Renal Response to Egg White Protein Loading in Healthy Young Adults

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Background: *Renal disease has progressively affected Thai people. Protein diet has been well documented to induce renal hyper-filtration. Therefore, recommendation to patients with kidney disease should be clear. Egg white is indicated as complete protein. However, comparative study of its effect on renal function with protein of animal meat has been rarely reported.*
Objective: *Evaluate renal response to egg white protein load as compared to chicken protein load.*
Material and Method: *High protein loading from different sources was evaluated in 11 healthy volunteers. They were enrolled in two separate experiments conducted within 1-week interval. Baseline GFR was examined by 24 hour C_{cr} before each protein challenge. Then the subject randomly received a protein rich meal of 0.8 g/Kg.BW of steamed egg white or boiled chicken breast. The spot C_{cr} was performed every 60 minutes for 3 hours for finding peak GFR after high protein intake.*
Results: *Baseline GFR of both experiments was not different. After two protein meals, GFR was significantly increased and reached the peak values at 60 minutes. There was no difference of peak GFR between both protein sources. The renal reserve was indicated as 64% and 58% increments from baseline values in egg white and chicken protein respectively.*
Conclusion: *In normal subjects, egg white protein stimulated as high renal response as chicken protein when challenged with the same amount of protein.*

Keywords: *Egg white protein, Protein loading, Glomerular filtration rate, Renal reserve*

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Glomerular filtration rate (GFR) is a good indicator for overall renal function. However, its value is altered between individual according to several physical differences *e.g.* age, gender, body size and pregnancy[1]. Normal variation of dietary protein intake also affects the individual GFR. There is a considerable difference in habitual dietary protein consumption among people around the world. This contributes to changes of resting GFR of those in discrete areas. The previous investigations have indicated that low protein intake caused lower GFR when compared to normal or high protein intake[2-4]. Additionally, decrease in GFR was also reported in people who consume a vegetarian diet or patients with malnutrition and renal disease[3,5,6]. An acute oral protein load or intravenous amino acid infusion has been recognized to enhance renal function in both humans and animals[2,7,8]. The increment of GFR on high protein challenge is due to physiological reactions of a kidney containing renal reserve[2]. The decrement and loss of renal reserve were revealed in patients with renal damage[6,9].

Various sources of protein have been used to evaluate renal reserve such as meat, poultry and plant. Animal meat protein has been reported to significantly increase GFR, while that from plants showed inconclusive responses[10,11]. Egg is an inexpensive source of high quality protein. People can easily access it. Thus, it is recommended for patients with some renal diseases. However, the performance on renal stimulation has rarely been reported and a comparative study to other protein sources in the same group of subjects has not been done. The present study was aimed to examine the effect of egg white protein loading on renal response compared to animal meat protein loading and to report as renal reserve.

Material and Method

The present study protocol was approved by the Intuitional Review Broad of Human Research Ethics

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Subjects

Eleven healthy volunteers participated in the present study, five males and six females, age range from 21 to 28 years. All of them gave their signed consents before enrolling in the present study. The participants had good nutritional status. None of them had a history of diabetes mellitus, renal diseases, hypertension, heart disease or other diseases. No medication was allowed for two weeks prior to or during the present study.

Protocols

All subjects were enrolled in two experiments of high protein loading, which were done within one-week interval. Egg white and chicken breast were used as sources of high protein tests. Baseline GFR evaluation was performed by 24 hour-endogenous creatinine clearance (C_{cr}) starting one day before each protein loading.

At 8 am of the experimental day, the subject arrived at the laboratory after fasting over night. After resting for at least 10 minutes, the blood pressure, weight and height were measured. They were asked to void the last aliquot of 24 hour urine collection as complete as possible. After that, the first venous blood collection was performed at peripheral superficial vein of a forearm. The heparin solution (Heparin: NSS 0.9%; 1:10 v/v) was applied to the blood vessel in order to avoid vessel blockage. The level of creatinine in both urine and serum were evaluated to calculate the 24 hour C_{cr} and blood chemistry data.

