The Effect of High Protein Low Phosphorus Snacks on Nutritional Status among Thai Children and Adolescents Receiving Continuous Ambulatory Peritoneal Dialysis

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Objective: *To develop high protein low phosphorus snacks (HPLPS) and to investigate the effect of HPLPS on nutritional status among Thai children and adolescents with continuous ambulatory peritoneal dialysis (CAPD).*
Material and Method: *The present study was divided into two phases. The first phase, HPLPS were developed by adding high protein and low phosphorus ingredients into favorite snacks. Sensory evaluation and nutritional values of each snack were determined. For the second phase, a randomized, crossover study was conducted. Fourteen children with CAPD, aged 3 to 19 years were randomly assigned into group A (n = 7), received HPLPS for 12 weeks, washout for four weeks and received regular snacks (RS) for 12 weeks and group B (n = 7), received RS for 12 weeks, washout for four weeks and received HPLPS for 12 weeks. Each snack was provided to participants (two servings/day) as a dietary supplement. The data of nutritional assessments were collected at baseline (week 0) and at the end of supplementation period (week 12).*
Results: *Five food items of HPLPS were developed including potato chips, crispy prawns, butter cookies, tuiles cookies, and cupcakes. The overall acceptability score for the developed snacks range from good to super good with the mean score of 4.16$\pm$0.55 to 4.39$\pm$0.49. The protein content of HPLPS were 7.04 to 7.81 g and phosphorus content were 12.39 to 37.51 mg per serving. At baseline, all nutritional parameters were not significantly different between groups. At the end of the study, the tricep skinfold (TSF), mid upper arm circumference (MUAC), and mid arm muscle circumference (MAMC) in HPLPS group were significantly higher than RS group. For HPLPS group, the energy and protein intake were significantly increased from 25.12 kcal/kg/day at baseline to 30.19 kcal/kg/day at the end of the study and from 0.69 g/kg/day to 1.09 g/kg/day, respectively. In addition, the present study found that the protein intake of participants was significantly increased in HPLPS group, however, their level of serum phosphorus was not increased.*
Conclusion: *Use of HPLPS as a dietary supplement is an alternative choice for improving nutritional status among children with CAPD.*

Keywords: *High protein low phosphorus snacks, Nutritional status, Children, Continuous ambulatory peritoneal dialysis*

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Kidney diseases, generally occur in adult and elderly, but it can occur in all ages from birth[1]. According to the Thailand Renal Replacement Therapy Report, the prevalence of end stage renal disease (ESRD) with renal replacement therapy (RRT) in children and adolescents increased from 116 cases in 2011 to 152 cases in 2012 and 62.5% of them received continuous ambulatory peritoneal dialysis (CAPD)[2]. CAPD is an effective RRT for the ESRD children to prolong and improve quality of life. However, the main disadvantage of CAPD is malnutrition due to protein loss during dialysis, which affect the child's growth. According to the study of Alberto C et al[3], it was found that children with CAPD lose the free amino acid approximately 0.02 to 0.03 g/kg/day which consistent with the study of Brem AS et al[4], reporting 35.9% of hypoalbuminemia in children with CAPD. Therefore, the dietary strategies focus on increasing energy and protein intake of CAPD patients for improving malnutrition. Unfortunately, most of high in protein foods are also high in phosphorus content, which contributed to increase serum phosphorus of patients. Therefore, developed snacks that contain high protein with low phosphorus as dietary supplement may be an alternative choice for children with CAPD. The previous studies for investigation the effect of dietary

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supplement for children with CAPD on nutritional status are still limited. Most studies focused the effect of commercial formula on nutritional status among adults and elderly[5-9]. Therefore, the present study aimed to develop high protein low phosphorus snacks, and to investigate the effect of HPLPS on nutritional status among Thai children and adolescents with CAPD.

