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Association of a Low Serum Albumin with Infection and Increased Mortality in Critically Ill Patients

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Abstract. 214 patients among 282 consecutive admissions had at least one measurement of serum albumin (SA) during their stay on the ICU and were classified according to their lowest value of SA. Mean SA was 2.88 ± 0.74 g/100 ml. Survivors had a mean SA (3.18 ± 0.60) higher than non-survivors (2.35 ± 0.68 g/100 ml) ($p < 0.05$). 64% of patients were admitted with an abnormally low SA (less than 3.5 g/100 ml) and in 56% of these the initial value was higher than the last. Mortality increased in the groups with lower SA and the level of SA was associated with infection ($x^2 = 73.9$) and mortality ($x^2 = 69.7$) ($p < 0.05$). The percentage of infected patients who died increased in groups with lower SA.

Key words: Serum albumin – Hypoalbuminemia – Infection – Septicemia – Mortality on ICU

Introduction

Serum albumin (SA) reflects the state of visceral protein [2, 7] and has been used alone or with anthropometric measures as an indicator of the nutritional situation [3, 4, 6, 8, 19]. Infection complicates the management and leads to death in many intensive care patients, at the same time posing a catabolic burden [1, 14].

Patients and Methods

The records of 282 consecutive admissions (267 patients) to the Intensive Care Unit (ICU) were reviewed. Two hundred and fourteen patients had at least one SA measurement and they were classified according to their lowest value (Table 1). In 99 patients with only one SA measurement, this was considered as the lowest.

Forty-six percent of the patients were admitted from the Emergency Room, and 54% were transferred from within the hospital. Respiratory failure, acute or chronic (30%), neurological problems (23%), uncompensated diabetes (8%), shock (7%), cardiac (7%), hepatic (6%) and renal failure (5%) were the most frequent diagnoses. No patient was excluded from the analysis.

Serum albumin was determined by a colorimetric method using bromcresol green in an automated technique*. Every sample taken for culture was included as "cultures", except blood samples that were handled as a discrete group. Tracheal aspirates were obtained routinely twice a week, urine samples once a week and the other samples when clinically indicated. A patient was considered as infected with a positive blood culture; with a negative blood culture in association with temperature (>38 °C) and leukocytosis (>12000/mm^3) and with a positive culture (other than blood) in conjunction with fever and/or leukocytosis.

Blood for chemical and haematological tests was withdrawn in most instances on admission and thereafter at least once a week. Statistical analysis included Student's t-test for non paired observations and chi-square for categorical data.

Results

There were 172 males and 110 females. The overall mortality was 36%; it was not associated with the availability of SA determinations ($x^2 = 0.17$) and was

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Table 1. General data of the population

Group		I	II	III	IV	V
Lowest serum albumin (g/100 ml)		>3.5	3.4–3.0	2.9–2.5	2.4–2.0	<2.0
Number of patients		56	44	51	40	23
Age (years)	$\bar{x}$	47.2	49.7	53.9	62.2	60.8
	s.d.	20.6	19.2	17.3	12.2	9.1
Number of albumin determinations	$\bar{x}$	1.3	1.8	3.4	3.7	3.9
	s.d.	0.7	1.7	4.1	3.2	2.6
Lowest serum albumin (g/100 ml)	$\bar{x}$	3.81	3.22	2.67	2.24	1.61
	s.d.	0.27	0.14	0.15	0.13	0.32
Highest temperature (°C)	$\bar{x}$	37.4	37.8	38.3	39.0	38.8
	s.d.	0.8	0.9	1.3	1.2	1.4
Highest leukocytes ($\times 1000/mm^3$)	n	51	41	49	39	23
	$\bar{x}$	11.7	13.0	16.7	13.7	16.7
	s.d.	5.4	6.8	7.6	7.0	9.0
Bands and juvenile neutrophils (%)	$\bar{x}$	1.0	1.8	4.1	5.7	11.0
	s.d.	2.2	2.9	5.6	8.0	13.7
Lowest lymphocytes ($/mm^3$)	$\bar{x}$	1504	1081	677	512	315
	s.d.	818	529	503	352	246

