Randomized, Controlled Study On Supplementation Of Ketoanalogues In Predialysis Patients To Prevent Decline In Glomerular Filtration Rate (GFR)

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Low Protein Diet

- In chronic kidney disease (CKD), hyperfiltration appears in the remnant glomeruli with subsequent histological lesions and decreased glomerular filtration[1].
- Low-protein diet is a means to protect residual renal function and to slow down progression of CKD to end-stage-renal-disease (ESRD) by reducing protein-related glomerular hyperfiltration, leading to reduction in glomerular capillary pressure and filtration[2-16]. and hypertrophy[2].
- Early 1980s highlighted the importance of protein restriction in the reduction of phosphorus intake in moderate to advanced CKD[14].
- Moderate dietary protein restriction is an effective way of delaying functional renal deterioration[14]
- Studies report an improvement in clinical and nutritional status in patients with a low protein diet supplemented by ketoanalogues[7-16].

Very Low Protein Diet (vLPD)

Modification Of Diet In Renal Disease (MDRD Study)[3,4] showed that in predialysis period CKD stage I,2,3, very low protein diet (vLPD 0.3g/kg/d + 5mg/kg bw KA) in combination with Ketoanalogues (one tablet 50 mg EAA)

Reduces uremic symptoms

Reduces proteinuria

Preserves residual renal function

Slows down rate of progression of disease

Delays onset of dialysis

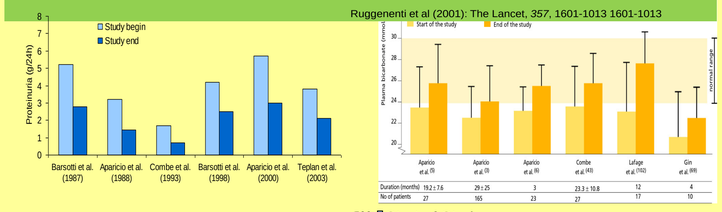
Improves metabolic complications[5]

Preserves nutritional status.

Studies Showing Benefits of (V)LPD Supplemented with Keto/amino Acid

By the end of the study reduction in proteinuria, correction of metabolic acidosis, lower ing of serum phosphate and triglyceride levels is reported.

Ruggenenti et al (2001): The Lancet, *357*, 1601-1013 1601-1013



Objectives

To evaluate

i) effect of combined therapy of very low protein diet (vLPD) and ketoanalogues on renal function of patients in CKD stages 1-3, and

ii) to study compliance to very low protein diet.

Material And Methods

Study Design: Prospective randomized controlled study.

Ethics Committee Approval: The clinical trial was approved by ethics committee of the institute.

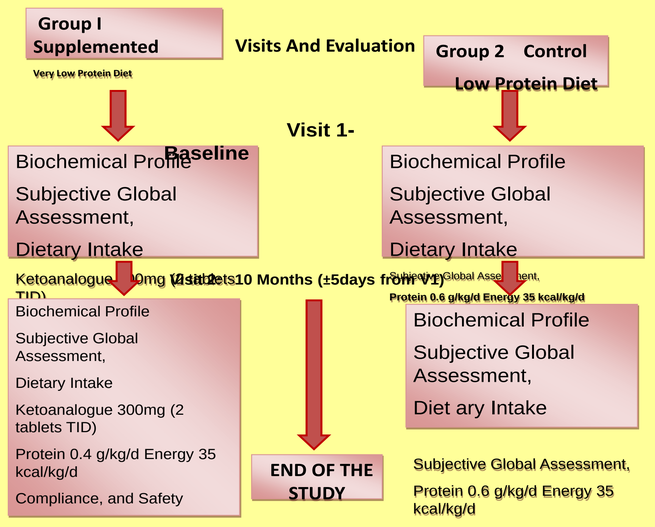
The project was funded by the institute as intramural research grant of Rs 3,00,000 (USD 4,615). Ketoanalogue tablets were purchased from the grant and patients were provided medicine free of cost.

Sample size: Minimum sample size derived using Student's T test was 19 (10 patients in each group 0.05 % significance level and power of 85%).

Therefore we recruited **40 patients**, 20 (15 males and 5 females) in each group.

Inclusion criteria: CKD patient with GFR <60 but >30 ml/minute as calculated by Cockroft's formula[6]

Exclusion Criteria was **p**atients with cancer, systemic disease, obstructive uropathy and rapidly progressive glomerulonephritis.



Biochemical Investigations And Nutritional Biochemical Investigations And Nutritional Intake

•Biochemical investigations were done at baseline (visit 1) and at 10 months (Visit 2).

Hemoglobin
Serum creatinine
Serum sodium
Serum potassium
Serum calcium
Serum phosphorus
Serum albumin and
Random blood glucose

•The nutritional status was assessed using Subjective Global Assessment (SGA) scores at visit 1 and visit 2.

