Retrospective Clinical Research Report

Single-center analysis of the inappropriate use of human albumin and nutritional support in hospitalized patients with hypoproteinemia in China

Jin Zhang, ZheTao Zhang and TianLu Shi

Abstract

**Background:** This study used single-center analysis of human serum albumin clinical usage and enteral-parenteral nutritional support to establish clinical application standards for the rational use of human serum albumin.

**Methods:** A total of 1984 patients receiving human serum albumin were enrolled in this retrospective study to analyze the rational application of human serum albumin and enteral-parenteral nutritional support.

**Results:** Among 1984 patients, 1044 (52.6%) were found to have irrational applications for human serum albumin use. Major indications for irrational applications were hypoproteinemia (30.0%) and nutritional support (21.9%). Surgical departments including thoracic surgery, orthopedics, and neurosurgery had the most irrational applications, occupying 18.4%, 8.4%, and 4.2%, respectively. A total of 1627 patients (82%) required nutritional support and 745 (45.8%) had irrational nutritional support. Moreover, 694 patients (35.0%) received human serum albumin as the only source of nutritional support.

**Conclusions:** Clinical training and the establishment of an approval system should be used to enhance the rational use of human serum albumin, ensuring medication safety, reducing medical costs, and avoiding the waste of medical resources.

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Introduction

Albumin is a negatively charged globular protein synthesized by hepatocytes that constitutes almost 50% of total human proteins and is the most abundant protein of extracellular fluid. As a physiological plasma volume dilator, albumin is a crucial determinant of plasma colloid osmotic pressure and regulates the balance of plasma volume and interstitial fluid. It is also involved in the transport of endogenous free bilirubin and exogenous drugs, and plays important roles in multiple physiological processes, including anti-oxidation, anti-inflammation, blood coagulation mediated by platelet aggregation, heman-giectasis, and pH regulation.

Human serum albumin is one of the blood products extracted from human venous plasma or the placenta. Hypoproteinemia is diagnosed when the concentration of serum albumin is less than 35.0 g/L, resulting in the clinical symptoms of malnutrition and edema. Nutritional support is a form of medical nutritional intervention used to alleviate or prevent malnutrition via oral, enteral, and parenteral channels. It is an important part of medical treatment that aids recovery and improves health and the quality of life.

Enteral and parenteral methods of nutritional support are often under-utilized during hospitalization. Moreover, when parenteral nutritional support is used, the delivery of amino acids or fat emulsion preparations alone without the integration of glucose can lead to insufficient energy supplies and increased adverse drug reactions in patients. Additionally, the improper application of human serum albumin as nutritional support to replace enteral and parenteral nutritional support is unreasonable clinical practice, and it cannot be used alone as nutritional support for the improvement of serum albumin levels.

Therefore, in consideration of the high production costs of human serum albumin, there is an urgent need to establish standards for the clinical application of human serum albumin.

Materials and methods

Patients

Between July and December 2018, 1984 patients being administered human serum albumin at the First Affiliated Hospital of University of Science and Technology of China were randomly selected for enrollment in this retrospective study. Human serum albumin was purchased from Tonrol Biopharmaceutical (Hefei, China) (20%, 25 mL: 5 g) or Hualan Biological Bacterin Co., Ltd. (Xinxiang, China) (10%, 50 mL: 5 g). The research was performed in accordance with the Declaration of Helsinki and was approved by the Human Ethics Committee of the First Affiliated Hospital of University of Science and Technology of China (date of approval: January 1, 2018 to December 31, 2018). All patients provided their written informed consent to receiving treatment and study participation, and have
been de-identified. The study was conducted in accordance with the Declaration of Helsinki and the review board of the First Affiliated Hospital of University of Science and Technology of China approved the study.