Table 2. Infection and survival according to the lowest serum albumin

Group	I	II	III	IV	V	Total
Number of patients	56	44	51	40	23	214
Lowest serum albumin (g/100 ml)	>3.5	3.4–3.0	2.9–2.5	2.4–2.0	<2.0	–
Infected patients/all patients	11/56	19/44	40/51	36/40	23/23	129/214
% of infected patients	20	43	78	90	100	60
Infected non survivors/all infected	1/11	5/19	18/40	18/36	22/23	64/129
% of infected non survivors	9	26	45	50	96	50
Survivors non infected/all survivors	42/52	23/37	7/29	1/19	0/1	73/138
% of survivors non infected	81	62	24	5	–	53

similar in patients with or without SA measurements (36% and 38% respectively).

The mean SA was 2.88 ± 0.74 g/100 ml and survivors had a mean value (3.18 ± 0.60 g/100 ml) higher than non-survivors (2.35 ± 0.68 g/100 ml) ($p < 0.05$). Only 36% of patients were admitted with SA in excess of 3.5 g/100 ml. In 56% of the 115 patients with more than one SA measurement, values of SA lower than the initial were observed. Among fatalities the admitting SA was higher than the last in 67%, while survivors presented this finding in 74%.

In groups with lower SA the mean highest temperature and mean highest leukocyte count were raised. Lymphocyte counts were significantly higher in groups I and II than in the others ($p < 0.05$) (Table 1). Survivors had a mean lymphocyte count ($n = 129$, $\bar{x} = 1117 \pm 715/mm^3$) significantly higher than non survivors ($n = 74$, $\bar{x} = 635 \pm 1274/mm^3$) ($p < 0.05$).

The percentage of patients considered as infected and the mortality rate increased in groups with lower SA (Figs. 1 and 2). The lowest level of SA was associated with mortality ($x^2 = 69.7$) and with infection ($x^2 = 73.9$) ($p < 0.05$). Infection was statistically related to mortality ($x^2 = 26.7$) ($p < 0.05$) and the mortality rate of infected patients (50%) exceeded that of non-infected patients (14%).

Discussion

Although in 10% of our patients a low SA might have reflected the basic pathology, thus not representing malnourishment, hypoalbuminaemia, whatever its cause, cannot be considered as an index of adequate nutrition [4, 6] and usually a low albumin reveals a significant protein deficit [4]. We have considered, as other workers have done [3–6, 10], a level of SA

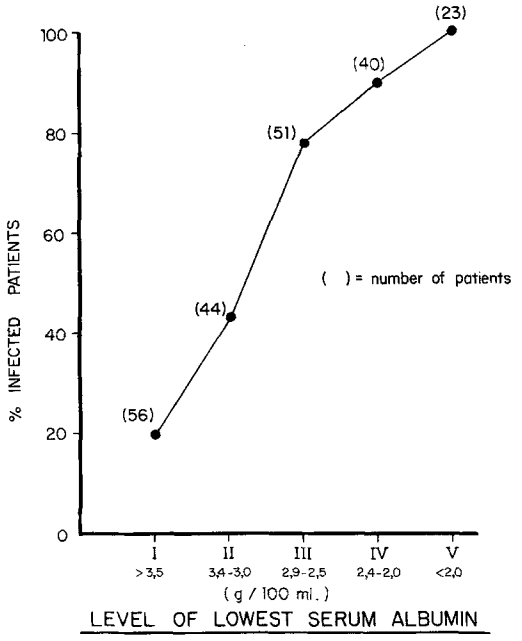

Fig. 1. The percentage of patients considered as infected raised progressively up to a 100% in the lowest serum albumin group

