CLINICAL RESEARCH STUDY

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Serum Albumin and Prealbumin in Calorically Restricted, Nondiseased Individuals: A Systematic Review

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ABSTRACT

PURPOSE: Undernutrition is often suspected in patients when serum albumin or prealbumin levels are low. We asked whether these measures are indeed low in undernourished people if no inflammatory illness is present.

METHODS: We did a systematic review to identify otherwise healthy subjects who were severely nutrient-deprived due to poor access to food or unwillingness to eat. We excluded children and pregnant women. We tabulated available measures of nutrient intake, anthropometry, serum albumin and prealbumin, and, when available, changes in these measures during nutritional intervention.

RESULTS: In otherwise healthy subjects, serum albumin and prealbumin levels remained normal despite marked nutrient deprivation until the extremes of starvation, that is, body mass index <12 or more than 6 weeks of starvation.

CONCLUSIONS: In these otherwise healthy subjects, serum albumin and prealbumin levels are not "markers of nutritional status." The "markers" failed to identify subjects with severe protein-calorie malnutrition until extreme starvation. That is, they failed to identify healthy individuals who would benefit from nutrition support, becoming abnormal only when starvation was already obvious. In contrast, serum albumin and prealbumin levels are known to fall promptly with injury or illness regardless of nutrient intake. They are negative acute-phase reactants. When these measures are low in sick patients, this cannot be assumed to reflect nutritional deprivation. Decisions about nutrition support should be based on evidence of meaningful benefit from this treatment rather than on assessment of "nutritional markers."

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KEYWORDS: Albumin; Malnutrition; Nutrition; Nutrition screening; Prealbumin

Malnutrition is considered a common, serious problem among ill patients. Serum albumin and prealbumin often are used to identify malnutrition and evaluate the success of nutrition support. For example, federal regulations for care in nursing homes explicitly require that "The facility must ensure that a resident: 1) maintains acceptable parameters of nutritional status, such as body weight and protein levels, unless the resident's clinical condition demonstrates that this is not possible; and 2) receives a therapeutic diet when there is a nutritional problem."[1] The Centers for Medicare and Medicaid Services also put forth a guide for long-term care surveyors evaluating nutrition and sanitary conditions, which states that "albumin and pre-albumin may help in some cases in deciding to initiate nutritional interventions …"[2] These regulations and this guide are very influential during nursing home surveys, and as a result they are influential in the nutritional treatments provided by nursing homes. A 2014 article recommends use of albumin and prealbumin levels to identify malnutrition before orthopedic surgery and to guide preoperative nutritional management, noting that

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normalization of levels should reduce perioperative complications.[3] Another finds serum albumin level to be the optimal guide for predicting malnutrition in heart transplant patients.[4] A third notes that "Amongst the nutritional biomarkers used, serum albumin has been, by far, the most extensively studied serum protein in patients on maintenance dialysis."[5]

Serum albumin and prealbumin also are affected by inflammatory illness, however, and their value in diagnosing malnutrition in sick patients has long been questioned; "When there is evidence of an acute-phase response (eg, increased CRP [C-reactive protein]), decreased concentrations of plasma proteins such as albumin, transferrin, retinol-binding protein and prealbumin cannot be assumed to reflect malnutrition."[6] Low albumin and prealbumin levels are recognized particularly as "reverse acute phase reactants," lowered during many inflammatory illnesses regardless of nutrient intake.[6-8]

CLINICAL SIGNIFICANCE

- Serum levels of albumin and prealbumin continue to be used as "markers of nutritional status."
- They remain normal during starvation, however, and are low in inflammatory illness.
- Initiating nutrition support because these measures are low has no evidence base and leads to significant waste.

We asked whether starvation affects albumin and prealbumin levels in the absence of inflammatory illness. We reviewed studies of healthy subjects with markedly restricted caloric intake, usually due to poor access to food or because of unwillingness to eat for psychiatric, political, research, or other reasons.

We use "malnourished" to mean "undernourished" as is common. We do not discuss albumin or prealbumin kinetics, acknowledging that serum levels are affected by synthesis, degradation, loss, and volume of distribution; we simply present the measures used in clinical practice. Children, pregnant women, and patients with known inflammatory illness are not considered here.

METHODS

Search Strategy

We developed a written protocol before our review following the standards listed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[9]

We searched PubMed, Embase, CINAHL, and Cochrane Library databases for published studies from inception up to the last search date of August 28, 2013. We did not use any restrictions on language, study type, or publication year. We hand-searched the reference lists of included studies for other articles possibly relevant to our topic. We did not incorporate data from unpublished studies, conferences, dissertations, or other grey literature.

We used a combination of keywords and headings related to albumin, prealbumin, and caloric restriction. A complete list of the search strategy for each database can be found in Appendix 1, available online. The results of the searches were then transferred into the RefWorks (2013; ProQuest LLC, Ann Arbor, MI) online database. Duplicates were removed using the RefWorks exact duplicates and close duplicates function. Two authors (JLL and RWL) then independently reviewed the remaining studies for exclusion/inclusion criteria.

Study Selection

Studies were considered, regardless of study design, if they included human subjects aged 13 years and older. We tabulated and graphed the results of studies of participants who had both 1) evidence of undernutrition, based on anthropometric measures, history of marked caloric restriction, or both; and 2) measurements of serum albumin, prealbumin, or both. We excluded studies that involved children, pregnant women, hospitalized patients, or patients with known injury or acute or chronic inflammatory disease, such as malignancy, acute infection, specific organ failure, and surgery.

Data Abstraction

Detailed reasons for exclusion are documented in the flow diagram (Figure 1). Articles that were categorized discordantly between the 2 reviewers or designated "uncertain" had their full text reviewed and discussed. If disagreement remained, then a third reviewer (TEF) cast the tie-breaking vote.

All articles included in the final analysis underwent a double data extraction process by the reviewers. We extracted demographic information, anthropometric measurements, information about caloric intake, and measures of serum albumin/prealbumin. If multiple albumin measurements were reported, we used the mean values measured during caloric restriction. We also recorded the change in albumin and prealbumin levels after any nutritional interventions. As is common in clinical practice, we used serum albumin levels <3.5 g/dL and prealbumin levels <20 mg/dL as the lower limits of normal.[2,10-12]

RESULTS

A total of 63 articles were included in the final data extraction process, with the complete details listed in Appendix 2, available online.[13-75] The studies were a mix of case reports, case control, cross-sectional, observational, and cohort studies, and clinical trials, with dates ranging from 1944 to 2012. A total of 2125 mostly female patients between the ages of 13 and 50 years were studied. Most of