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Role of Oral Activated Charcoal in decreasing Blood Urea, Creatinine and Phosphorous in Chronic Kidney Disease

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ABSTRACT
Background: In recent years, chronic kidney disease (CKD) has become a worldwide public health issue.
Objective: The main aim of this study was to explore the ability of oral activated charcoal to adsorb uremic toxins limiting the progression of CKD and delaying the need for hemodialysis in patients with CKD stages III and IV and to compare its effect with the effect of dry seeds (lentils) as absorbents of uremic toxins.
Patients and methods: A randomized controlled clinical trial was conducted on 90 patients with CKD stages III and IV. The patients were divided into 3 groups as following; Group (A): 30 patients received oral activated charcoal in a dose of 3 gm/day, Group (B): 30 cases received dry seeds (raw lentils) in a dose of 30 gm/day, and Group (C): 30 cases as control group on usual conservative treatment. **Results:** *Group A* showed that there was significant decrease in serum urea, creatinine, phosphorus and potassium throughout follow up period (12 weeks) compared to *Group B* and *Group C* (control group). *Group B* showed there was significant decrease in serum urea and creatinine throughout follow up period (12 weeks), while there was no significant difference in serum phosphorus and potassium, compared to *Group A* and *Group C*. **Conclusion:** The use of oral activated charcoal and uncooked lentils could be of value in lowering uremic toxins in patients with CKD stages III and IV. Future studies are warranted to confirm such results.
Keywords: Chronic kidney disease, Activated charcoal, Lentils, Creatinine, Urea.

INTRODUCTION
Chronic kidney disease (CKD) has grown in importance as a global public health concern in recent years. The consequences of chronic kidney disease, such as atherosclerotic syndrome, anaemia, malnutrition, inflammation, cardiovascular and cerebrovascular illnesses, are what have the most impact on a patient's prognosis [1].

The advancement of renal failure and cardiovascular disease is attributed to the buildup of uremic toxins such indoxyl sulphate and p-cresyl sulfatases. It seems sense to stop this trend using therapeutic strategies that lower uremic toxin levels [2]. Numerous studies have been conducted in an effort to find alternatives to chronic hemodialysis, particularly for elderly patients who face financial or psychological challenges. One such study looked at the use of gum Arabic in the treatment and amelioration of kidney dysfunction and end-stage renal disease. Increased sweat production from sweat glands can enhance kidney function by excreting a significant portion of the urea that the kidneys normally eliminate [3, 4].

Through the adsorption of indole formed in the gastrointestinal tract from dietary tryptophan, the oral charcoal adsorbent lowers serum levels of indoxyl sulphate while increasing serum creatinine and urea levels [5]. In the current work we aimed to explore the ability of oral activated charcoal to adsorb uremic toxins limiting the progression of chronic kidney disease and delaying need for hemodialysis in patients with CKD stages III and IV, and to compare its effect with the effect of dry seeds as absorbents of uremic toxins.

PATIENTS AND METHODS
Type of the study and design: Randomized controlled clinical trial was conducted at Internal Medicine Outpatient Clinic of Assiut University Hospital.

Selection criteria:
Any patients with CKD stages III/IV with age more than 18 years old was enrolled in the study. Patients on regular hemodialysis and/or age less than 18 years old were excluded.

Participants
A total of 90 patients with CKD stages III and IV on same usual treatment will divide into 3 groups:
- 1st group of 30 patients received oral activated charcoal in a dose of 3 gm/day.
- 2nd group of 30 cases received dry seeds in a dose of 30 gm/ day.
- 3rd group of 30 cases as control group.

Methodology
All patients were subjected to full history taking, clinical examination. Laboratory investigation for all 90 cases with follow up twice monthly for 3 months: urea, serum creatinine, phosphors and potassium and estimated glomerular filtration rate (eGFR) of all patients will be calculated.

Research outcome measures:
Primary (main): Mean of blood urea, creatinine and phosphorous in patients with CKD before and after oral activated charcoal.
Secondary (subsidiary): Ccompare dry seeds with activated charcoal as alternative natural cheap methods that may help in limiting progression of CKD by measuring blood urea, creatinine, and phosphorous in all 3 groups of the study.

