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Original article

Interrelations of immunological parameters, nutrition, and healthcare-associated infections: Prospective study in elderly in-patients

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Background & aims: Healthcare-associated infections [HAI] are common in elderly individuals and may be related to both nutritional deficiencies and immunosenescence. Here, we assessed whether overall malnutrition and/or specific nutrient deficiencies were associated with HAI via alterations in immune parameters.
Methods: Prospective observational cohort study in patients aged ≥70 years admitted to the geriatric rehabilitation unit of a teaching hospital in France between July 2006 and November 2008. Clinical and laboratory parameters reflecting nutritional status and immune function were collected at baseline. Flow cytometry was used to assess blood lymphocyte subsets including the naive CD4 T-cell count, naive and memory CD8 T-cell counts, effector CD8 T-cell count, and CD4/CD8 ratio. Patients were monitored for HAI for 3 months or until discharge from the geriatric unit or death.
Results: Of 252 consecutive in-patients aged ≥70 years [mean age, 85 ± 6.2 years], 181 [72%] met French National Authority for Health criteria for malnutrition and 97 [38%] experienced one or more HAI. Patients who subsequently experienced HAI had significantly lower baseline values for energy intake [odds ratio (OR), 0.76; 95% confidence interval (95%CI), 0.59–0.99], serum albumin [OR, 0.43; 95%CI, 0.32–0.58], serum zinc [OR, 0.77; 95%CI, 0.62–0.97], selenium [OR, 0.76; 95%CI, 0.61–0.95], and vitamin C [OR, 0.71; 95%CI, 0.54–0.93]. Associations linking these five variables to HAI were not significantly changed by adjusting for flow cytometry T-cell subset values.
Conclusion: Our results suggest a direct effect of nutritional parameters on HAI rather than an indirect effect mediated by immune parameters.

Abbreviations: BMI, body mass index; HAI, healthcare-associated infection; HAS, French National Authority for Health (Haute Autorité de Santé); MAC, mid-arm circumference; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; Se, selenium; TST, triceps skinfold thickness; Zn, zinc.

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1. Introduction

Healthcare-associated infections [HAI] and malnutrition are both prevalent in elderly in-patients and are associated with increased morbidity and mortality rates and with high healthcare costs.[1,2] The increased susceptibility to severe infections and decreased efficacy of immunizations in older individuals are partly ascribable to an age-related remodelling of the immune system known as immunosenescence. Although immunosenescence affects both the innate and the adaptive components of the immune system,[3] the alterations in cell-mediated immunity seem to play the main role.[4,5] Thus, we found in a previous study that elderly patients with HAI had significantly lower values for the CD4/CD8 ratio and naive CD4 and CD8 T-cell counts, as well as higher memory CD8 T-cell counts with significantly increased CD28-negative CD8 T-cells, compared to those without HAI.[6]

Several studies reported HAI as complications of malnutrition in various populations, mainly patients in surgical wards[7] and geriatric rehabilitation units.[8] Malnutrition may play a key role in increasing the susceptibility to infections.[9] Poor nutrition with an inadequate global food intake and/or deficiencies in specific micronutrients [vitamins and trace minerals] may adversely affect the immune system, most notably its cellular component,[10] thereby increasing the risk of infection. Inadequate intakes of specific nutrients are associated with adaptive immunity impairments in elderly individuals.[10,11]

The mechanisms underlying the link between malnutrition and infection remain poorly understood. We hypothesised that malnutrition might increase the risk of infection in elderly patients by exacerbating the immunosenescence process. To assess this hypothesis, we studied the impact of overall malnutrition and specific nutrient deficiencies on the risk of HAI in a cohort of patients admitted to a geriatric rehabilitation unit. We then sought to determine whether this impact was mediated by immunophenotypic parameters.

2. Methods

2.1. Patients and study design

The study methods have been described elsewhere.[12] Briefly, consecutive patients aged 70 years or over who were referred to the geriatric rehabilitation unit of a teaching hospital in the Paris metropolitan area between July 2006 and November 2008 were prospectively included in a cohort and followed-up until death or discharge from the geriatric unit. The study complied with the Declaration of Helsinki and was approved by the Ile-de-France IX ethics committee, Paris, France. Written informed consent was obtained from each patient before study inclusion.