**Survey methods**

The Prescription Automatic Screening System was used to investigate the records of patients involved in the study to collect the following information: age, sex, diagnosis, hospital department, human serum albumin level before and after treatment, the total use and expenditure of human serum albumin, course of treatment, NRS-2002 scoring, and the classification and type of enteral and parenteral nutritional support. This information was used to analyze the rationality of human serum albumin clinical applications and enteral and parenteral nutritional support. This survey follows Equator network guidelines.11

**Standards of human serum albumin clinical application rationality evaluation**

Published guidelines were used to establish standards for human serum albumin clinical application rationality evaluation.12–16 Indications for the rational use of human serum albumin include the shock induced by hemorrhage, trauma, and burns, the increased brain pressure induced by encephal edema and cerebral lesions, edema or ascites induced by liver cirrhosis and nephropathy, neonatal hyperbilirubinemia, adjuvant therapies for cardiopulmonary bypass, burns and hemodialysis, adult respiratory distress syndrome, severe hypoproteinemia (human serum albumin level <20.0 g/L), cardiac surgery, paracentesis, spontaneous bacterial peritonitis, and diuresis.12–14 Indications for the irrational use of human serum albumin include nutritional support, hypoproteinemia (human serum albumin level 20.0–35.0 g/L), peripheral edema, anemia, serious infection, post-operative wound healing, pancreatitis, and pleural effusion.12–14 Intravenous drip or injection were used as the main methods of human serum albumin administration.

**Standards of nutritional support rationality evaluation**

If body mass index (BMI) cannot be calculated because of disease, NRS-2002 scoring is an alternative means of determining nutritional risk screening. NRS-2002 scoring of 3 means that serum albumin levels are lower than 35.0 g/L to meet the standards for nutritional support. NRS-2002 scores of patients were collected and analyzed. Published guidelines were used to establish standards for nutritional support rationality evaluation, including ‘ESPEN Guidelines on Enteral Nutrition: intensive care’, ‘ESPEN Guidelines on Parenteral Nutrition: intensive care’, ‘Clinical Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients 2009’, and ‘Clinical diagnosis and treatment guide for parenteral and enteral nutrition support in China’.17–19 According to the rational nutritional support program, patients with NRS-2002 ≥3 were diagnosed as having nutritional risk, so an individualized nutritional support plan was developed according to their clinical circumstance, including enteral nutrition, parenteral nutrition, and enteral-parenteral nutrition. When NRS-2002 <3, patients were diagnosed as having no nutritional risk, and NRS-2002 Nutritional Risk Screening was conducted weekly for each inpatient. Once NRS-2002 was found to be ≥3, nutritional support was given immediately.20,21 The rationality analysis and evaluation of human albumin application was conducted on the basis of indications for the irrational use of human serum albumin and nonstandard clinical nutritional support, and
included inpatients without nutritional risk screening or weekly NRS-2002 scoring or completed NRS-2002 scores. Patients with NRS-2002 ≥3 but not using nutritional support and patients with NRS-2002 <3 but using nutritional support were deemed to be following irrational applications.

Results

Data on the use of human serum albumin and nutritional support

According to the survey results shown in Table 1, there were 1984 patients using human serum albumin with 32,339.2 U. The per capita amount was 16.3 U and the per capita treatment course was 5.7 days. A total of 1134 patients were men (57.2%) and 850 were women (42.8%). Patients aged from 60 to 74 years old represent 44.5% of the total and had the highest per capita amount of 18.4 U and the per capita treatment course of 6.3 days compared with other age groups.

Human serum albumin was widely used in 21 departments including in 405 patients in neurosurgery, 366 patients in thoracic surgery, and 299 patients in cardiac surgery. The neurosurgery department used 27.7 U per capita overran average treatment course of 8.4 days, thoracic surgery used 23 U per capita over 7.7 days, and critical care medicine used 18.9 U per capita over 6.3 days. Regarding irrational human serum albumin use, the departments of thoracic surgery, orthopedics, and neurosurgery comprised 18.4%, 8.4%, and 4.2%, respectively. These results show that the surgery departments in the surveyed hospital had the most human serum albumin users, and total and per capita use.

