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Nutritional Considerations in Indian Patients on PD

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1. Introduction

Malnutrition inevitably accompanies Chronic Kidney Disease (CKD) and dialysis. Markers of malnutrition like low serum albumin have been shown to correlate independently with higher mortality in dialysis patients (1). Malnutrition is seen in both Hemodialysis (HD) and Peritoneal Dialysis (PD) patients. The incidence has been described at 10-70% in HD and 18-51% in PD patients (2,3). The causes of malnutrition in dialysis patients can be manifold- dialysis factors, biochemical factors, gastrointestinal factors, miscellaneous factors, and low socio-economic status (4). Miscellaneous factors include depression, multiple medications, recurrent hospitalizations, and underlying illness. Modality of dialysis also affects nutritional status. There are factors unique to each both PD and HD that may contribute to the overall malnutrition. In PD, loss of albumin in PD fluid may range from 5.5-11.8 gms per day (5). In comparison, low flux dialysers account for amino acid losses of 5.6-7.1 gm/day in HD patients (6). Thus PD patients maintain lower serum albumin than age and weight controlled HD patients. Other causes responsible for hypoalbuminemia in PD patients include older age, etiology of renal failure, transport status, and chronic inflammation. Anorexia can result from distention due to fluid in the abdomen. Episodes of peritonitis can cause protein losses of upto 15 gm per day (7). Overhydration, and early satiety due to absorption of glucose from PD fluid can also be a cause of malnutrition in PD (8). Hospitalisation of dialysis patients is estimated to lead to them missing upto 20% of their lunches and dinners, with calorie deficits of upto 3000kcal/week (9). Other factors may ultimately impinge upon a dialysis patients nutritional well being. Blindness, amputations, dementia, depression and stroke are some factors adding to the nutritional challenges. Disabilities are more in HD patients than in PD, and is also more common in diabetics than non diabetics (10). As the number of diabetics on PD increased exponentially, malnutrition is also expected to increase with the same rate. Even though malnutrition is very common and strongly predicts outcome, malnutrition is not thought to directly cause death. Rather, a combination of malnutrition, inflammation and cardiovascular disease may be interrelated in dialysis (11,12). Serum levels of CRP and interleukin-6 (IL-6, which is a pivotal proinflammatory cytokine involved in systemic inflammation) were found to be significantly elevated in malnourished HD and PD patients. As a marker of systemic inflammatory reaction, serum CRP is now regarded as the best predictor for development of cardiovascular disease in the general population as well as in dialysis patients. These factors led to the proposal that malnutrition be characterised as Type 1 and Type 2 (12). Type 1

malnutrition is related to the uremic syndrome per se and can be corrected by adequate dialysis. It is characterised by a normal/low serum albumin, absence of inflammation and comorbidity, low food intake and decreased protein catabolism. Type 2 malnutrition is thought to be 'cytokine driven' and is clinically more severe, characterised by hypoalbuminemia, inflammation, comorbidity and increased protein catabolism. Thus, it is clear that malnutrition and co morbidities play a major role in determining outcomes in patients on PD. Assessment and treatment of nutritional problems in PD may lead to overall better performance on PD, better quality of life, and increased longevity. Methods of assessment of nutritional status, the interpretation and limitations of the same, approaches towards the optimum treatment strategies, and future directions in the management of nutritional status in PD patients is dealt with at length in this chapter in the following pages.