Ethical consent
An approval of the study was obtained from Assiut University Academic and Ethical Committee. Every patient signed an informed written consent for

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acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using SPSS (Statistical Package for Social Sciences) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA). While categorical data were reported as numbers and percentages and compared using the Chi square test. Continuous data were expressed as mean and standard deviation (SD), and compared using the ANOVA test followed by post-hoc analysis. P value <0.05 was considered significant.

RESULTS

This prospective randomized controlled study was conducted on 110 patients with CKD stages III and IV on same usual treatment. A total of 20 patients were excluded during the follow-up period; hence, 90 patients were included in the final analysis.

Characteristics among the studied groups (Table 1):

The majority of the studied patients was males and had stages III. Different groups had insignificant difference as regard baseline data (*p* >0.05).

Table (1): Characteristics among the studied groups

Variable		Group (A) (n.= 30)		Group (B) (n.= 30)		Group (C) (n.= 30)		P-value
		No.	%	No.	%	No.	%	
Gender	Male	14	46.7%	18	60%	13	43.3%	0.393
	Female	16	53.3%	12	40%	17	56.7%	
Age (years)	Mean ± SD	25.43 ± 2.92		25.13 ± 2.91		26.57 ± 3.15		0.622
	Range	21 - 30		20 - 30		21 - 31		
Stage III		21	70%	17	56.7%	18	60%	0.541
IV		9	30%	13	43.3%	12	40%	

Data expressed as frequency (percentage), mean (SD). P *value was significant if* ≤ 0.05

Comparison between the studied groups regarding serum urea at different follow-up periods (Table 2):

There was significant decrease in serum urea throughout follow up in *Group A* and *Group C* (p<0.001). Also, there was significant increase in serum urea throughout follow up in *Group C* (p<0.001).

After 6, 8, 10 and 12 weeks, *Group A* and *Group C* showed significant decrease in serum urea compared to *Group B* and *Group C* while there was no statistically significant difference between the three groups regarding serum urea at baseline, after 2 weeks and after 4 weeks (p>0.05).

Table (2): Comparison between the studied groups regarding serum urea at different follow-up periods.
Data expressed as mean (SD). P value was significant if ≤ 0.05.

Serum urea (mg/dL)	Group (A) (n.= 30)		Group (B) (n.= 30)		Group (C) (n.= 30)		Test value	P-value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	109.03	13.11	105.87	13.54	103.17	12.91	2.917	0.233
After 2 weeks	103.93	14.48	102.87	12.16	101.33	13.06	2.194	0.749
After 4 weeks	100.27	15.67	104.20	14.16	103.87	13.30	3.889	0.527
After 6 weeks	88.03	13.11	98.43	15.38	106.03	13.93	17.22	**<0.001** P_{A-B}**=0.026** P_{A-C}**<0.001** P_{B-C}**=0.047**
After 8 weeks	86.77	12.44	97.80	15.35	109.90	12.39	28.65	**<0.001** P_{A-B}**=0.017** P_{A-C}**<0.001** P_{B-C}**=0.003**
After 10 weeks	76.77	12.44	89.50	16.81	111.90	12.39	49.11	**<0.001** P_{A-B}**=0.012** P_{A-C}**<0.001** P_{B-C}**<0.001**
After 12 weeks	58.77	12.44	79.10	9.11	114.90	12.39	61.84	**<0.001** P_{A-B}**=0.006** P_{A-C}**<0.001** P_{B-C}**<0.001**

Comparison between the studied groups regarding serum creatinine at different follow-up periods (Table 3):

There was significant decrease in serum creatinine throughout follow up in *Group A* and *Group B* ($p<0.001$) while there was no statistically significant difference in serum creatinine throughout follow up in group C ($p>0.05$).

After 6 weeks, *Group A* showed significant decrease in serum creatinine compared to *Group B* while After 8, 10 and 12 weeks, *Group A* and *Group B* showed significant decrease in serum creatinine compared to group C. There was no statistically significant difference between the three groups regarding serum creatinine at baseline, after 2 weeks and after 4 weeks ($p>0.05$).

