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Guidelines for the Clinical Use of Albumin: Comparison of Use in Two Italian Hospitals and a Third Hospital Without Guidelines

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ABSTRACT

Background: In the absence of clinical practice guidelines prior to 1999, the consumption of human albumin in the Liguria region of Italy was very high, despite possible adverse effects, limited supply, and significant cost.

Objective: The purpose of this study was to assess the impact of comprehensive guidelines on the amount of albumin used in 2 general hospitals and to compare it with that of a third general hospital that did not adopt the guidelines.

Methods: We analyzed the influence of the guidelines on albumin use in 2 general hospitals (hospitals 1 and 2) in the Liguria region by comparing albumin consumption during the year before the distribution of the guidelines (1999) with consumption in the 2 years after their distribution (2000 and 2001). We compared these data with those of a third general hospital that did not adopt the guidelines (hospital 3). The parameters considered were total consumption of albumin, consumption per bed, consumption per hospital stay, mean time to discharge, expenditure per bed, and mortality rate.

Results: In the years 2000 and 2001, the adoption of guidelines reduced albumin consumption in hospitals 1 and 2. In hospital 1, where the release of albumin was carefully controlled by the transfusion service, albumin use per hospital stay decreased 8.7% in 2000 and 7.6% in 2001 from 1999; in hospital 2, use decreased 73.8% and 77.4%, respectively, from 1999. In hospital 3, rejection of the guidelines was coupled with an increase of 2.9% and 8.4%, respectively, in the amount of albumin used per hospital stay. In the years 2000 and 2001, the savings in the expenditure for albumin was ~17,000 euro in hospital 1 and ~200,000 euro in hospital 2.

Conclusion: This study confirms that the adoption of guidelines may substantially reduce the inappropriate use of albumin and relative costs. (*Curr Ther Res Clin Exp.* 2003;64:676–684) Copyright © 2003 Excerpta Medica, Inc.

Key words: clinical use of albumin, guidelines, efficacy of guideline application.

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INTRODUCTION

The role of the infusion of human albumin in treating patients with critical illnesses has been debated for ≥20 years because of the possible adverse effects, significant cost, and limited supply. In an observational study[1] in 15 academic health centers in the United States, the appropriateness of the use of albumin and nonprotein colloids was assessed using 969 case reports. The administration of these products was found to be appropriate in 24% of cases, inappropriate in 62%, and unevaluable in 14%. Two meta-analyses[2,3] published in 1998 demonstrated that the use of albumin and nonprotein colloids in critically ill patients was associated with increased mortality. The first meta-analysis,[2] based on the systematic review of 37 randomized controlled trials, of which 26 compared colloids with crystalloids, indicated that resuscitation with colloids was associated with an increased absolute risk for mortality of 4% (95% CI, 0%–8%). The second meta-analysis,[3] based on 30 randomized controlled trials comparing administration of albumin or plasma protein fractions with or without crystalloid solutions, indicated that with albumin the pooled difference in the risk for death was 6% (95% CI, 3%–9%). Finally, a cumulative meta-analysis[4] demonstrated that in patients treated with albumin, the increase in mortality was already significant in studies published before 1993 and was confirmed year after year by subsequent studies. Several letters[5] questioned the absence of a critical analysis of the studies considered in the above-mentioned meta-analyses; however, as expressed in an editorial,[6] it seems more appropriate to plan new large trials than simply to defend current practice.

In view of these considerations, and taking into account the high albumin consumption in hospitals of the Liguria region of Italy (732 kg in 1997 and 812 kg in 1998), as well as the wide differences in its use among various hospitals, guidelines for the use of albumin and nonprotein colloid and crystalloid solutions were developed through a systematic, literature-based consensus process by a multidisciplinary group of clinicians and researchers with experience in the use of these products.

These guidelines and the new form for requesting albumin, which has a summary of the guidelines printed on the back, were distributed to all hospitals in the Liguria region in December 1999. The purpose of this study was to assess the impact of these guidelines on the amount of albumin used in 2 general hospitals and to compare it with that of a third general hospital that did not adopt the guidelines.