2. Global perspective

The prevalence of malnutrition in PD patients varies based upon the method of assessment used(13).For unclear reasons, longitudinal studies have shown that after initiation on PD, following an initial improvement, nutritional status gradually declines (14,15,16). There is clear association between malnutrition and poor outcome in PD patients, but the relevant studies including the much quoted CANUSA study (17) were based on Caucasian populations. It is not yet known whether the relationship is also applicable for Asian populations and whether Asian PD patients have distinct and unique nutritional issues compared to their Western counterparts. Also, it is not clear whether the reported superior survival of Asian patients can be related to better preservation of nutritional status (18,19).There is a general feeling that the incidence of malnutrition is essentially similar in Western and Asian populations, but the incidence of severe malnutrition is lower in Asian populations (20,21,22,23). Lesser activation of a systemic inflammatory reaction in Asian PD patients is suggested, and that circumstance may partially explain their lower incidence of malnutrition as compared with Western PD patients(24)Lesser incidence of metabolic acidosis in Asian patients has also been reported (25). It appears that correction of metabolic acidosis improves the nutritional status of Asian PD patients, which is consistent with the results from earlier reports in Western PD patients. Reported data indicate that dietary protein and energy intakes are not much different, although actual dietary intake of nutrients is independently influenced by the delivered dialysis dose and RRF in Asian PD patients(26). The effect of peritoneal membrane transport characteristics on long-term nutritional status remains controversial (27).Establishing a relationship between dialysis adequacy and nutritional status (and clinical outcome) would give nutrition a central role and thus have important therapeutic implications. Important nutritional issues that need further investigation in Asian PD patients include determining daily diet requirements for maintenance of a positive nitrogen balance, establishing an optimum method to assess nutritional status, and developing preventive and therapeutic strategies to manage malnutrition.

3. Indian scenario

The lack of a Renal Registry system in India prevents an exact estimation of the incidence of renal failure and ESRD in India. Estimates suggest that an average of 160,000 new patients

require dialysis every year in India (28). Several problems mar the optimum use of PD in our patients. An initial prescription is usually limited to 3 exchanges of 2-L bags (29). Most patients are unable to afford 4 exchanges, or the use of newer/biocompatible solutions. Currently about 6000 patients are receiving PD in the country. Malnutrition in Indian patients is often severe and multifactorial. Reasons include late initiation of PD, protein restriction in the pre dialysis period, intercurrent infections, comorbidity, and dietary factors. Patients almost invariably fall short of recommended dietary intakes (30). The mean age of our CAPD patients is lower than that of PD patients in Western countries (31), and most of our PD patients are malnourished at PD initiation (20). Comorbidities may also be different in Indian PD patients. Vegetarianism is very common in India which means that patients do not get animal source protein in their diet. Dietary habits in India are complex with many patients being pure vegetarians, some who occasionally partake of meat in the diet and some who are regular non vegetarians. This makes nutritional assessment and management difficult. Data on Indian patients nutritional status is scant. A recent trial showed that malnutrition at initiation of PD was predictive of higher incidence of peritonitis. Patients were categorized into malnourished or well-nourished groups on the basis of Subjective Global Assessment (SGA) scores. Malnourished patients experienced significantly more peritonitis episodes (1 vs. 0.2 annually) than did patients with a normal nutritional status. On univariate analysis, SGA, nutritional risk index, serum albumin, and daily calorie intake were significantly associated with peritonitis. On multivariate regression analysis, only SGA was a significant predictor of peritonitis. Peritonitis-free survival was better in patients showing normal nutrition than showing malnutrition (32). Indian PD patients are thought to consistently fail to achieve NKF-KDOQI recommended calorie and protein intake, which was confirmed in some Indian studies (31). There is an overall paucity of good data from India. Assessment of nutritional status, and the management of malnutrition, all remain suboptimal at present.

4. Assessment of nutritional status in PD patients

An ideal assessment of nutritional status of a patient draws from a detailed history, clinical examination including anthropometry and biochemical tests. There is no ideal and 100% effective method available at present. Current strategies of evaluating nutritional status vary from centre to centre and depend on many factors including economic considerations. In a country like India it is impossible to perform too frequent and cumbersome investigations especially when they are expensive. The different available tools for nutritional assessment are discussed here