Table (3): Comparison between the studied groups regarding serum creatinine at different follow-up periods

Serum creatinine (mg/dL)	Group (A) (n.= 30)		Group (B) (n.= 30)		Group (C) (n.= 30)		Test value	P-value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	1.99	0.30	1.91	0.28	1.93	0.26	1.295	0.523
After 2 weeks	1.94	0.29	1.96	0.25	1.92	0.24	0.468	0.791
After 4 weeks	1.86	0.31	1.84	0.27	1.98	0.24	4.037	0.133
After 6 weeks	1.77	0.32	1.86	0.19	1.95	0.25	6.177	**0.024** P_{A-B}=0.910 P_{A-C}=**0.040** P_{B-C}=0.446
After 8 weeks	1.72	0.30	1.96	0.23	2.00	0.24	16.36	**<0.001** P_{A-B}=**0.006** P_{A-C}=**0.001** P_{B-C}=1.00
After 10 weeks	1.62	0.30	1.82	0.29	2.04	0.23	25.05	**<0.001** P_{A-B}=0.062 P_{A-C}**<0.001** P_{B-C}=**0.022**
After 12 weeks	1.42	0.30	1.63	0.33	2.01	0.26	37.08	**<0.001** P_{A-B}=0.058 P_{A-C}**<0.001** P_{B-C}=**0.001**

Data expressed as mean (SD). *P* value was significant if ≤ 0.05.

Comparison between the studied groups regarding serum Phosphorous at different follow-up periods (Figure 1):

There was significant decrease in serum phosphorous throughout follow up in *Group A* ($p<0.001$) and *Group C* ($p<0.001$) while there was no significant difference in serum phosphorous throughout follow up in *Group B* ($p>0.05$).

Serum phosphorous was significantly lower in *Group A* compared to *Group B* and *Group C* after 4, 6, 8, 10 and 12 weeks. Meanwhile, *Group B* showed significant elevation in serum phosphorous compared to *Group C* after 10 and 12 weeks. *Group A* showed significant decrease in serum phosphorous compared to *Group B* after 2 weeks. There was no statistically significant difference between the three groups regarding serum phosphorus at baseline ($p>0.05$).