METHODS

We analyzed the influence of the guidelines on albumin use (summarized below) in 2 general hospitals (hospitals 1 and 2) in the Liguria region by comparing albumin consumption during the year before the distribution of the guidelines (1999) with consumption in the 2 years after their distribution (2000 and 2001). To verify whether changes in albumin use were a consequence of the guidelines,

albumin consumption in the same 3 years was analyzed in a third general hospital that did not adopt the guidelines (hospital 3). The parameters considered were total consumption of albumin, consumption per bed, consumption per hospital stay, mean time to discharge, expenditure per bed, and mortality rate. The consumption of albumin was obtained from the hospital pharmacy, and the number of beds and hospital stays from the hospital administration.

A quantitative analysis of the effect of the reduction in albumin use attributable to the adoption of the guidelines was not performed. Rather, interviews with physicians at both hospitals were used to determine changes in mean time to discharge, expenditure per bed, and mortality rate.

Summary of Guidelines

The following is a summary of the guidelines adopted by hospitals 1 and 2.

Hemorrhagic Shock

Crystalloid solutions should be the initial choice for the treatment of hemorrhagic shock. Colloids are appropriate in conjunction with crystalloids when blood products are not available. Nonprotein colloids, due to better cost-effectiveness, should be favored over albumin, except when sodium must be restricted (25% albumin diluted to 5% with 5% dextrose) or when nonprotein colloids are contraindicated.[7–10]

Nonhemorrhagic (Maldistributive) Shock

Crystalloid solutions should be considered the first-line therapy for nonhemorrhagic shock. Nonprotein colloids may be used in the presence of capillary leak with pulmonary and/or peripheral edema or following administration of ≥2 L of crystalloid solution without effect. Albumin may be used when nonprotein colloids are contraindicated.[7,11]

Major Surgery

Crystalloid solutions are recommended to maintain circulating volume after >40% hepatic resection. The administration of nonprotein colloid or albumin solutions may be appropriate if required, depending on the amount of residual hepatic and hemodynamic function. In these cases, nonprotein colloids are the favored cost-effective alternative. Albumin administration may be indicated when the serum albumin level is <20 g/L after correction for volemia.[7]

Thermal Injury

Crystalloid solutions should be used within the first 24 hours after thermal injury. The administration of colloids in conjunction with crystalloids is appropriate if all the following conditions are met: (1) burns cover >50% of the body surface area; (2) at least 24 hours have passed since the occurrence of the burn; and (3) crystalloid treatment did not correct hypovolemia. Albumin should be used only when nonprotein colloids are contraindicated.[7,12,13]

Cerebral Ischemia

Colloid (both nonprotein and albumin) solutions should not be used in ischemic stroke or subarachnoid hemorrhage, except in patients whose hematocrit is <40% on admission. Crystalloid solutions should be administered to patients with elevated hematocrit to create hypervolemia and hemodilution and thus maximize cerebral perfusion.[7,12]

Cardiac Surgery

Crystalloids should be considered the first choice as the priming solution for cardiopulmonary bypass pumps. The addition of nonprotein colloids may be preferable when it is extremely important to avoid pulmonary interstitial fluid accumulation. Crystalloids are the first-line treatment for postoperative volume expansion, nonprotein colloids are the second choice, and albumin is the third choice. Nonprotein colloids may be useful in reducing systemic edema.[7,14,15]

Neonatal Hyperbilirubinemia

Albumin should not be administered in conjunction with phototherapy or prior to exchange transfusion. Albumin has been used with mixed results as an adjuvant to exchange transfusion. Crystalloids and nonprotein colloids do not bind bilirubin and therefore should not be considered alternatives to albumin.[7]