5. Subjective Global Assessment (SGA)

This is probably the most widely used method of nutritional assessment. It is simple and inexpensive. It is based on the clinicians ability to make an assessment of the overall nutritional status based on a medical history and clinical examination, to derive a final score. In general, 60% of the clinician's rating of the patient is based on the results of the medical history, and 40% on the physical examination. The clinician rates each medical history and physical examination parameter as either an A, B, or C. Although originally used to categorize surgical patients, this nutritional classification system has been shown to be a reliable nutritional assessment tool for dialysis patients(14,33). SGA is limited by the very

fact that it is subjective and may not be entirely reproducible due to observer variability. In addition, its ability to detect small variations in nutritional status is limited. One parameter, the degree of anorexia, has been reported to be a strong predictor of mortality in haemodialysis patients [34].

6. Serum Albumin and Prealbumin

Serum albumin has been, by far, the most commonly used marker of nutrition status in CKD patients, and it is a powerful predictor of mortality in PD patients (17). However Serum albumin as a marker of malnutrition has several caveats. The low serum albumin level observed in PD patients may reflect mostly the acute-phase response and resulting albumin losses in dialysate and urine, and only to a lesser extent poor nutrition status. The patient's clinical status must be examined when evaluating changes in the serum albumin concentration, which is weakly and inversely correlated with serum acute phase proteins (35). Prealbumin is thought to be a better marker than serum albumin due to its shorter half life, and better correlation to the nutritional status. However Prealbumin is also a negative acute phase reactant (36). Also the prealbumin levels are related to the residual renal function (36,37). Hence both these markers may not be the ideal reflection of nutritional status.

7. Serum Transferrin

Serum Transferrin, though initially thought to reflect nutritional status, is now not widely used. It is almost universally low in dialysis patients and reflects iron status predominantly.

8. Protein equivalent of total nitrogen appearance (nPNA)

The use of nPNA as an estimate of protein intake is simple to use in the clinical setting. nPNA approximates DPI only when the patient is in nitrogen equilibrium or steady state. It will change in anabolic or catabolic situations and needs to be interpreted accordingly.

9. Anthropometry and hand grip strength

The anthropometric parameters that are generally assessed include body weight, height, skeletal frame size, skin-fold thickness, midarm muscle circumference, percentage of the body mass that is fat, the percentage of usual body weight, the percentage of standard body weight and the body mass index (BMI) [38,39,40]. These various measures provide different information concerning body composition, and it is therefore advantageous to measure more than one of these parameters. Moreover these tests are cheap and easy to perform. There is focus on hand grip strength as a nutritional assessment tool as it has been demonstrated to predict mortality on PD patients (41). It is recommended to use some of these tests singly or in combination, for diagnosis of malnutrition and also for follow up of patients.

10. Body composition measurements

A-dual energy xray absorptiometry

This is considered superior to other currently available techniques. With DEXA, bone mineral, fat mass (FM), and LBM distribution are estimated directly, without making

assumptions about the two-compartment model. However, the assessment of LBM by DEXA is subject to flaws, because it assumes that 72% of the LBM compartment is water. Given that PD patients can exhibit abnormal hydration status, DEXA might not be a very precise method for assessing LBM in dialyzed patients. Therefore, measurement of LBM by DEXA should be combined with estimation of the extracellular fluid volume by the tracer dilution technique. Provides accurate data on body composition which are superior to anthropometry, creatinine kinetics and bioelectrical impedance [42,43].

B-Bioimpedance Analysis (BIA)

Bioimpedance analysis is based on the measurement of resistance and reactance when a constant alternating electrical current is applied to a patient, by empirical equations. However BIA is highly influenced by the hydration status. It is recommended that BIA be attempted only when the patient is at his oedema free weight. Our own experience with the use of BIA in CAPD patients showed good results (44).

C-creatinine kinetics

Creatinine kinetics is based on creatinine excretion in urine and dialysate. LBM estimated from creatinine kinetics depends on the creatinine content in the diet and the metabolic degradation of creatinine. Variations observed during repeated measures of LBM estimated using creatinine kinetics is unacceptably high (45).