Material and Method

Study design and participants

The present study was divided into two phases. For the first phase, a survey of favorite snacks among children with ESRD at Phramongkutklao Hospital was conducted and the top five of favorite snacks were selected including potato chips, crispy prawn, butter cookies, tuiles cookies, and cupcakes for developing the high protein low phosphorus snacks (HPLPS). In the developing step, the definition of HPLPS was defined as the snacks must contain 7 g or more of protein and 50 mg or less of phosphorus per serving. HPLPS were developed by adding egg white powder into regular recipes and replacing high phosphorus ingredients to low phosphorus content. The egg white powder used in the present study was Albumin Plus®. Each one ounce (28 g) serving of Albumin Plus® contained 107 kcal, 24 g protein, 2 g carbohydrate, 25.23 mg phosphorus, 316.38 mg potassium, and 358 mg sodium. The nutritional values of HPLPS and RS were calculated by using the INMUCAL-N V. 2.0 program[10], Institute of Nutrition, Mahidol University. A five-point facial hedonic scale[11] was used to evaluate sensory evaluation of all snacks including general appearance, color, tastes, odor, and overall acceptability.

For the second phase, a 28-week randomized crossover study was conducted in 14 children on CAPD aged between 3 to 19 years attending the pediatric renal clinic, Department of Pediatrics, Phramongkutklao Hospital, Bangkok, Thailand. The number of participants was at least 14 patients, which were calculated based on the study of Ian JR et al[12]. Fourteen children with CAPD, aged 3 to 19 years were randomly assigned into group A (n = 7), received HPLPS for 12 weeks, washout for four weeks and received RS for 12 weeks and group B (n = 7), received RS for 12 weeks, washout for four weeks and received HPLPS for 12 weeks. Each snack was provided to participants (2 servings/day) as a dietary supplement.

Anthropometric assessment

Anthropometric assessment was performed and included body weight, height, triceps skinfold (TSF), mid upper arm circumference (MUAC), mid arm muscle circumference (MAMC), and body composition at baseline (week 0), week 4, week 8, and week 12 of each supplementation period.

Body weight was measured by using electric automatically weighting scales (Model 769, SECA, USA). The participants were asked to measure their weight after filled peritoneal solution and taken to the nearest 0.1 kg. However, the volume of filled peritoneal solution was noted for calculating the dry weight of each participant. Height was measured in a standing position by using a stable stadiometer (Model 217, SECA, USA). Height was recorded to the nearest 0.1 cm. In additional, body weight and height of all participants were plotted in the growth curve of Bureau of Nutrition, Department of Health, Ministry of Public Health, Thailand.

Triceps skinfold (TSF) was measured by using a caliper (Baseline®, Fabrication Enterprises Inc., USA). Body composition was measured by using bioelectrical impedance analysis (Model 720, Inbody Co., Ltd., Korea).

Biochemical assessment

Venous blood was obtained from each participant after 8 to 12 hours fasting at baseline (week 0), week 4, week 8, and week 12 of each supplementation period. Serum albumin (Alb), serum phosphorus (PO_4), serum 25 (OH) D, and interleukin-6 (IL-6) were determined.

Dietary assessment

The participants were asked to keep an estimated record of all foods and beverages consumed over a 3-day dietary record at baseline (week 0), week 4, week 8, and week 12 of each supplementation period. For under 6-year-old children, the parents would record their dietary intake. Before starting the study, all participants and their parents were instructed and tested how to collect a 3-day dietary record. Data were analyzed by the INMUCAL-N V.2 program (Institute of Nutrition, Mahidol University, Thailand).

The study protocol was approved by the Committee on Human Rights Related to Human Experimentation, Mahidol University (No. MU-IRB 2013/043.1704) and the Institutional Review Board, Royal Thai Army Medical Department (No. Q007h/56).

Statistical analyses

The SPSS for windows v.16.0 was used for

analyzing the data. Descriptive data were expressed as mean ± standard deviation (SD) and percentage. To test for baseline condition differences, independence sample t-test was used for continuous variables. Data at difference time points within group were analyzed by paired t-test. The independence sample t-test was used to compare the difference between groups. A *p*-value less than 0.05 was considered statistically significant.