Among 1984 patients using human serum albumin, 3.7% received enteral nutritional support, 4.5% received parenteral nutritional support, 62.2% received enteral-parenteral nutritional support, and 29.6% lacked enteral or parenteral nutritional support. A total of 922 patients (46.5%) received irrational nutritional support, 771 of whom (38.9%) received human serum albumin alone as nutritional support (9.3% in neurosurgery, 7.2% in cardiac surgery, and 7.1% in orthopedics). Furthermore, 141 patients (7.1%) received amino acids alone as nutritional support (1.8% in gastroenterology, 1.4% in thoracic surgery, and 1.0% in critical care medicine), and 325 patients received fat emulsion alone as nutritional support (10.5% in cardiac surgery, 4.4% in neurosurgery, and 0.3% in thoracic surgery). Because of insufficient nutritional support training, 747 patients (37.7%) had false or missing NRS-2002 scoring. These data show that the surgery departments in the surveyed hospital also had the most patients receiving irrational nutritional support.

Data on the indications for using human serum albumin

Among all patients using human serum albumin, 1044 (52.6%) had irrational indications for its use. Hypoproteinemia (serum albumin 20.0–35.0 g/L) and nutritional support were the two most common irrational indications, seen in 597 patients (30.0%) and 434 patients (21.9%), respectively. Other irrational indications included pleural effusion, peripheral edema, serious infection, postoperative wound healing, anemia, and pancreatitis. Overall, the irrational use of human serum albumin represented 48.66% of the total (Table 2).

As the major indications for the irrational use of human serum albumin, hypoproteinemia and nutritional support constituted 20.83% and 27.13% of the total amount used, respectively (Table 2). Additionally, 59.1% of patients with hypoproteinemia and 16.6% of patients with nutritional support received irrational nutritional support. The irrational use of
Table 1. Patient information on the use of human serum albumin and nutritional support