•Three days Dietary Intake was taken by a dietician on both the visits.Data were analyzed using SPSS windows Version 12

Results

Table 1 Disease Profile Of Patient

Disease	Group 1 (Ketanalogue) N=20	Group 2 (Control) N=20
CKD	5	10
CKD HTN	6	6
CKD DM	2	1
CKD DKD	1	-
CKD HTN DKD	5	-
CKD HTN DM	-	3
CKD HTN RA	1	-

CKD Chronic kidney disease; HTN Hypertension, DM Diabetes mellitus, RA Rheumatoid arthritis.

Table 2 Dietary Intake Of Patients At Visit 1 and 2

Parameter	Group1 (Ketoanalogue)	Group 2 (Control)
Dietary Energy kilocalories/d	1104.59±212.29	991.21±258.49
Dietary Energy kilocal/kg/d	19.48±6.84	16.15±5.85
Dietary Protein gram/d	35.11±7.80	30.72±6.76
Dietary Protein gram/kg/d	0.62±0.24	0.50±0.16
Carbohydrate gram/d	186.45±40.31	171.09±54.75
Fat gram/d	26.03±12.59	18.91±13.46
Dietary Sodium mg/d	222.94±102.26	200.95±174.84
Dietary Potassium mg/d	1187.86±338.27	1123.76±430.73
Dietary Calcium mg/d	443.25±271.33	446.18±248.67
Dietary phosphorus mg/d	999.50±238.42	836.41±238.17
Dietary Iron mg/d	17.53±22.06	11.00±3.29

Results

Table 3 Biochemical Profile Of The Patients

Parameter	Group 1 (Ketoanalogue)		Group 2 (Control)	
	Visit 1	Visit 2	Visit 1	Visit 2
Age years	52.26±13.17	No change	46.86±13.64	No change
Weight kg	61.53±13.49	No change	61.95±10.85	No change
Hemoglobin g%	12.19±1.95	14.20±1.00	12.35±1.48	12.50±1.00
Serum Creatinine mg%	1.61±0.52	1.40±0.52	2.20±0.29	2.47±0.33
GFR ml/min *	47.79±13.2	47.65±13.26*	51.14±15.1	37.8±10.0 *
Blood Sugar Fasting	117.77±33.2	92.00±31.1	139.71±90.2	120.00
Serum Albumin g/dL	4.11±0.43	4.03 ±0. 52	3.8±0.90	3.09±0.38 *
Serum Sodium mg	137.5±3.39	140.3±2.52	138.9±4.12	138.00
Serum Potassium mg	4.43±0.63	4.35±0.62	4.43±0.63	4.35±0.62
Serum Calcium mg	8.55±1.98	9.87±1.04	8.62±2.05	8.55±0.78
Serum Phosphorus mg	3.67±0.86*	3.88±0.88	3.54±0.89	4.00±0.28
Systolic BP mmHG	130.35±15.06	136.6±25.17	127.44±15.5	116.50±9.19
Diastolic BP mmHG	81.29±7.55	81.33±10.26	82.78±8.95	74.00±5.66

*Significance (2-tailed) Significant difference in serum albumin level (p =0.000) between visit 1and 2 in group 2. Significant difference between visit 1 and 2 in GFR in group 2. In group 1 GFR remained stable at 47.65±13.26 ml/minute and there was a significant difference in the GFRs of group1 and 2 at visit 2. Significant difference (p = 0.023) in GFR of groups 1 and 2 at visit 2.

Figure 1 Hemoglobin Level of Patients at Visit 1 and 2 Results cont...