After the first blood collection, subjects were derived a high protein meal as breakfast. The protein was prepared in the form of steamed egg white or boiled chicken breast given in the dose of 0.8 g/Kg.BW. The subject was requested to complete the meal within 10 minutes. To encourage urine output during the experimental period, 10 ml/Kg.BW of water were given to the subject as starting hydration. Blood samples were obtained from the kept vein and urine samples were collected by spontaneous voiding every 60 minutes for 3 hours. These will be further used for chemical analysis to find peak GFR after protein rich meal. The urine volume was measured and the same amount of water was replaced orally to stimulate the next urine excretion. In order to avoid the effect of posture on changes of renal hemodynamic, the subject was asked to stay in supine position throughout the experimental period except for urine voiding.

Laboratory analysis

Triglyceride, cholesterol, blood urea nitrogen and creatinine in serum and urine were analyzed by standard reactions performed by auto-analyzer of a commercial company.

The GFR analysis was assessed by using endogenous creatinine clearance. The calculation was carried out by using the following equation.

$$C_{cr} = \frac{U \times V}{P}$$

where U = creatinine concentration in urine (mg/dl)
V = urine flow rate (ml/min)
P = creatinine concentration in plasma (mg/dl)

The body surface area (BSA) of the subject was obtained by using the standard normogram that determines BSA from height and weight.

The calculated GFR was corrected to the standard surface area of 1.73 m^2.

The peak GFR was obtained from the highest C_{cr} after protein loading.

The renal reserve was calculated as the difference between peak and baseline GFR.

Statistical analysis

All data are expressed as mean $\pm$ SEM. The Student paired and unpaired t-test were used to evaluate the difference of C_{cr} within the same group at different time periods and between groups of the same time period respectively. p-value < 0.05 was accepted as statistical significance difference.

Results

The clinical and biochemical parameters of 11 volunteers are shown in Table 1. The mean age of the healthy young adults was a 23.36 $\pm$ 0.71 year ranging from 21-28 years. The mean weight and height were 56.27 $\pm$ 2.75 Kg and 165.09 $\pm$ 2.57 cm respectively. The average body surface area presented as 1.61 $\pm$ 0.05 m^2. They are all in normotensive conditions during the time course of study with the average SBP as 105.64 $\pm$ 1.72 mmHg and DBP as 67.82 $\pm$ 1.80 mmHg. Biochemical parameters were observed in the group of subjects. The mean value of serum cholesterol level was 169.82 $\pm$ 10.22 mg/dl and fasting glucose level was 75.36 $\pm$ 2.13 mg/dl. These results indicated that all participants were healthy during participation in the present study.

Table 1. Clinical characteristics and biochemical parameters of all 11 healthy volunteers

	Mean ± SEM	Range
Age (year)	23.36 ± 0.71	21-28
Weight (Kg)	56.27 ± 2.75	44-72
Height (cm)	165.09 ± 2.57	154-177
BSA (m^2)	1.61 ± 0.05	1.39-1.88
SBP (mmHg)	105.64 ± 1.72	100-112
DBP (mmHg)	67.82 ± 1.80	60-80
Cholesterol (mg/dl)	169.82 ± 10.22	116-210
Hct (%)	41.91 ± 1.20	38-49
FBS (mg/dl)	75.36 ± 2.13	70-86

SEM = standard error of mean; BSA = body surface area; SBP = systolic blood pressure; DBP = diastolic blood pressure; FBS = fasting blood sugar