Results

Development of high protein and low phosphorus snacks

After the survey for favorite snacks among children with ESRD, the top five of favorite snacks including potato chips, crispy prawns, cupcakes, butter cookies, and tuiles cookies were developed for HPLPS by adding high protein and low phosphorus ingredients whereas the same food items of RS were prepared as a control. The nutritional values and the overall acceptability score of HPLPS and RS were shown in Table 1. The range of nutritional values per a serving of RS were as follows: energy 100.86 to 127.70 kcal, protein 1.25 to 3.41 g, and phosphorus 25.00 to 66.74 mg. For HPLPS, the range of nutritional values per a serving were as follows: energy 126.76 to 132.55 kcal, protein 7.04 to 7.81 g, and phosphorus 12.39 to 37.51 mg. The mean ± SD of protein contents of HPLPS were significance higher than RS, whereas the means ± SD of phosphorus content of HPLPS were significance lower than RS ($p<0.05$). The overall acceptability scores of both HPLPS and RS were found to be good (4.16±0.55) to super good (4.39±0.49) and did not show significant difference between HPLPS and RS.

Nutritional status of subjects before and after receiving dietary supplement

At baseline, all nutritional parameters were not significantly different between group A and B. Anthropometric and biochemical parameters at baseline and at the end of each HPLPS and RS supplementation period for 14 participating patients were presented in Table 2. Both HPLPS and RS showed significantly increased dry weight when compared between baseline and the end of each supplementation period ($p<0.05$) but did not find any significant difference between

Table 1. The nutritional values and the overall acceptability score of HPLPS and RS

Type of snacks	The nutritional values per serving			The overall acceptability score (n = 38)
	Energy (kcal)	Protein (g)	Phosphorus (mg)	
Potato chips				
HPLPS	127.70	7.04	30.12	4.18±0.37
RS	100.86	1.25	25.00	4.26±0.45
Crispy prawn				
HPLPS	132.55	7.22	26.47	4.16±0.55
RS	127.70	2.12	31.11	4.39±0.49
Butter cookies				
HPLPS	127.99	7.81	12.88	4.16±0.55
RS	124.85	3.41	54.64	4.24±0.54
Tuiles cookies				
HPLPS	129.36	7.15	12.39	4.18±0.56
RS	117.46	2.56	29.19	4.31±0.47
Cupcake				
HPLPS	126.76	7.10	37.51	4.21±0.58
RS	117.37	3.21	66.74	4.39±0.49
Mean ± SD				
HPLPS	128.87±2.33	7.26±0.31	23.87±11.00	4.18±0.02
RS	117.65±10.43	2.51±0.87	41.34±18.31	4.32±0.07
p-value HPLPS vs. RS	0.62	<0.001*	<0.001*	0.89

HPLPS = High Protein Low Phosphorus Snacks; RS = Regular Snacks

* *p*-value considered significant at <0.05

Five-point facial hedonic scale (1 = super bad, 2 = bad, 3 = maybe good or maybe bad, 4 = good, 5 = super good)

groups. At the end of the study, the mean tricep skinfold (TSF), mid upper arm circumference (MUAC), and mid arm muscle circumference (MAMC) in HPLPS (15.32±7.31 mm, 18.55±5.05 cm, and 13.73±3.29 cm, respectively) were significantly higher than RS (14.99±7.39 mm, 18.24±5.14 cm, and 13.53±3.33 cm, respectively) (p<0.05).

The total energy and protein intake of participants at baseline, HPLPS and RS supplementation period were calculated from the 3-day dietary record as shown in Table 3. The means energy intake with supplement of both HPLPS and RS were significantly increased from 1,097.23±229.43 kcal/day at baseline to 1,325.43±230.47 kcal/day in HPLPS group, and 1,296.50±23.16 kcal/day in RS group at the end of the study (p<0.05), however, no significant difference of energy intake was found between the two groups. For HPLPS group, the mean protein intake with supplement was also significantly increased from 29.16±15.66 g/day at baseline to 39.93±16.81 g/day at the end of the study (p<0.05). In addition, the mean protein intake at the end of the study in HPLPS group

Table 2. Anthropometric and biochemical measurements (mean ± SD) of participants (n = 14) at baseline, HPLPS and RS supplementation periods