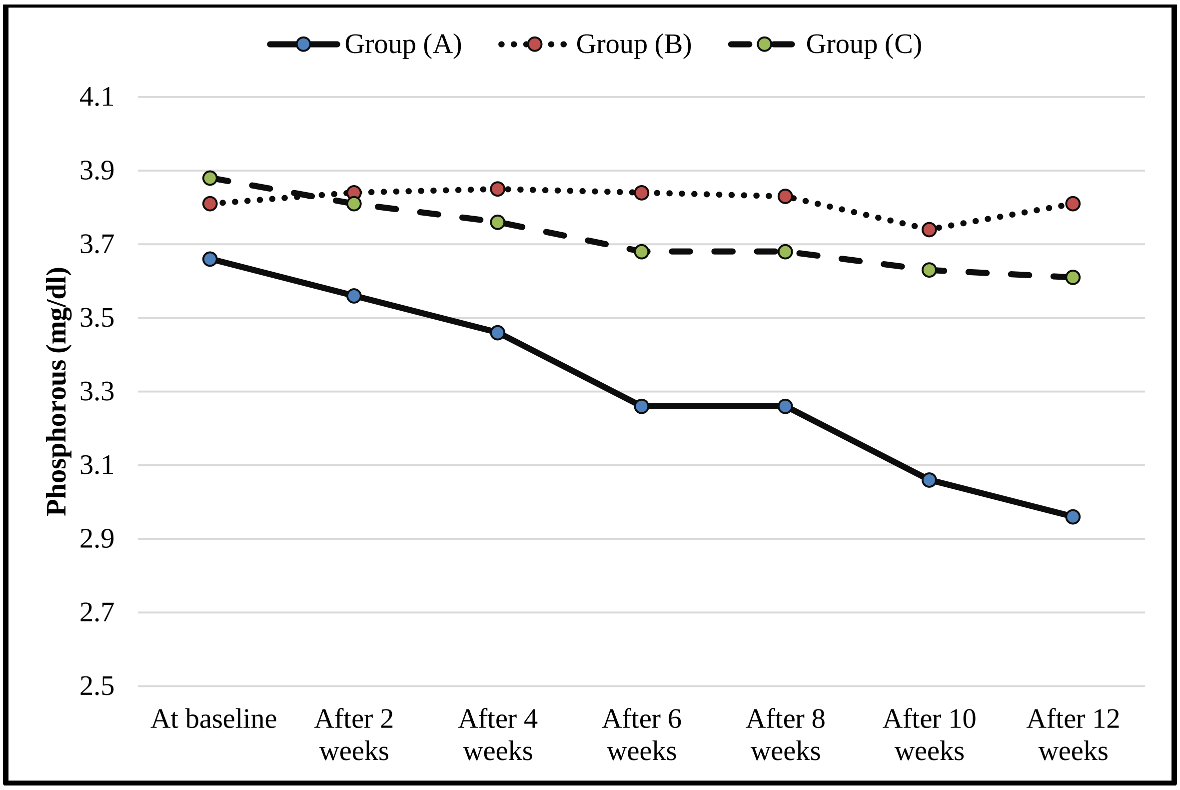

Figure (1): Comparison between the studied groups regarding serum phosphorous at different follow-up periods.

Comparison between the studied groups regarding serum potassium at different follow-up periods (*Figure 2*):

There was significant decrease in serum potassium throughout follow up in *Group A* ($p<0.001$) while there was no statistically significant difference in serum potassium throughout follow up in *Groups B and C* ($p>0.05$).

Serum potassium was significantly lower in *Group A* compared to *Group B* after 6, 8, 10 & 12 weeks. Also, *Group A* showed significant decrease in serum potassium compared to *Group C* after 10 and 12 weeks. There was no statistically significant difference between the three groups regarding serum potassium at baseline, after 2 weeks and after 4 weeks ($p>0.05$).