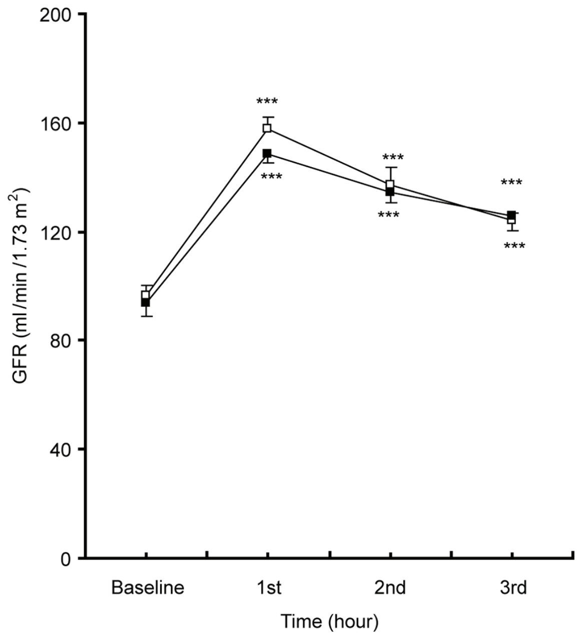

Fig. 1 Changes of GFR before and after high protein challenge (opened square for egg white and closed square for chicken); The data are shown as mean ± SEM. *** p < 0.001 vs. baseline values

Table 2 and Fig. 1 show the serial changes of GFR before and after protein loading. In the period prior to protein challenge (baseline), there was no difference in GFR of two protein sources. The values between egg white and chicken meals were 96.22 ± 4.13 and 93.98 ± 5.14 ml/min/ 1.73 m^2 ($p > 0.05$) respectively. After protein load, GFR increased significantly throughout the course of the present study. The highest GFR was observed 1 hour after the meals and were similar in both protein sources. After that, the renal response decreased progressively to a level significantly higher than that of baseline value of each experiment. The values of baseline and peak GFR for egg white was 96.22 ± 4.13 vs. 157.50 ± 4.63 ml/min/1.73 m^2 ($p < 0.001$) and for chicken was 93.98 ± 5.14 vs. 148.56 ± 3.04 ml/min/1.73 m^2 ($p < 0.001$). Two protein sources stimulated high renal reserve. The values of egg white and chicken were 61.28 and 54.58 ml/min/ 1.73 m^2 or 64% and 58% increment of baseline values respectively.

High protein challenge also caused progressively increased urinary urea excretion (Fig. 2). The peak times of both protein loads were observed at 3 hours after the meals. The values of baseline and peak for egg white were 370.21 ± 51.53 vs. 643.50 ± 62.65 ($p < 0.01$) and for chicken were 332.70 ± 33.66 vs. 717.59 ± 51.33 ($p < 0.001$) respectively. There was no difference of urea excretion rate between two protein

Table 2. Alteration of GFR before and after protein ingestion (ml/min/1.73 m^2) (n = 11)

	Time (hour)			
	Baseline	1st hour	2nd hour	3rd hour
Egg white	96.22 ± 4.13	157.50 ± 4.63***	137.00 ± 6.38***	124.62 ± 2.94***
RR (ml/min/1.73 m^2)	61.28			
Chicken	93.98 ± 5.14	148.56 ± 3.04***	134.26 ± 3.63***	125.77 ± 5.22***
RR (ml/min/1.73 m^2)	54.58			

Data are depicted as mean ± SEM
RR = renal reserve
*** p < 0.001 compared with baseline value of each experiment

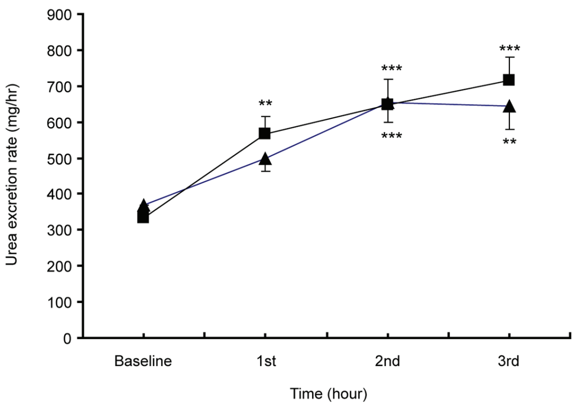

Fig. 2 Changes of urinary urea excretion rate before and after protein loading, egg white (triangle) and chicken (square). The values are shown as mean ± SEM, ** $p < 0.01$, *** $p < 0.001$ vs. baseline values

meals within the same time period. These results indicated that high protein intake causes an elevated load of urea excretion to the kidney.

