身體蛋白質作爲消耗性疾病預防指標的作用

Role of body protein as a prognostic indicator in wasting disease

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Malnutrition is associated with many chronic diseases, though its extent and effect is not well known. Measurement of body protein provides a quantitative and reproducible means of monitoring malnutrition. Results for anorexia nervosa, end stage renal failure value and asymptomatic and symptomatic HIV positive subjects are presented to show that, with the exception of asymptomatic HIV subjects, substantial protein depletion does occur.

A more difficult problem is to determine the relation between body protein, the effects of treatment and prognosis. In the case of CAPD patients, 20% protein depletion was found to be associated with a poor prognosis. For anorexia nervosa subjects, readmission probability was found to be correlated with body protein. However, monitored refeeding and exercise achieved a more normal body composition and quality of life. The critical effect of protein depletion in AIDS remains to be determined, but once ascertained, the role of enteral and parenteral supplementation can then be quantitatively examined.

Introduction

In a likelihood of malnutrition (LOM) study[1], the following definitions were applied:
–serum albumin <3.5 g/dl,
–total lymphocyte count <1500/mm^3
–height/weight <80% normal,
–description of cachexia, wasted, or protein-depleted,
–weight loss >4.5 kg or 15% in 3 months.

Prevalence of LOM was 55% of 771 patients examined. These patients have:
– x3 probability of complications,
– x4 probability of death,
– longer hospital stay of 1-13 days,
– extra cost of $1700-3500 without complications,
– with complications, extra cost of $3000-6000.

The LOM analysis involves a time-consuming investigation of many parameters, none of which have major significance. While clearly identifying the effects of malnutrition, LOM does not provide a simple method for quantifying malnutrition.

In clinical practice, it is necessary to identify patients who may be at risk of malnutrition sequelae. The following questions need to be asked:
– which patients are malnourished,
– is dietary supplementation working,
– how to judge the efficacy of the management of patients with wasting disease,
– how to select patients at risk?

The underlying hypothesis in this paper is that protein status is a measure of nutritional status. If this is the case, then a further set of questions can be posed relating to specific diseases, such as:

– are end-stage renal failure patients protein-depleted,
– what is the effect of major surgery,
– do hospitalized anorexia nervosa patients recover fat in preference to protein?
– does protein loss precede loss of CD4 count in AIDS?

These questions can be addressed by measurement of total body protein (TBP)[2,3]. Body protein is composed of nitrogen-containing amino acids and proteins, with 1g nitrogen per 6.25 g protein.

Nitrogen can be detected by neutron capture analysis, with the prompt emission of characteristic gamma rays. Thus in vivo measurement of total body protein by prompt neutron capture reactions in nitrogen and hydrogen can be made with a body protein monitor (BPM).

The BPM provides the time-integrated change of nitrogen and hence protein. This is a much more sensitive and reliable indicator then differential measurements of blood proteins, nitrogen balance and creatinine clearance, all of which depend on the current condition of the patient.

Two-thirds of body nitrogen is found in the metabolic tissues, ie skeletal muscle and viscera, and one-third in connective tissue[4]. Only 0.06% of nitrogen is found as urea in the bladder. Thus when changes of TBP are observed, it is the metabolic compartment that is changing at a rate 50% greater than the TBP.

Skeletal muscle

Skeletal muscle is a metabolic organ with a regulatory role in the production of amino acids[5] for:
– synthesis of proteins for repair processes after trauma,
– hepatic glucose production from gluconeogenic amino acids,

- glutamine to combat acidosis in kidneys,
- glutamine for RNA, DNA synthesis and multiplication of lymphocytes and rapidly dividing cells,
- increased secretory activity, eg macrophages, on immune challenge.

Skeletal muscle is therefore a fundamental part of the immune system.

Anorexia nervosa

Previous studies in refeeding of famine victims and of nutrient support in cancer, septic shock, acquired immunodeficiency and peritoneal dialysis in end-stage renal failure demonstrate that in all these conditions fat is gained preferentially to protein. The relative contributions to this process of intercurrent disease, altered activity levels and specific metabolic effects of the primary condition are as yet unclear. Yet despite the apparent advantage of anorexia nervosa patients as a model for these studies, only one report has directly addressed the issue of body protein changes during refeeding. Several papers[6-8] report studies which examine the effect of undernutrition, weight restoration and exercise on body composition in patients with anorexia nervosa.

Twenty-eight control subjects were studied on one occasion and 32 patients before and after refeeding. Eighteen patients declined to take part in the study. There were no significant differences in age, BMI at admission, weight gain or body fat before or after refeeding between patients who agreed to participate and those who refused. Results are given in Table 1.

The results confirm that the self-induced weight loss with characterises anorexia nervosa causes fat to be depleted to a greater degree than protein. At hospital admission the average fat mass of the patient group was 41.6% of that of the control subjects whereas protein mass was 75.5% of that of controls. Protein and fat were regained throughout refeeding and at its completion (ie when a minimum healthy weight was achieved for the majority of subjects, albeit a weight significantly less than that of controls), fat was still proportionately more depleted than protein, the fat mass being 78.2% of the control value whereas the protein mass was 89.4%.

Table 1. Body composition of controls and anorexia nervosa patients (ANP) (n=32) before and after feeding (SD).