From the available tests we recommend relying on a panel of nutritional markers rather than any one particular test. We recommend assessment of nutritional status at least every 6 months. Ideally, body weight, serum albumin, SGA, protein intake as assessed from dietary recall or nPNA, and an assessment of protein stores and iron stores (serum transferrin) would be necessary. A prospective decline in nutritional status would prompt a detailed evaluation. A cost effective but complete strategy for Indian patients would be a 6 monthly battery of tests that includes

- Serum albumin
- Serum Transferrin Saturation
- SGA
- Anthropometrics/Hand Grip Strength.

While inexpensive, these tests would enable assessment of all necessary parameters.

11. Nutritional intervention strategies

It is important to individualise strategies for each patient rather than slavishly adhere to guidelines or formulae. Considerations towards cost, palatability, culture, and comorbidity should be considered. We recommend using the services of a renal dietician in addition to the expertise of the treating Physician. In consultation with the patient, a unique and exclusive plan is drawn up for each patient.

12. Daily Protein Intake

While a Daily Protein Intake(DPI) of 1.3g/kg/day is recommended, there is no conclusive evidence to show that lower protein intakes impact upon nutritional status in PD. Some studies have shown that a DPI of 1.0-1.2g/kg/day is adequate to maintain positive nitrogen balance (46,47). We would recommend a daily protein intake of > 1.0g/kg/day as sufficient if the patient has no declining trend in nutritional parameters. At a DPI of < 0.9g/kg/day, we would reassess the patients nutritional status. Our own experience with the use of 0.8

g/kg/day of protein, supplemented with keto analogues 0.4g/kg/day, when compared with a traditional protein diet of 1.2g/kg/day showed that the keto-group had improvement on parameters like appetite, anthropometry, serum albumin and a decrease in serum cholesterol and fasting blood sugar (48).

<p>MANAGEMENT OF MALNUTRITION IN PD PATIENTS-</p> <p>NON DIALYTIC MEASURES</p> <p>Preserve residual renal function</p> <p>Prevent catabolic factors</p> <p>Correct acidosis</p> <p>Treat comorbidity and inflammation</p> <p>Maintain optimal nutrition</p> <p>Nutritional counseling</p> <p>Nutritional supplementation (oral, enteral, or parenteral)</p> <p>Correct anemia</p> <p>Encourage exercise</p> <p>Emotional and social support</p> <p>DIALYSIS RELATED MEASURES</p> <p>Optimize dialysis dose</p> <p>Avoid potential sources of inflammation</p> <p>during the PD procedure</p> <p>Peritonitis</p> <p>Bioincompatible PD solutions</p> <p>Attention to fluid, electrolyte and acid base balance.</p> <p>Encourage anti-inflammatory diets</p> <p>NOVEL APPROACHES</p> <p>Use PD fluids with nutritional supplements</p> <p>Appetite stimulants</p> <p>Anti inflammatory diets</p> <p>Dietary fibre, Phytoestrogens, Omega-3 fatty acids</p> <p>Glycation End Product Inhibitor, PPAR-agonist, Antioxidants</p>

Table. 1.

13. Dietary energy intake

A dietary energy intake of > 35kcal/kg/day is essential for PD patients. In elderly patients 30 kcal/kg/day may suffice. It is important to consider glucose absorption from the PD fluid. This can account for upto 100-200 g/24 hours.

LIPIDS

A diet with no more than 30% of total calories from fat should be encouraged. No more than 10% should derive from saturated fat.

CARBOHYDRATES

Complex carbohydrates are encouraged over refined carbohydrates.

SODIUM AND WATER

This is individualised based upon urine output, fluid status and blood pressure. We recommend 3-4 grams of salt intake /day in patients where ultrafiltration is easily achieved.

POTASSIUM

With residual renal function, we allow upto 100 meq/day of K unless the patient is on ACE inhibitors or ARBs. As dialysate contains no potassium, even in anuric PD patients we allow upto 100 meq/day.