Organ Transplantation

A conclusive demonstration that albumin and nonprotein colloids are effective during or after renal transplantation is still lacking. Albumin may be useful in controlling ascites and peripheral edema in the postoperative period of hepatic transplantation if all of the following conditions are met: (1) serum albumin level <25 g/L; (2) pulmonary capillary wedge pressure <12 mm Hg; and (3) hematocrit >30%.[7]

Plasmapheresis

Albumin administration is appropriate only in conjunction with large-volume plasma exchange (>20 mL/kg in 1 session) and only in the second phase of the procedure.[7,16]

Cirrhosis and Paracentesis

Albumin administration is useful in preventing complications associated with large-volume paracentesis (3–4 L). In this case, 4 to 8 g of albumin/L of ascitic fluid removed should be used.[7] Albumin 12.5 g/d is effective in improving the rate of response and preventing recurrence of ascites in cirrhotic patients with ascites who are receiving diuretics.[17] In patients with cirrhosis and spontaneous bacterial peritonitis, treatment with albumin in addition to an antibiotic reduces the incidence of renal impairment and death compared with treatment with an antibiotic alone.[18]

Nephrotic Syndrome
Short-term administration of albumin in conjunction with diuretic therapy should be considered appropriate in patients with acute severe pulmonary or peripheral edema.[7,16]

Hemodialysis
Albumin for the treatment of hypotension in patients undergoing hemodialysis seems to be useful in only 2% of patients.[19,20]

Nutritional Intervention
Albumin should not be used as a source of protein in patients requiring nutritional intervention. However, albumin may be appropriate in patients with diarrhea associated with intolerance to enteral feeding if all of the following conditions are met: (1) significant diarrhea (>2 L/d); (2) serum albumin <20 g/L; and (3) persistence of diarrhea despite administration of short-chain peptides and elemental formula.[7]

RESULTS

Albumin consumption in hospitals 1 and 2 is shown in Table I. In 1999, albumin consumption per bed and per stay in hospital 1 was markedly lower than in hospital 2. In hospital 1, the consumption per hospital stay was 36.5% of that of hospital 2. Therefore, it is not surprising that in the years after the distribution of the guidelines (2000 and 2001), albumin consumption per hospital stay decreased in hospital 1 by only 8.7% in 2000 and 7.6% in 2001 compared with 1999. In hospital 2, where albumin was and still is distributed by the hospital pharmacy, the reduction that occurred in albumin consumption per hospital stay after the distribution of the guidelines was more marked (73.8% in 2000 and 77.4% in 2001).

Table I. Albumin consumption in 2 general hospitals before the distribution of the guidelines (1999) and in the 2 years after their distribution (2000 and 2001).

	Hospital 1			Hospital 2		
Parameter	1999	2000	2001	1999	2000	2001
Beds, no.	653	650	629	553	574	556
Hospital stays, no.	211,800	204,966	192,236	179,627	179,098	171,731
Albumin consumption, kg	19.59	17.20	16.28	45.24	11.76	9.71
Albumin consumption per bed, g	30.00	26.46	25.88	81.81	20.49	17.46
Albumin consumption per hospital stay, g	0.092	0.084	0.085	0.252	0.066	0.057

Table II shows albumin consumption as a percentage of total consumption in the different divisions of hospitals 1 and 2. If these percentages are compared with albumin consumption per hospital stay listed in Table I, it appears that in hospital 1 the limited reduction in albumin consumption was mainly due to the lower use of albumin by anesthesiologists in both 2000 and 2001 and by the transfusion service in 2001. In the same 2 years, a marked reduction in albumin use took place in all divisions of hospital 2, with the exception of the transfusion service.

Physician interviews revealed that mean time to discharge, expenditure per bed, and mortality rate did not change much after distribution of the guidelines. In the years 2000 and 2001, the savings in the expenditure for albumin was ~17,000 euro in hospital 1 and ~200,000 euro in hospital 2.

The data listed in Table III indicate that in hospital 3, where the guidelines were not adopted, albumin consumption per hospital stay was consistently higher than in the other 2 hospitals. In 1999 albumin use was 5.96-fold that of hospital 1 and 2.17-fold that of hospital 2; in 2000 and 2001 it increased 2.9% and 8.4%, respectively.