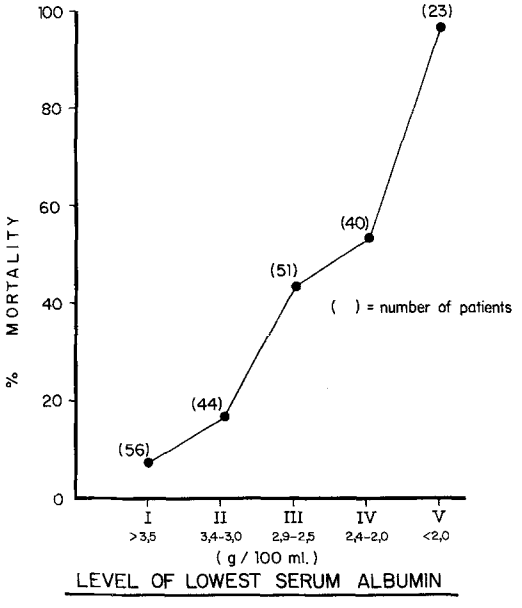

Fig. 2. Mortality rate raised as the level of serum albumin diminished, reaching 96% in the group of patients with the most severely depressed albumin

below 3.5 g/100 ml as abnormally low and indicative of malnutrition, although anthropometric variables were frequently taken into account in these studies [4, 6, 8].

Low SA levels are frequent in hospitalized patients [3, 4, 6] with greater reductions in the more severely ill [3]. More than half of our patients were admitted from hospital wards and two thirds of all cases had a reduced initial SA. Fifty six percent of ICU patients presented a low SA, but liver diseases were excluded [8]. We have not excluded any patient and nearly 66% of all subjects presented a low SA. Our survivors, as others have found [18] had a higher SA than non survivors, but in the present report all SA values were more depressed than in other series of ICU patients [18, 19].

The low SA may reflect the difficulty in maintaining a reasonable nutritional state in the presence of chronic or severe disease and also, possibly, a low level of attention towards the nutritional situation of these patients, while in hospital. Therefore we again emphasize the need for greater consideration of nutrition in hospitalized patients [4–6, 15].

Two factors might have been involved in the reduction of SA. Firstly a deficient protein intake; nutrition is most important in the regulation of albumin synthesis, an adequate nitrogen intake being essential [16]. Reduction in the rate of synthesis of albumin has been shown in human volunteers on low protein diets, and this soon reversed after it had been raised [9]. Secondly metabolic demands are increased; elevated temperature increases energy requirements and infection and sepsis raise urea nitrogen excretion as a reflection of hypercatabolism [1, 14] with a higher protein catabolism [12]. At the same time an anabolic demand is occurring during infection and protein synthesis has been found to be increased in sepsis [12].

An association between a low SA and infection has been found in ICU patients [8, 18] and serum albumin has been noted to be low in sepsis [19]. In our patients the incidence of infection increased as the level of SA decreased reaching 100% with SA below 2.0 g/100 ml.

Depressed cellular immunity has been found in malnourished hospitalized patients [5, 11] and in severely ill or injured patients [13]. Lymphopenia below 1200/mm^3 reflects a broad defect of cellular immunity [17] and lymphocyte counts have been found to be severely depressed in septic patients [19]. In our patients only those with SA higher than 3.5 g/100 ml exceeded 1200 lymphocytes/mm^3, which supports the idea of deranged cellular immunity in the lower SA groups. Interestingly, survivors had a higher lymphocyte count than non-survivors, as previously reported [18].

An association between infection, septicemia and mortality from infection was found in anergic patients who had a great risk of postoperative infectious complications [13] and an increased

mortality among ICU patients [18]. Appropriate protein repletion can increase their immune response [11].

The treatment of ICU patients represents a major challenge. Adequate nutrition whether enteral or parenteral may influence the evolution and prevent or retard nutritional deterioration with the consequences of infection and increased mortality.

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