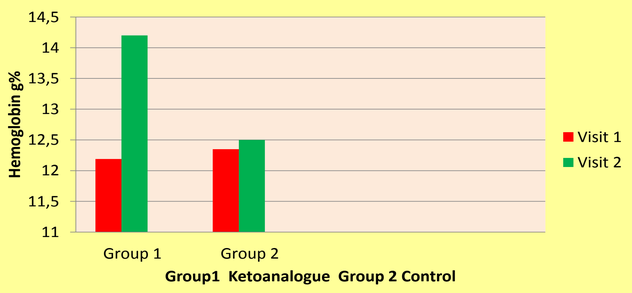


Figure 2 Fasting Blood Sugar of Patients at Visit 1 and 2

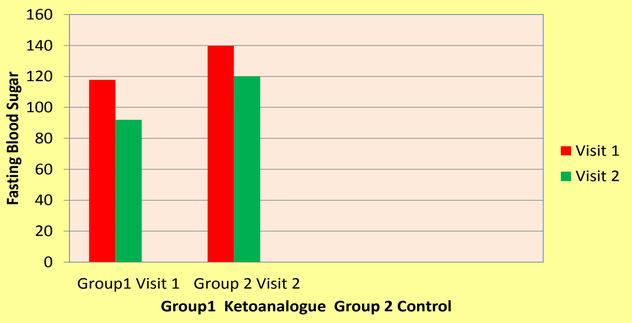


Figure 3 Serum Creatinine of Patients at Visit 1 and 2

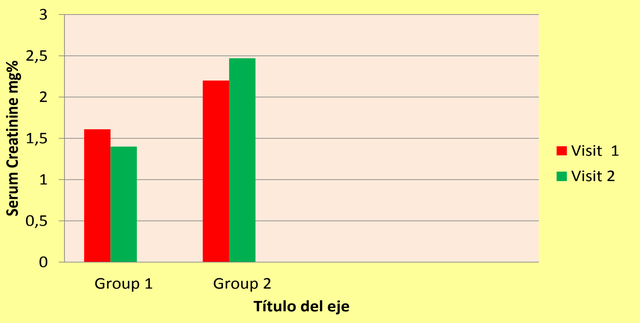


Figure 4 Glomerular Filtration Rate of Patients at Visit 1 and 2

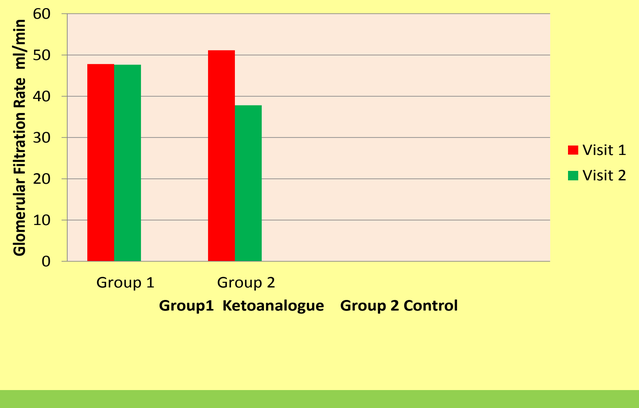
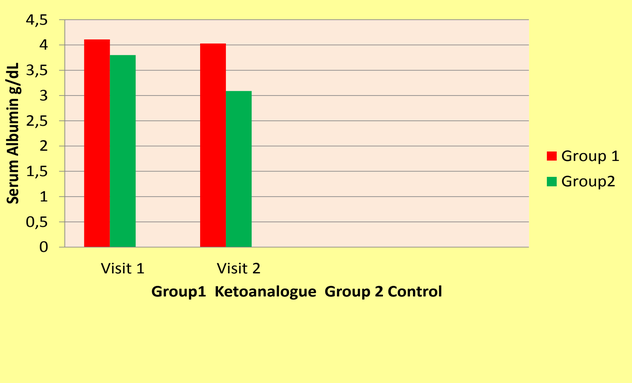


Figure 5 Serum Albumin Level of Patients at Visit 1 and 2



Conclusion

GFR was preserved at 47.0 ml/min in the intervention group while in the control the GFR decreased from 51.1±15.1ml/minute to 37.8±10.0 ml/minute in 10 months.

At the end of the study, the serum albumin level was higher in the intervention group compared to control group.

Supplementation with ketoanalogues can prevent decline in renal function even without adherence to very low protein diet.

Right dosage of the ketoanalogue supplements is required in addition to ensuring strict compliance of dietary restrictions[3].

While prescribing vLPD supplemented with ketoanalogues is important to ensure optimal intake of energy in order to preserve nutritional status.

Discussion

- Despite obvious benefits of protein restriction, concern has been raised in patients on VLPDs, which could lead to deterioration in the nutritional status of CKD patients[3].
- In present study, patients were noncompliant to vLPD. However, despite the fact that the protein intake was normal 0.62±0.24 g/kg/d (instead of 0.4 g/kg/d as advised) to group 1, the GFR remained stable at 47.7 ml/min over 10 months in intervention group.
- The energy intake was 19.48±6.84 kcal/kg/d and 16.15±5.85 kcal/kg/d in group 1 and 2 respectively, which is significantly low compared to recommended dietary allowance for CKD patients.
- It is possible that the extra 0.2g/kg/d of protein that the ketoanalogue group took, it was utilized for providing energy as energy intake was 50% less than recommended. **Yet, GFR remained stable**.
- The serum albumin level was well preserved 4.11±0.43 g/dL at visit 1 and 4.03 ±0.52 g/dL at 10 months in ketoanalogue group.
- This study shows that even without vLPD, ketoanalogue supplementation even with standard low protein diet can preserve renal function. The nutritional status was preserved as per the SGA scores.
- At baseline, GFR was higher in control group (51.14±15.1 ml/minute) compared to ketoanalogue group (47.79±13.2 ml/minute). The GFR declined significantly in controls from 51.14 ml/min at baseline to 37.8 ml/minute over a period of 10 months.
- The serum calcium, phosphorus, sodium and potassium remained unaffected with ketoanalogue supplementation.
- The fasting blood glucose was better controlled in supplemented group (117.77±33.2 mg% at visit 1 and 92.00±31.1 mg% at visit 2) at 10 months compared to controls (139.71±90.2mg % at visit 1 and 120.00mg % visit 2).

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