Parameter	Baseline	The end of study (week 12)		*p*-value (HPLPS vs. RS)
		HPLPS	RS	
Body weight (kg)	30.07±17.27	31.23±16.36	31.49±16.51	0.838
TSF (mm)	14.20±7.36	15.32±7.31	15.18±7.37	0.001*
MUAC (cm)	17.51±5.01	18.55±5.05	18.37±5.17	0.001*
MAMC	13.05±3.23	13.73±3.29	13.60±3.36	0.001*
SMM	13.86±5.42	13.90±5.61	14.00±5.41	0.715
Serum albumin	3.56±0.66	3.60±0.52	3.51±0.53	0.899
Serum phosphorus	5.44±1.58	5.62±1.17	5.39±1.26	0.929
25 (OH) D	24.15±7.08	25.44±11.86	21.93±9.11	0.312

TSF = Tricep skinfold; MUAC = Mid upper arm circumference; MAMC = Mid arm muscle circumference; SMM = Skeleton muscle mass; 25 (OH) D = 25-hydroxy vitamin D
* *p*-value considered significant at <0.05

Table 3. Energy and protein intake (mean ± SD) of participants (n = 14) at baseline, HPLPS and RS supplementation periods

Parameter	Baseline	The end of study (week 12)		*p*-value (HPLPS vs. RS)
		HPLPS	RS	
Energy intake with supplement (kcal/day)	1,097.23±229.43	1,325.43±230.47	1,296.50±23.16	0.417
Energy intake with supplement (kcal/kg/day)	25.12±3.02	30.19±4.16	28.24±2.45	0.405
Energy intake without supplement (kcal/day)	1,097.23±229.43	1,119.85±222.28	1,086.37±228.88	0.866
Protein intake (g/day)	29.16±15.66	39.93±16.81	30.33±15.05	0.0001*
Protein intake (g/kg/day)	0.69±0.05	1.09±0.11	0.82±0.09	0.001*
Protein intake without supplement (g/day)	29.16±15.66	28.46±15.22	27.98±16.60	0.642
Phosphorus intake (mg/day)	459.91±130.79	433.90±126.86	474.53±116.19	0.054

* *p*-value considered significant at <0.05

(39.93±16.81 g/day) was significantly higher than RS group (30.33±15.05 g/day) (p<0.0001). For HPLPS, the energy and protein intake were significantly increased from 25.12±3.02 kcal/kg/day at baseline to 30.19±4.16 kcal/kg/day (p<0.05) at the end of the study and from 0.69±0.05 g/kg/day to 1.09±0.11 g/kg/day (p<0.001), respectively. However, both HPLPS and RS groups received inadequate energy intake compared to their energy requirements.

Discussion

In the present study, high protein low phosphorus snacks (HPLPS) were developed and the main finding of a 28-week randomized crossover study to investigate the effect of HPLP on nutritional status among Thai children and adolescents with CAPD showed that when the participants supplemented two servings of HPLPS per day for 12 weeks, the tricep skinfold (TSF), mid upper arm circumference (MUAC), and mid arm muscle circumference (MAMC) in HPLPS group were significantly increased by 7.13%, 5.34%, and 4.88%, respectively. Moreover, the energy and protein intake in HPLPS group were also significantly increased from 25.12 kcal/kg/day to 30.19 kcal/kg/day and 0.69 g/kg/day to 1.09 g/kg/day, respectively. In addition, the present study found that although the protein intake of participants was increased in HPLPS group, their level of serum phosphorus was not increased.

The present study is the first study to develop HPLPS for children with CAPD to improve their nutritional status. In children with CAPD, malnutrition is a common nutritional problem and contributes to morbidity and mortality. The factors for malnutrition in these patients are multi-factorial including decreased food intake related to poor appetite, complications of disease, depression, and the consequence of treatment such as protein losses in dialysis[13,14]. According to KDOQI guidelines in nutrition for children[15], CAPD patients may lose protein during dialysis around 5.8 to 17.4 g and they should increase protein intake 0.15 to 0.3 g/kg/day depended on the patient's age and at least 50% of protein intake for these patients should be of high biologic value and energy intake should be 35 kcal/kg/day. Therefore, the dietary strategies of patient with CAPD almost focus on increasing protein intake for preventing malnutrition especially hypoalbuminemia and muscle mass loss. However, increasing high protein intake may also lead to high phosphorus intake because most foods that contain high protein usually have high phosphorus such as milk, egg yolk, soy, and soy products. In some CAPD patients, hyperphosphatemia is a common complication of end-stage renal disease (ESRD) patients and stimulates the development of secondary hyperparathyroidism and renal osteodystrophy. According to the study of Kalantar ZK et al[16] reported protein-rich foods have high phosphorus content resulting in a positive correlation between dietary protein intake and phosphorus intake and suggested that egg white based diets are high in protein and low phosphorus with the lowest phosphorus to protein ratio 1.4 mg phosphorus/g protein among all natural sources of protein rich diets. For the present study, HPLPS are high in protein content (greater than 20% of total energy per serving) with a phosphorus-to-protein ratio of 3.28.