Measurement	Controls	ANP	
		Before	After
Age (years)	23.2(5.4)	18.8(4.1)[a]	
Height (cm)	164(6.2)	165(5.7)	
Weight (kg)	57.8(7.3)	42.0(0.9)	51.9(4.4)[a,b]
BMI (kg/m^2)	21.6(2.7)	15.4(1.3)	19.1(1.2)[a,b]
Lean body mass (kg)	42.2(4.2)	35.4(3.4)	39.7(3.6)[a,b]
Fat:			
Weight (kg)	15.6(4.3)	6.5(2.6)	12.2(2.4)[a,b]
Percent of weight	26.6(4.6)	15.2(5.0)	23.4(3.8)[a,b]
Nitrogen:			
Weight (Kg)	1.527(0.183)	1.153(0.172)	1.365(0.16)[a,b]
Percent of weight	2.65(0.21)	2.74(0.19)	2.63(0.21)[b]
Index for females	1.01(0.11)	0.74(0.11)	0.88(0.02)[a,b]
Lean body mass (g/kg)	36.5(3.0)	32.5(3.0)	34.4(2.5)[a,b]

a=different from control, P <0.001, ANOVA (DF=1,59)
b=different before refeeding, P <0.001, ANOVA (DF=1,59)

Nitrogen constituted a larger proportion of lean body mass after refeeding although this too remained significantly below that of controls. However, after refeeding, the body composition of anorexia nervosa patients, and in particular the composition of their lean body mass became more normal. Protein repletion is more significant in view of the fact that approximately 30% of protein is relatively nonexchangeable.

Body protein had the largest correlation (r=0.8) with chronicity (number of hospitalizations) of all measured parameters[8].

Further studies are needed to investigate advanced cases of anorexia nervosa who have frequent hospitalizations and poor prognoses. These cases are difficult to bring into the study.

Effects of surgery

Protein catabolism in post-trauma response and cancer cachexia are manifestations of an accelerated loss of nitrogen with injury. This occurs even when the body is in positive energy balance as in elective surgery with exogenous provision of nutrients.

Dramatic losses of metabolic protein in the range 0-30% have been observed after aortic surgery[9]. However, only six patients were in the study and it was not possible to determine the important determinants which influence protein catabolism. Further studies are needed to investigate the determinants of body protein depletion and the effect of this depletion on prognosis.

HIV + and AIDS

Body composition and lymphocyte counts were measured for both asymptomatic and symptomatic subjects[10]. Results are shown in Table 2. While symptomatic subjects showed a 13% weight loss, which is comparable to the 15% loss of nitrogen, the 23% loss of metabolic protein shows that conventional measures can markedly underestimate the effects of concurrent disease. Thus TBN is an essential parameter in the management of AIDS.

Table 2. Average values (SEM) for asymptomatic and symptomatic HIV + subjects

HIV+	Asymptomatic	Symptomatic	S/AS %
n	28	13	
Age y	37.2 (9.2)	41.1 (7.4)	
CD4	596 (168)	49 (101)	
Wt kg	71.4 (10.6)	59.6 (5.6)	83.5
LBM kg	56.9 (6.7)	49.7 (3.4)	87.3
N g	2170 (295)	1815 (214)	83.6
NIM	1.00 (0.11)	0.84 (0.11)	84.4
%BFat	19.9 (4.7)	16.3 (4.2)	81.9
TBW/Wt	59.7 (6.2)	65.2 (4.6)	109

A group of 13 asymptomatic subjects were followed over 12 months to monitor changes in the above parameters. However, no significant changes were observed, as shown in Table 3 below.

Table 3. Longitudinal study of asymptomatic group (n=13). Values are measured ±SEM.

Time months	0	6	12
CD4	540 (150)	520 (180)	545 (190)
Wt kg	72.9 (5.9)	73.1 (8.6)	72.9 (6.7)
N g	2195 (232)	2220 (336)	2220 (241)
LBM, kg	58.2 (6.0)	57.9 (6.5)	59.1 (5.9)

It remains to be answered whether or not loss of body protein precedes the fall of the CD4 lymphocyte count? If so, then maintenance of TBP would become a primary task of HIV+ management.

End-stage renal failure

Major protein depletion in excess of 15% is observed in a

fraction of peritoneal and haemodialysis patients[11,12]. Evidence was found for a cross-sectional dependence with time on dialysis, suggesting that patients may enter ESRF in a depleted state. Further studies are needed to determine whether protein is lost before end stage failure is reached and dialysis commenced.

Protein depletion in excess of 20% in CAPD was found to be associated with poor prognosis[12], whereas good prognoses were observed for the bulk of patients with <7%> protein depletion.

Proteinuria

A high protein diet would be recommended to optimize protein synthesis, but low protein diet slows progression to end-stage renal failure. Thus there is a fine balance to be reached with respect to protein intake.

The nutritional status of some patients may be impaired on entry into dialysis if protein intake is too low, with subsequent poor quality of life and prognosis.

Conclusions

Malnutrition is an important factor in patient prognosis and the cost of patient care. Measurement of total body nitrogen and hence body protein provides a quantitative means of monitoring malnutrition and optimisation of patient management.

With respect to prognosis, CAPD patients are found to have poor prognoses for 20% protein depletion, and the incidence of chronicity in anorexia nervosa patients is correlated with body protein. In the case of major surgery, substantial loses of protein occur, but the effect on prognosis remains to be investigated. A similar situation prevails in AIDS. However, metabolic protein depletion is found to be much greater than weight loss. For asymptomatic subjects, neither protein nor CD4 depletion is observed in a longitudinal study over 12 months.

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