Discussion

Increased renal response to an acute oral protein load or amino acid infusion was extensively reported[1-3]. The postprandial increase in GFR was recognized with the increment of plasma amino acid concentration, renal plasma flow and decrement of renal vascular resistance[6,12,13]. It has been suggested that some amino acids for example glycine, alanine and arginine are important for augmented renal hemodynamic to a large protein meal[14]. Therefore, increased serum amino acid level, especially some important amino acids, is responsible for renal effect of protein challenge. However, the mechanism enhancing GFR is not clearly explained. It could mediate renal hyper-filtration by both direct and indirect mechanisms. An augmentation of plasma levels of some blood-borne factors induced by a rich protein meal such as glucagon, growth hormone and prostaglandins was indicated as a factor affecting to increased renal hemodynamics[15,16]. Several lines of evidence have suggested that glucagon is important for renal hyperfiltration following protein or amino acid challenges because the investigations in both humans and animals showed that its peak serum level was observed at the same time of increased renal blood flow and renal hyper-filtration[13,17,18]. Furthermore, renal effect of protein meal was suppressed by infusion of somatostatin, an inhibitory peptide of glucagon[19].

The previous studies have indicated that peak time of postprandial GFR varied from 30 minutes to 3 hours after the meal and there is no definitely normal value of renal reserve[8,9,12]. The variation depends on the method of study, amount and type of protein load, amount of daily protein intake and functional status of the subject's kidney or residual nephron. The healthy kidney indicates high renal reserve.

Egg white contains wonderful protein that mostly constituents albumin, a small amount of fat and no cholesterol[20,21]. In the present study, egg white protein stimulated renal response as high as chicken protein. This finding is different from that reported by Nakamura and colleagues in 1990. They loaded 0.7 g/Kg.BW of egg white protein to normal subjects whose mean age was 49 years and claimed that this kind of protein could not enhance GFR to a significant degree[10]. It was suggested that age is related to renal function. The GFR is reduced 10% for a decade after the age of 30 years without renal reserve increment[1]. Therefore, age may be a factor affecting to renal response to protein loading in that case. In addition, the process of protein cooking may cause the loss of some amino acids that could be significant to increased renal hemodynamics after the protein meal[11].

The renal effect of each protein depends mostly on amino acid constituent that modulates renal blood flow[11]. Egg white contains a high amount of important amino acids relating to increased renal hemodynamics. This is supported by the analyzing data of amino acid content from different protein sources performed by The Ministry of Public Health of Thailand, which shows that one gram of protein from egg white and chicken meat contains more or less the same amount of arginine, glycine and alanine[22]. As egg white protein is easily digested and absorbed in the GI tract, the peak GFR was observed within an hour and similar to that of chicken. It could be expected that there was no delay of protein assimilation. Therefore, plasma amino acid level was increased to the high level and renal hemodynamic was modulated.

Nakamura et al have additionally reported the effect of egg white protein on plasma glucagon, which was done in healthy subjects whose age ranged between 23 and 28 years. They found that 0.7 g/Kg. BW of egg white protein load significantly augmented plasma level of glucagon and peaked at one hour after a meal[10]. Unfortunately, the renal effect of that protein was not evaluated in this group of subjects. Together with the finding of the present study, it is possible to be assumed that glucagon could be a candidate of important mediators responsible for renal effect of egg white protein. However, changes in renal hemodynamics and plasma glucagon of egg white protein challenge are needed to be evaluated in the same group of subjects. Finally, the renal reserve of both protein loads was similar and presented in a considerable degree. This indicates the same quality of both protein sources in renal stimulation and high performance of the subject's kidney.