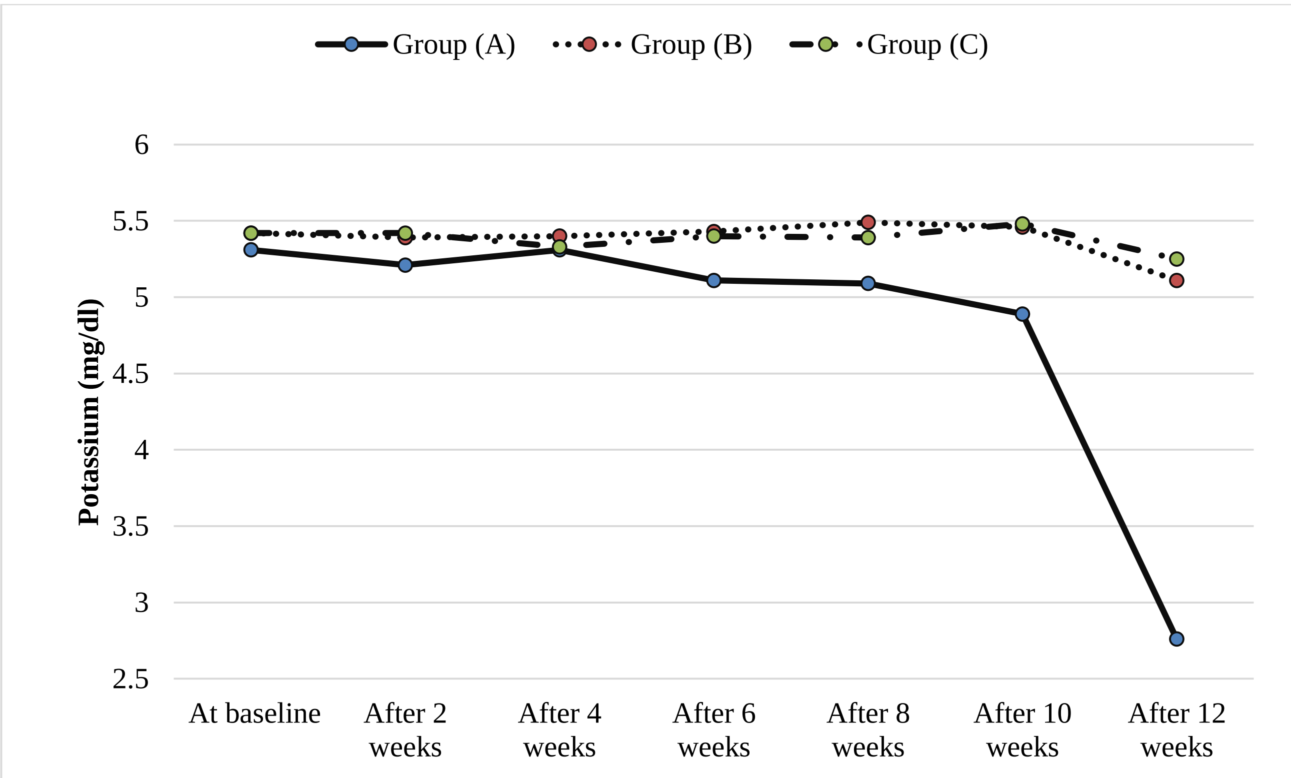

Figure (2): Comparison between the studied groups regarding serum potassium at different follow-up periods.

DISCUSSION

The main aim of this study was to explore the ability of oral activated charcoal to adsorb uremic toxins limiting the progression of chronic kidney disease and delaying the need for hemodialysis in patients with CKD stages III and IV and to compare its effect with the effect of dry seeds (lentils) as absorbents of uremic toxins.

The process of activating charcoal involves subjecting it to an oxidizing gas mixture at high temperatures, which results in the formation of pores and an increase in surface area. The surface area of 50 grams of activated charcoal is equivalent to 10 football fields [6].

The process known as "intestinal dialysis" is caused by the binding of urea and other waste products to charcoal and their excretion in the feces, which creates a concentration gradient for continuous diffusion. Carbamazepine, digoxin, furosemide, mycophenolate, theophylline, and olanzapine have all been documented as having minor side effects besides vomiting, acute appendicitis, allergic response, and luminal drug adsorption [6].

The current study showed that in the comparison between studied groups regarding serum urea, creatinine, serum phosphorous and serum potassium at different follow-up periods. There was significant decrease in serum urea, creatinine, phosphorus and potassium throughout follow up in group A ($p<0.001$).

Study by **Gao *et al.*** [7], which revealed that the initial part of the follow-up is 12 months, corroborated our findings. The phosphorus levels of the OAC group started to fall below those of the placebo group starting in the third month and stayed there through the completion of the experiment.

Additionally, **El-Kafoury *et al.*** [8] investigated the potential benefit of activated charcoal in slowing the progression of CKD in albino rats by limiting the uptake of intestinal bacterial toxins into the systemic circulation. They found that the charcoal-treated groups displayed a significant decrease in serum urea and creatinine when compared to the nephrectomy group.

Lentils are small, disc-shaped legumes are a low-fat, cholesterol-free source of high-quality protein, complex carbohydrates and several vitamins and minerals. Lentils are considered a diabetic-friendly, heart-healthy food because their high fiber content promotes normal blood sugar and cholesterol levels, lentils as a type of dry seeds used in this study in its raw form - as novel research - to test its ability to absorb uremic toxins, added to its value in management of different risk factors in CKD patients [9,10].

In a 2010 study by **Abdel-Rahim and El-Beltagi** [11]**,** it was found that using lentils as a therapeutic diet against lipidemia and cholesterolemia significantly improved blood results as well as liver and kidney functioning.

The current study showed that in the comparison between studied groups regarding serum urea, creatinine, phosphorus and potassium at different follow-up periods. There was significant decrease in serum urea and creatinine throughout follow up in *Group B* ($p<0.001$), while there was no significant difference in serum phosphorus and potassium throughout follow up in *Group B* ($p >0.05$).

A cup of 30 grams of raw (uncooked) lentils has 203 mg of potassium and 84.3 mg of phosphorus, making them a food high in potassium, phosphorus, purines, and oxalate that may limit their use or need the use of phosphate binders and potassium-lowering medications [12].

Our study regarding using raw lentils as an absorbent for uremic toxins considered a novel research with no old comparable studies or references. The study limitations included single center nature, small sample size and no long term follow up of those patients.

In conclusion, activated charcoal and dry seeds (Lentils) could be useful therapeutic alternatives in order to manage CKD patients, improve their quality of life and may delay their need for hemodialysis because of its effect in decreasing serum urea and creatinine.

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