2.2. Conceptual framework

Figure 1 displays the conceptual framework of the analyses. Exposures were defined as nutritional parameters [body mass index (BMI), serum albumin, energy intake, protein intake, and serum micronutrient levels] and the outcome as HAI. To assess whether the links between exposures and HAI were mediated by immune parameters, we computed odds ratios [ORs] using sequential adjustment for immune parameters known to be associated with HAI.

2.3. Data collection

For each patient, the following variables were collected routinely on a standardised form at admission to the geriatric rehabilitation unit: age and gender, reason for admission,

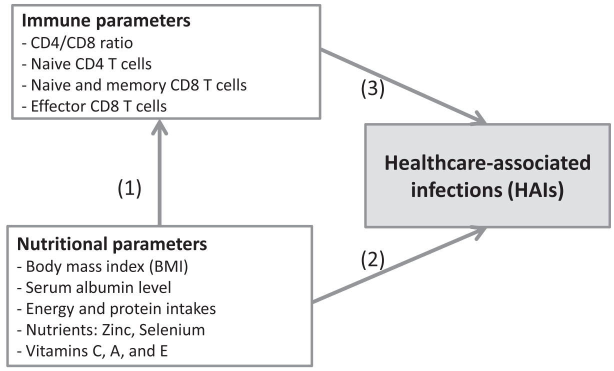

Fig. 1. Conceptual framework. (1) Direct effect of nutritional parameters on immune parameters; (2) Direct effect of nutritional parameters on HAI; (3) Indirect effect of nutritional parameters on HAI mediated by immune parameters.

cognitive impairment [defined as a Mini-Mental State Examination score <24], and the nutritional and immunological variables listed below.

2.3.1. Nutritional assessment

Body weight, height, and BMI [weight/height^2] were recorded. Mid-arm circumference [MAC] and triceps skinfold thicknesses [TST] were measured by a single examiner using a Harpenden calliper; the mean of three consecutive measurements was used for the study. The Mini Nutritional Assessment score [MNA] was recorded and daily dietary intakes were estimated over a 3-day period in the week following admission.

During their hospital stay, the patients received the usual diet given in hospitals of the Paris teaching-hospital network [AP-HP], which supplies 2200 kcal/day on average with 55% carbohydrates, 30% fat, and 15% protein. Foods and fluids were given orally. Additional helpings, beverages, and snacks were offered routinely. A single dietician recorded the energy and protein intakes immediately after each meal based on portion-size estimates and on food-composition information from the CIQUAL database, using Mac 2 Win software 1990–2000 [Altura Software Inc., Pacific Grove, CA, USA]. Oral supplements were also recorded with the help of the ward nurses. Dietary intakes were estimated in grams over a 3-day period in the week following admission.

Serum albumin was measured using a BNII analyser [Siemens, Saint-Denis, France] and C-reactive protein was measured by immunoturbidimetry using an Advia 1650 analyser [Siemens]. Serum was collected simultaneously for assays of Zn, Se, and vitamins A, C, and E. Serum vitamin C was assayed using high-performance liquid chromatography with fluorometric detection, after stabilisation and extraction with a metaphosphoric acid solution; the detection limit was 4 μmol/L and the normal range for the laboratory was 28–85 μmol/L. After deproteinisation with pure ethanol and extraction with hexane, vitamins A and E were separated using reverse-phase high-performance liquid chromatography and quantified using dual-wavelength spectrophotometry; normal ranges for the laboratory were 1.50–2.70 μmol/L for vitamin A and 21–35 μmol/L for vitamin E. Blood was collected in heparin tubes [Trace Element Vacutainer® Royal blue stopper, Becton Dickinson, Rungis, France] for measurement of serum Zn and Se using flame atomic absorption spectrometry with the AA 1100 analyser [Varian, les Ulis, France]; normal ranges for the laboratory were 12–18 μmol/L for Zn and 0.9–1.5 μmol/L for Se.

As recommended in guidelines for elderly individuals issued by the French National Authority for Health [HAS],[13] malnutrition was

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