Conclusion

In healthy young adults, egg white protein, when used in the same amount of protein load, can stimulate a similar degree of renal response as chicken protein did. It should be a protein source of choice used for renal functional test, especially in the people who omit animal meat in their diet *e.g.* ovovegetarian. However, egg white is not the major source of habitual dietary protein. People may consume 6-12 gram of protein from one or two eggs/day, so it may share less effect on resting GFR. This would be a benefit for use in patients whose protein diet is restricted to reduce progression of renal disease.

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การตอบสนองของไตต่อการกระตุ้นด้วยโปรตีนจากไข่ขาวในคนปรกติ

อัญญานีย์ บุโรดม

***ภูมิหลัง**: ในปัจจุบันโรคไตมีผลกระทบต่อชีวิตคนไทยเพิ่มขึ้นเรื่อย ๆ เป็นที่ทราบกันดีว่าอาหารโปรตีนมีผลเพิ่มการทำงานของไต ดังนั้นการให้อาหารโปรตีนกับผู้ป่วยโรคไตจึงควรคำนึงถึงผลกระทบต่อการทำงานของไตส่วนที่ยังเหลืออยู่ ไข่ขาวมีคุณสมบัติเป็นโปรตีนสมบูรณ์ แต่การศึกษาคุณสมบัติของไข่ขาวในแง่การกระตุ้นการทำงานของไตเปรียบเทียบกับโปรตีนจากเนื้อสัตว์ยังไม่แพร่หลายมากนัก*

***วัตถุประสงค์**: การศึกษานี้ต้องการเปรียบเทียบผลของการรับประทานโปรตีนสูงแบบเฉียบพลันจากไข่ขาวและเนื้อไก่ต่อการทำงานของไต*

***วัสดุและวิจัย**: ทำการทดสอบในอาสาสมัครจำนวน 11 คน ผู้ร่วมวิจัยทุกคนเข้าร่วมการทดสอบ 2 ครั้ง โดยมีระยะห่างกัน 1 สัปดาห์ ทำการวัดอัตราการกรองของไตขณะพักจากอัตราการชำระครีอาตินิน 24 ชั่วโมง ก่อนการทดสอบด้วยโปรตีน จากนั้นผู้ร่วมวิจัยจะได้รับอาหารโปรตีนสูงขนาด 0.8 กรัม/น้ำหนักตัว 1 กิโลกรัม จำนวน 1 มื้อ ซึ่งเตรียมจากไข่ขาวนึ่งสุก หรือ เนื้ออกไก่ต้มโดยวิธีการสุ่ม จากนั้นวัดอัตราการกรองของไตเป็นระยะทุก 60 นาที ติดต่อกันเป็นเวลา 3 ชั่วโมง*

***ผลการศึกษา**: อัตราการกรองของไตขณะพักก่อนการทดสอบด้วยโปรตีนทั้งสองชนิดไม่แตกต่างกัน หลังได้รับอาหารโปรตีนสูงจากสองแหล่งแล้ว พบว่าอัตราการกรองของไตเพิ่มขึ้นอย่างมีนัยสำคัญ และเพิ่มสูงสุดที่เวลา 60 นาที โดยมีค่าไม่แตกต่างกัน พบว่าไข่ขาวกระตุ้นการทำงานของไตโดยมีค่ากำลังสำรองเป็น 64% ของขณะพัก ส่วนเนื้อไก่มีค่ากำลังสำรองเป็น 58% ของขณะพัก*

***สรุป**: ในคนปรกติโปรตีนจากไข่ขาวมีศักยภาพในการกระตุ้นไตได้สูงเท่ากับโปรตีนจากเนื้อไก่ เมื่อใช้ทดสอบในปริมาณเท่ากัน*