertension is evaluated by serum creatinine, urinary protein/creatinine ratio, and urine microalbumin clinically. However, serum creatinine increased only after kidney impairment [15]. Urinary

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Table 6. Analysis of risk factors of 24-hour urine microalbuminuria

Variable	Beta coefficient	Standard error	Wald χ^2	df	P	OR	95% CI	
							Lower limit	Upper limit
Salt intake (g/d)	2.57	0.60	15.18	523	<0.001	16.54	2.49	25.36
Course of disease (year)	0.78	0.45	2.25	523	0.07	2.25	0.87	6.85
Gender	0.82	0.40	2.27	1	0.08	2.25	0.81	6.75
Systolic pressure (mmHg)	1.25	0.32	4.39	523	0.04	10.58	1.05	12.69
Diastolic pressure (mmHg)	0.89	0.43	2.37	523	0.08	4.66	0.82	6.83
Blood glucose (mmol/L)	0.47	0.35	8.05	523	0.02	10.65	1.12	15.36
Serum creatinine (μ mol/L)	0.91	0.37	4.13	523	0.06	7.49	0.98	6.26
Blood uric acid (μ mol/L)	2.11	0.64	12.97	523	<0.001	10.26	3.46	24.24
Blood urea nitrogen (mmol/L)	0.92	0.40	4.27	523	0.07	6.37	0.85	6.39
Cystatin C (mg/L)	0.88	0.42	2.38	523	0.08	4.44	0.84	6.84
Triglyceride (mmol/L)	0.81	0.43	2.41	523	0.08	2.59	0.86	6.63
Total cholesterol (mmol/L)	0.90	0.47	2.37	523	0.09	4.56	0.87	6.56
HDL (mmol/L)	0.92	0.42	3.74	523	0.12	5.01	0.79	6.41
LDL (mmol/L)	0.86	0.39	4.15	523	0.08	4.25	0.75	6.39
Serum sodium (mmol/L)	0.94	0.40	4.28	523	0.08	5.38	0.85	6.36
Serum potassium (mmol/L)	0.86	0.43	2.35	523	0.09	4.62	0.84	6.63
Serum chlorine (mmol/L)	0.94	0.39	4.28	523	0.07	5.37	0.84	6.37

Note: HDL, high-density lipoprotein; LDL, low density lipoprotein; df, degree of freedom; OR, odds ratio; CI, confidence interval.

microalbumin was less affected by diet than urinary protein/creatinine ratio, which is more suitable as a gold standard for the evaluation of early kidney damage [10]. Numerous studies have shown that high salt intake has a damaging effect on the target organs of heart and kidney [6, 7]. Previous study has found that the incidence of early kidney damage is about 20-30% in all hypertensive patients [16]. In this research, the detection rate of early kidney damage in middle high intake group and high intake group were 20.16% and 30.46%, which was basically consistent with the results in previous studies. In the experimental studies, the urinary protein occurred and renal tubule injury was found after 10 weeks of continuous high salt diet for hypertensive rats [17]. A large number of clinical studies have also shown that high salt diet is an important risk factor for elevation of blood pressure and complications [18, 19]. In this research, 24-hour urine microalbumin as a gold standard for early renal damage was measured for comparison and found that, the levels of 24-hour microalbumin in the middle high intake group and high intake group were significantly higher than that in the low intake group and the medium intake group (all $P < 0.05$). It was also found that there was a positive correlation between salt intake and urine

microalbuminuria ($r=0.15$, $t=4.69$, $P<0.001$), consistent with previous studies.

In the analysis of related risk factors of 24-hour urine microalbuminuria, a previous study found that hypertension, diabetes, chronic kidney disease, lipid metabolism disorders, smoking, and race were all associated with urinary microalbumin [20]. This research found that high salt intake was closely related to urinary microalbuminuria, and the increase in systolic pressure was closely related to 24-hour urine microalbumin too. Previous studies have shown that high salt intake could increase the secretion of steroid hormones in the body, resulting in contraction of blood vessels and increased cardiac contractility, therefore leading to the increase of systolic blood pressure [21, 22]. After reducing the salt intake in patients with chronic kidney disease, the blood pressure was significantly decreased [23]. This research also found that elevated systolic blood pressure was closely related to 24-hour urine microalbumin. Serum uric acid and 24-hour microalbuminuria were closely related and led to kidney damage, which is consistent with previous study [24]. This research showed that the increase of blood glucose was associated with 24-hour urinary microalbumin, and previous study has also

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indicated that the increase of blood glucose is the risk factor for kidney damage, which is consistent with this research [25]. In this research, due to the lack of long-term follow-up observation, the data investigated were relatively limited and individual differences were large. Further increase of follow-up time, and a long-term follow-up observation are necessary for future research.

In summary, long-term high salt intake is an independent risk factor for early kidney damage in patients. The more the daily intake of salt, the heavier the degree of kidney damage that was observed. In addition, systolic blood pressure, blood uric acid, and blood glucose are closely related to 24-hour urine microalbumin.

Acknowledgements

This work was supported by the Young and Middle-aged Backbone Personnel Training Project of Fujian Health and Family Planning Commission (2016-ZQN-10) and the Guiding Project of Fujian Provincial Department of Social and Technology (2017Y0015).

Disclosure of conflict of interest

None.

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