

Enteric Dialysis- Stabilization of the Gut Microbiome using Probiotics and Prebiotics (Gut-Kidney Connection)

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INTRODUCTION

Recent scientific evidence from the human microbiome project has revealed that the trillions of gut microbiome exceed the human genome by a factor of 10. There are just 23,000 human genes as against the 3.3 million genes coded by the gut microbiome. This complex microbiome has a major role to play in health and diseases. Scientific evidence has shown that the imbalance in the ratio of this complex microbial community leads to dysbiosis a cause for various diseases. The use of beneficial microbes-probiotics and prebiotics is generally well recognized towards digestive, gut and immune health. However, novel and niche application of probiotics and prebiotics as a dietary supplement in stabilization of Gut Microbiome towards Chronic Kidney Disease(CKD) is relatively new. Many independent reviews in various scientific journals have reflected on various topics such as gut Microbiome, its dysbiosis, impact of the altered intestinal characteristics including small bowel bacterial overgrowth, newer uremic toxins, adsorbent drugs and several observational small scale clinical studies from Kibow and many others.

METHODS

‘RENADYL™’ a synbiotic dietary supplement was studied in randomized clinical trials in CKD 3 and 4 and ESRD patients. Other oral therapies for removal of uremic toxins include the use of keto acids and charcoal sorbents.

CLINICAL TRIAL 1-RESULTS

Multi center double blind placebo controlled crossover studies in CKD III and IV patients, for a 6 month period¹.

Dosage of 90 Billion CFU/day.

USA- SUNY and NYU school of Medicine(n=10), Canada- University of Toronto, Scarborough Hospital Ontario (n=13), Nigeria-National Hospital Abuja (n=15), Argentina-Hospital Italiano Bueno Aires(n=8)

Parameter	No of Patients showing positive response	% of patients showing positive response	p value
Blood Urea Nitrogen(BUN)	29	63	<0.05
Creatinine (Crn)	20	43	Not statistically significant
Uric acid	15	33	
Quality of life	39	85	

CLINICAL TRIAL 2-RESULTS

Open label dose escalation study in 28 patients for a period of 6 months at Thomas Jefferson University showed no adverse effects with doses of 90,180 and 270 Billion CFU/day². There was a significant reduction in creatinine and C-reactive protein (CRP) an inflammatory biomarker. Reduction was also seen in urea, potassium and improvement in quality of life (QOL) were also observed.

Parameter	Month	Mean	p value
Blood Urea Nitrogen(BUN)-mg/dL	0	48.82	0.0889
	4	44.85	
Creatinine (Crn)-mg/dL	0	2.38	0.52
	4	2.29	
C reactive protein (CRP)-mg/L	0	0.44	0.58
	4	0.4	
Hemoglobin(Hb)-mg/dL	0	10.79	0.0084
	4	10.93	
	6	11.06	
Potassium(K)-mmol/L	0	4.52	0.39
	4	4.44	
	6	4.39	
Quality of life			
Physical Function	0	60.27	0.0852
	4	69.1	
	6	71.16	
Pain	0	36.2	0.66
	4	33.91	
	6	26.63	