CALCIUM

We attempt to achieve calcium balance with supplementation of calcium/ Vit D as needed.

PHOSPHORUS

Phosphorus restricted diets are often impractical to achieve as they lead to malnutrition. Ideally phosphorus intake should be limited to 0.6-1.2g/day. Most PD patients need the use of Phosphate binders. We target a serum phosphorus of 4.5-5.5 mg/dL. The choice of phosphate binders is individualised.

IRON

We target a serum transferrin saturation of 20% or higher. We prefer the intravenous route of iron supplementation, for reasons of ease, compliance and effectiveness.

14. Correction of metabolic acidosis

Metabolic acidosis is an important stimulus for net protein catabolism and elicits the transcription of genes for proteolytic enzymes in muscle including the ubiquitin-proteasome pathway. The correction of metabolic acidosis decreases protein degradation and improves nitrogen balance. This has been proven for PD patients (49). Oral sodium bicarbonate can be used to achieve this goal.

15. Dose of dialysis

The relationship between delivered dose of dialysis and nutrition is controversial. Overall, prospective studies of adequacy and nPNA or DPI have not shown any correlation.

16. Additional nutritional support

PD patients who may need additional support include patients with peritonitis, hospitalisation or gastroparesis. We recommend support with oral supplements of fortified energy and protein, intraperitoneal amino acids, nasogastric feeding or parenteral nutrition.

17. Amino acid based PD fluids

In a prospective, randomized, open-label study that evaluated the role of amino-acid dialysate on the nutrition status of malnourished PD patients, patients who replaced 1 daily exchange of traditional dialysate with amino-acid dialysate showed better evolution in markers of nutrition than did patients who continued to use dextrose dialysate only (50).

18. Appetite stimulants

The use of appetite stimulants such as megestrol acetate, cannabinoids, and cyproheptadine may be a tempting part of a new strategy for malnourished PD patients. Megestrol acetate has been suggested for use as an appetite stimulant in HD and PD patients (51,52); however, it is associated with several side effects, including hypogonadism, impotence, and increased risk of thromboembolism.

ANTI INFLAMMATORY DIET

A recent study with HD patients suggested a trend toward a reduction in the serum concentration of C-reactive protein (CRP) after 8 weeks' ingestion of an isoflavone soy-based supplement (phytoestrogen based diet) (53). High fiber consumption in non-renal subjects was shown to lower the risk of elevated CRP (54). The anti-inflammatory effects of the omega-3 fatty acids, mainly eicosapentaenoic acid, found in fish oil are also well recognized.

ANTI INFLAMMATORY PHARMACOTHERAPY

This includes statins, ACEIs, PPAR agonists, and anti-oxidative agents, such as α - and γ -tocopherol.

ANTICYTOKINE THERAPY

These are still experimental. Interleukin-1 receptor antagonists are in trial. Recombinant insulin-like growth factor (rhIGF-1) may induce an anabolic response in patients in whom the primary cause of malnutrition is a low protein intake (55).

19. Conclusions

Nutritional management of PD patients is challenging, and vital to the patients long term survival and well being. A multi disciplinary approach, with a patient centric plan is necessary to achieve long term compliance and success. Consideration to cultural, economic and medical issues is paramount to develop a workable plan, especially in a country as large and diverse as India.

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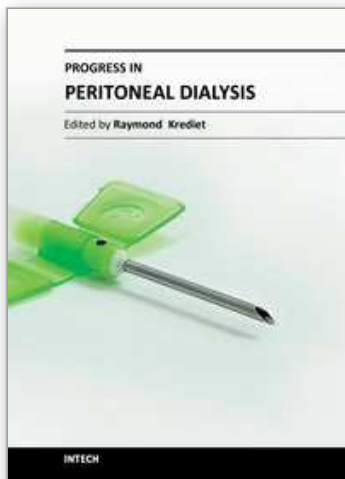
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