The main finding of the present study is similar to the results found in the study of Espinoza et al[6] investigated the effect of the egg albumin-based protein supplement to patients on CAPD and found a significant improvement on TSF (9.58%) and MUAC (4.51%) (p<0.05). Moreover, energy intake in CAPD patients received egg white powder was significantly increased from 21.64 kcal/kg/day at baseline to 30.44 kcal/kg/day at the end of study (p<0.05).

In the present study, there were no significant differences in biochemical parameters at the end of study in both groups. Although HPLPS provided approximately 14 g protein and 200 to 250 kcal per day which increased protein and energy intake of the participants, but it was found that participants received the average energy intake only 86.62% of their energy requirement, whereas the average protein intake was 99.09% of their protein requirement. Therefore, no change of serum albumin may be due to inadequate energy intake.

In conclusion, HPLPS showed a significant improvement in nutritional status of children with CAPD without increasing serum phosphorus. Use of high protein low phosphorus snacks as the dietary supplement was the alternative choice for improving nutritional status among children and adolescents with CAPD.

What is already known on this topic?

Dietary supplements, especially high protein foods are correlated to reduce and prevent malnutrition in CAPD patients. However, increasing high protein intake in some CAPD patients may lead to hyperphosphatemia. Thus, protein supplementation should consider the phosphorus to protein ratio.

What this study adds?

The present study is the first study in Thailand that developed high protein low phosphorus snacks (HPLPS), and investigated the effects of HPLPS on nutritional status among children and adolescents with CAPD. The supplementation in form of HPLPS is suitable for children with CAPD because patient's nutritional status is improved without increasing serum phosphorus. Moreover, children with CAPD can still enjoy their favorite snacks.

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Potential conflicts of interest

None.

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ผลของอาหารว่างโปรตีนสูงฟอสฟอรัสต่ำต่อภาวะโภชนาการในเด็กและวัยรุ่นไทยที่ได้รับการบำบัดทดแทนไตด้วยการล้างไตทางช่องท้อง

กรกต วีรเธียร, ชนิดา ปโชติการ, อดิสรณ์ ลำเพาพงศ์, สุนาฏ เตชางาม

วัตถุประสงค์: เพื่อพัฒนาอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำและศึกษาผลของอาหารว่างที่พัฒนาขึ้นต่อภาวะโภชนาการในเด็กและวัยรุ่นไทยที่ได้รับการล้างไตทางช่องท้อง