CLINICAL TRIAL 3-RESULTS

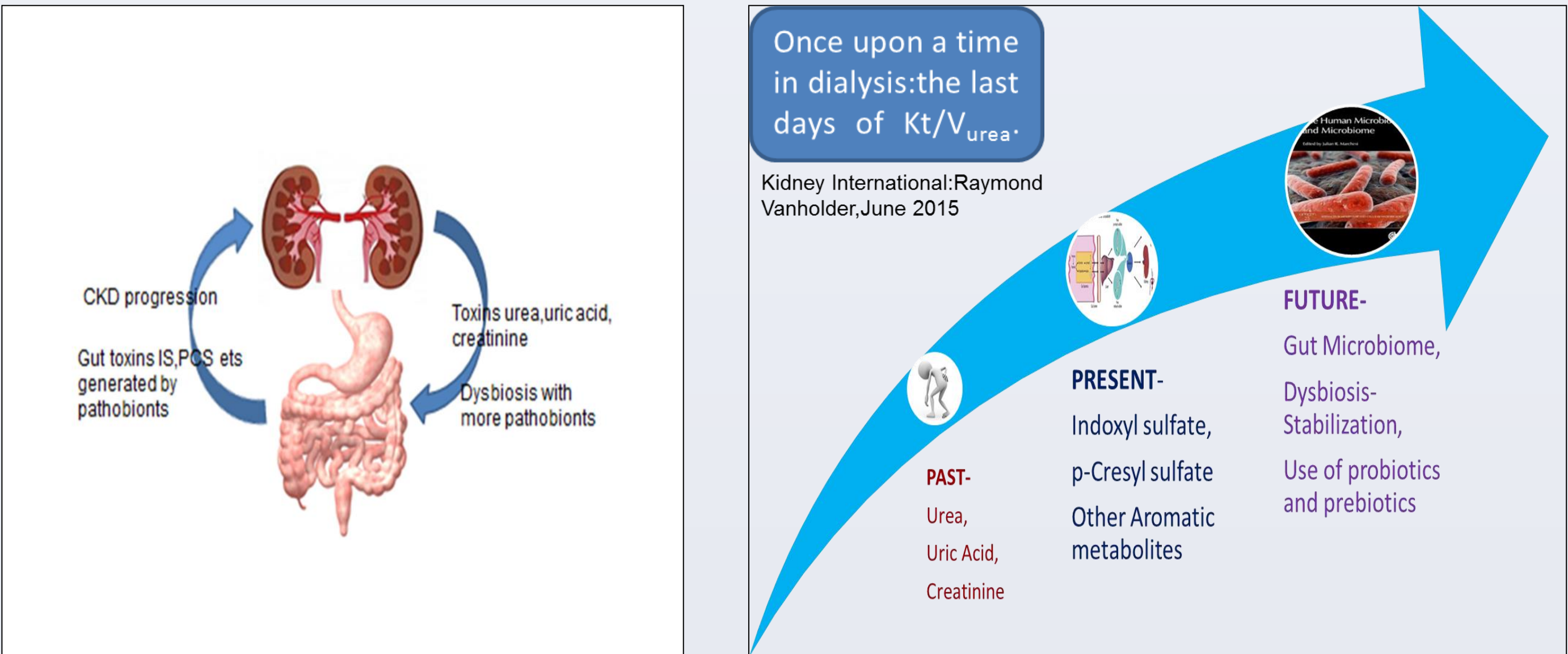
Double blind placebo controlled crossover studies in 22 dialysis patients over a 6 month period at the State University of New York showed reduction in CRP, serum total Indoxyl glucuronide (IG) and improved QOL with a dose of 180 Billion CFU/day³.

Variable	Tx period	N	Mean
White Blood Cells (WBC)	Base	22	6.36
	Placebo (PL)	21	6.07
	Treatment (Tx)	21	5.57
C-reactive protein (CRP)	Base	21	8.89
	Placebo (PL)	18	11.28
	Treatment (Tx)	19	5.1
Total Indoxyl Glucuronide (TIG)	Base	22	0.75
	Placebo (PL)	22	0.75
	Treatment (Tx)	22	0.67

Variable	Tx period	t value	Pr> t
White Blood Cells (WBC)	PL-Tx	2.03	0.0569
C-reactive protein (CRP)	PL-Tx	1.97	0.0707
Total Indoxyl Glucuronide (TIG)	PL-Tx	2.01	0.0579

SUMMARY

Our studies using Renadyl for Enteric Dialysis showed reduction in levels of various uremic toxins like urea and indoxyl glucuronide a gut microbiome derived uremic toxin. Levels of CRP also decreased with an improvement in the quality of life. Oral adsorbents and keto acids have other associated problems. This demonstrates the potential restoration of the gut microbiome dysbiosis with the use of specific strains of probiotic bacteria.



Treatment	Application/Advantage	Disadvantage
Ketoacids	Provide essential amino acids	Expensive. Not covered by insurance
Kremezin	Binds to Uric acid, creatinine, phenols and indoles. Does not bind to Urea	Dosage 9g/day. Cost \$270/month. Can bind to many other aromatic, steroidal and heterocyclic compounds including drugs.
Pro/Prebiotics	Restore gut balance. Reduce production of some toxins. Metabolize some uremic toxins. Safe and well tolerated.	Large number of RCT needed to get statistically significant data.

CONCLUSIONS

Levels of urea, uric acid, creatinine, CRP, and the lesser known toxic metabolite (IG) arising from protein putrefaction due to gut dysbiosis in CKD, can be reduced using some specific probiotic strains with improved QOL. Other methods of toxin removal like AST-120 and protein replacement by keto acid supplementation have disadvantages in comparison to probiotic usage which is safe and well tolerated, non invasive, less expensive and less painful to the patient population. Future research aims to focus on the more harmful gut derived uremic toxins like IS and PCS rather than Urea which has been the long term surrogate marker of renal failure.

REFERENCES

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