DISCUSSION

The results of this study indicate that in the absence of guidelines for albumin consumption the amount of albumin used probably was mainly dependent on the presence or absence of careful control of its delivery, as indicated by the markedly lower consumption in hospital 1, where the control of requests for albumin was exerted by the transfusion service through verification of patients' laboratory and clinical data, compared with consumption in hospital 2, where albumin was delivered by the hospital pharmacy. The adoption of the guidelines resulted in a reduction of albumin consumption in both hospitals; however, the reduction was markedly greater in hospital 2, where it was the consequence of both the increased appropriateness of the requests and of their more accurate control by the hospital pharmacy. Although progressive awareness by physicians

Table II. Percentage of total albumin consumption by division in the 2 hospitals in 1999, 2000, and 2001.

	Hospital 1			Hospital 2		
Division	1999	2000	2001	1999	2000	2001
Transfusion service	37.52	41.92	32.25	9.29	28.91	25.77
Internal medicine and medical specialties	29.51	25.35	37.78	21.69	27.55	35.67
General surgery and surgical specialties	23.58	25.46	23.77	53.43	33.08	29.90
Anesthesiology	9.39	7.27	6.20	15.59	10.46	8.66

Table III. Albumin consumption in 1999, 2000, and 2001 in the general hospital that did not adopt the guidelines.

Parameter	1999	2000	2001
Beds, no.	2112	2095	2084
Hospital stays, no.	692,787	685,380	659,125
Albumin consumption, kg*	379.96	386.71	391.36
Albumin consumption per bed, g	179.91	184.59	187.79
Albumin consumption per hospital stay, g	0.548	0.564	0.594

*This consumption does not include the unknown amount of albumin provided directly to the transfusion service without going through the hospital pharmacy.

of the proper use of albumin cannot be excluded as a cause of reduced albumin consumption, the important role of the guidelines in reducing albumin consumption is indicated by the fact that in the first 3 months after their distribution the amount of the reduction in albumin consumption was similar to that observed in the successive 21 months in both hospitals. Finally, it is worth noting that not only did the decrease in albumin consumption persist substantially unchanged in the 2 years after the adoption of the guidelines (2000 and 2001), but also the decrease continued in the year 2002, according to information provided by the 2 hospitals.

The importance of guidelines in ensuring appropriate use of albumin is confirmed by the comparison with a third general hospital in the Liguria region, in which the distribution of the guidelines and of the new request form did not take place despite several discussions with the hospital pharmacy. The high albumin consumption in this hospital, which in the 3 years considered caused a total expense of ~1 million euro/y, may be justified to a limited extent by the existence of some surgical divisions not present in the other 2 hospitals: the Division for Organ Transplantation and the Division of Plastic Surgery–Severe Thermal Injuries. However, in 1999 these 2 divisions consumed only 42% of the total amount of albumin used by all surgical departments. In addition, high albumin consumption in the Division of Hematology cannot be excluded, due to the high number of patients with severe blood diseases who choose this division because of their widely recognized skill in the therapeutic approach; however, the amount of albumin consumed was only 32% of the total amount used by the divisions of internal medicine and medical specialties. Therefore, it is evident that albumin consumption in this hospital was inappropriate and excessive in all 3 years considered.

CONCLUSIONS

This analysis of the consumption of albumin in 3 hospitals of the Liguria region of Italy supports the conclusion that the acceptance of the guidelines resulted

in a significant reduction in the inappropriate use of albumin. On the basis of our findings, we recommend that hospital 3 adopt the guidelines because of the increased risk for mortality in patients treated with albumin in the absence of an appropriate indication and the limited availability of resources, requiring careful assessment of the cost/benefit ratio. If albumin consumption per hospital stay in hospital 3 were reduced to 2-fold that of the hospital, the savings would be ~900,000 euro/y.

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