วัสดุและวิธีการ: การศึกษานี้แบ่งออกเป็น 2 ระยะ ระยะที่ 1 คือ การพัฒนาอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำโดยการเติมวัตถุดิบที่มีโปรตีนสูงและฟอสฟอรัสต่ำลงในสูตรอาหารว่างยอดนิยมของเด็กและวัยรุ่น ซึ่งอาหารว่างที่พัฒนาขึ้นจะได้รับการประเมินคุณภาพทางประสาทสัมผัสและได้รับการคำนวณคุณค่าทางโภชนาการ ส่วนระยะที่ 2 คือ การศึกษาแบบไขว้กลุ่มในอาสาสมัครเด็กและวัยรุ่นที่ได้รับการล้างไตทางช่องท้อง จำนวน 14 คน อายุระหว่าง 3 ถึง 19 ปี โดยอาสาสมัครทั้งหมดจะถูกสุ่มเพื่อแบ่งออกเป็น 2 กลุ่ม ดังนี้ กลุ่ม เอ (จำนวน 7 คน) ได้รับการเสริมอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำ ระยะเวลา 12 สัปดาห์ ตามด้วยช่วงล้างออก ระยะเวลา 4 สัปดาห์ และได้รับการเสริมอาหารว่างสูตรปกติ เป็นระยะเวลา 12 สัปดาห์ ในขณะที่กลุ่ม บี (จำนวน 7 คน) ได้รับการเสริมอาหารว่างสูตรปกติ ระยะเวลา 12 สัปดาห์ ตามด้วยช่วงล้างออก 4 สัปดาห์ และได้รับการเสริมอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำ ระยะเวลา 12 สัปดาห์ โดยอาสาสมัครทุกคนจะได้รับอาหารว่างแต่ละชนิด จำนวน 2 หน่วยบริโภคต่อวัน เพื่อใช้รับประทานเสริมเป็นอาหารว่างระหว่างมื้อ ข้อมูลจากการประเมินภาวะโภชนาการของอาสาสมัครจะถูกเก็บที่ก่อนเริ่มการเสริมอาหารว่าง (สัปดาห์ที่ 0) และเมื่อสิ้นสุดช่วงการเสริมอาหารว่าง (สัปดาห์ที่ 12)

ผลการศึกษา: อาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำจำนวน 5 ชนิดถูกพัฒนาขึ้น ประกอบด้วย มันฝรั่งทอด, ข้าวเกรียบกุ้ง, คุกกี้เนย, คุกกี้ลิ้นแมว และคัพเค้ก จากการประเมินคุณภาพทางประสาทสัมผัส พบว่าคะแนนการยอมรับโดยรวมต่ออาหารว่างที่พัฒนาขึ้นอยู่ในระดับดีถึงดีมาก โดยมีค่าเฉลี่ยคะแนนอยู่ที่ 4.16±0.55 ถึง 4.39±0.49 นอกจากนี้จากการคำนวณคุณค่าทางโภชนาการพบว่าอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำมีปริมาณโปรตีน 7.04 ถึง 7.81 กรัม และฟอสฟอรัส 12.39 ถึง 37.51 มิลลิกรัมต่อหนึ่งหน่วยบริโภค ผลการศึกษาในระยะที่ 2 พบว่าค่าตัวชี้วัดด้านโภชนาการระหว่างกลุ่มก่อนการศึกษาไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ หลังจากการเสริมอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำ ระยะเวลา 12 สัปดาห์ พบว่าไขมันใต้ผิวหนังบริเวณต้นแขนด้านหลัง, เส้นรอบวงบริเวณกึ่งกลางต้นแขน และเส้นรอบวงของมวลกล้ามเนื้อบริเวณกึ่งกลางต้นแขนเพิ่มขึ้นอย่างมีนัยสำคัญเมื่อเปรียบเทียบกับหลังจากการเสริมอาหารว่างสูตรปกติ จากการประเมินการบริโภคของอาสาสมัคร พบว่าเมื่อสิ้นสุดช่วงการเสริมอาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำ ค่าพลังงานเพิ่มขึ้นจาก 25.12 กิโลแคลอรี/กิโลกรัม/วัน เป็น 30.19 กิโลแคลอรี/กิโลกรัม/วัน และปริมาณโปรตีนที่ได้รับเพิ่มขึ้นจาก 0.69 กรัม/กิโลกรัม/วัน เป็น 1.09 กรัม/กิโลกรัม/วัน นอกจากนี้ยังพบว่า ถึงแม้อาสาสมัครจะได้รับโปรตีนในปริมาณที่เพิ่มขึ้น แต่ไม่ส่งผลต่อการเพิ่มขึ้นของระดับฟอสฟอรัสในเลือด

สรุป: การใช้อาหารว่างโปรตีนสูง ฟอสฟอรัสต่ำ ในรูปแบบอาหารว่างเสริมระหว่างมื้อเป็นอีกทางเลือกหนึ่งในการทำให้ภาวะโภชนาการของผู้ป่วยเด็กและวัยรุ่นไทยที่ได้รับการล้างไตทางช่องท้องดีขึ้น