| Information                        | Total users (%) | Irrational users (%) | Per capita use amount/treatment course | Total irrational nutritional support (%) | Human serum albumin alone (%) | Amino acids alone (%) | Fat emulsion alone (%) | False or missing NRS-2002 scoring (%) |
|------------------------------------|-----------------|----------------------|---------------------------------------|------------------------------------------|-------------------------------|----------------------|-----------------------|----------------------------------------|
| Total                              | 1984 (100%)     | 1044 (52.6%)         | 16.3/5.7                              | 922 (46.5%)                              | 38.9                          | 7.1                  | 16.4                  | 37.7                                   |
| Sex                                |                 |                      |                                       |                                          |                               |                      |                       |                                        |
| Male                               | 1134 (57.2%)    | 624 (31.5%)          | 17.2/6.1                              | 448 (22.6%)                              | 19.0                          | 4.0                  | 8.4                   | 18.5                                   |
| Female                             | 850 (42.8%)     | 420 (21.2%)          | 15.2/5.1                              | 474 (23.9%)                              | 19.9                          | 3.1                  | 8.0                   | 19.2                                   |
| Age range (years)                  |                 |                      |                                       |                                          |                               |                      |                       |                                        |
| 0–17                               | 41 (2.1%)       | 9 (3.0%)             | 3.2/1.9                               | 9 (0.5%)                                 | 0.3                           | 0.2                  | 0.1                   | 0.3                                    |
| 18–44                              | 230 (11.6%)     | 90 (30.0%)           | 13.6/4.6                              | 121 (61.1%)                              | 5.0                           | 0.5                  | 1.6                   | 4.8                                    |
| 45–59                              | 549 (27.7%)     | 231 (77.0%)          | 15.8/5.3                              | 288 (14.5%)                              | 11.6                          | 1.8                  | 5.9                   | 12.0                                   |
| 60–74                              | 882 (44.5%)     | 524 (26.4%)          | 18.4/6.3                              | 383 (19.3%)                              | 16.3                          | 2.6                  | 7.6                   | 17.4                                   |
| ≥75                                | 282 (14.2%)     | 190 (63.3%)          | 14.8/6.1                              | 212 (61.1%)                              | 11.6                          | 2.1                  | 1.2                   | 7.2                                    |
| Department                         |                 |                      |                                       |                                          |                               |                      |                       |                                        |
| Neurosurgery                       | 405 (20.4%)     | 84 (4.2%)            | 27.7/8.4                              | 212 (10.7%)                              | 9.3                           | 0.5                  | 4.4                   | 9.1                                    |
| Cardiac surgery                    | 299 (15.1%)     | 16 (0.8%)            | 8.4/2.5                               | 235 (11.8%)                              | 7.2                           | 0.1                  | 10.5                  | 7.2                                    |
| Thyroid breast surgery             | 3 (0.2%)        | 3 (0.2%)             | 5.0/1.3                               | 3 (0.2%)                                 | 0.2                           | 0                    | 0                     | 0.2                                    |
| Otorhinolaryngology head and neck surgery | 32 (1.6%) | 32 (1.6%)         | 17.2/8.9                              | 4 (0.2%)                                 | 0.2                           | 0.1                  | 0.1                   | 0.2                                    |
| Thoracic surgery                   | 366 (18.4%)     | 365 (18.4%)          | 23.0/7.7                              | 40 (2.0%)                                | 1.9                           | 1.4                  | 0.3                   | 5.1                                    |
| Orthopedics                        | 172 (8.7%)      | 166 (8.4%)           | 7.8/2.8                               | 161 (8.1%)                               | 7.1                           | 0.1                  | 0.2                   | 7.3                                    |
| Emergency surgery                  | 56 (2.8%)       | 52 (2.6%)            | 16.8/4.8                              | 5 (0.3%)                                 | 0.3                           | 0.2                  | 0                     | 0.8                                    |
| Obstetrics                         | 28 (1.4%)       | 24 (1.2%)            | 7.1/3.1                               | 28 (1.4%)                                | 1.4                           | 0                    | 0.1                   | 1.2                                    |
| Neurology                          | 67 (3.4%)       | 29 (1.5%)            | 16.7/6.9                              | 34 (1.7%)                                | 1.8                           | 0.3                  | 0                     | 0.7                                    |
| Vascularocardiology                | 30 (1.5%)       | 16 (0.8%)            | 7.5/4.6                               | 20 (1.0%)                                | 1.1                           | 0.2                  | 0.1                   | 0.6                                    |
| Gastroenterology                   | 78 (3.9%)       | 38 (1.9%)            | 10.2/5.1                              | 60 (3.0%)                                | 3.0                           | 1.8                  | 0.2                   | 0.9                                    |
| Respiratory medicine               | 16 (0.8%)       | 12 (0.6%)            | 6.0/3.9                               | 14 (0.7%)                                | 0.6                           | 0.3                  | 0                     | 0                                      |
| Nephrology                         | 64 (3.2%)       | 5 (0.3%)             | 8.1/5.1                               | 1 (0.1%)                                 | 0                             | 0.1                  | 0                     | 0.6                                    |
| Carcinoma chemotherapy             | 28 (1.4%)       | 18 (0.9%)            | 6.6/3.7                               | 14 (0.7%)                                | 0.6                           | 0.2                  | 0.2                   | 0.5                                    |
| Geriatric                          | 49 (2.5%)       | 44 (2.2%)            | 5.9/5.5                               | 22 (1.1%)                                | 1.0                           | 0.7                  | 0                     | 0.9                                    |
| Emergency medicine                 | 26 (1.3%)       | 18 (0.9%)            | 3.7/1.9                               | 11 (0.6%)                                | 0.7                           | 0.3                  | 0.1                   | 0.4                                    |
| Rehabilitation medicine            | 17 (0.9%)       | 13 (0.7%)            | 10.9/6.4                              | 5 (0.3%)                                 | 0.3                           | 0.2                  | 0.1                   | 0.3                                    |

(continued)
human serum albumin for hypoproteinemia mainly occurred in the departments of orthopedics (7.3%), neurosurgery (3.6%), critical care medicine (7.1%), and gynecology (7.1%), while its irrational use for nutritional support mainly occurred in thoracic surgery (17.1%), otorhinolaryngology head and neck surgery (1.5%), and orthopedics (1.0%).

Data on serum albumin levels for using human serum albumin

According to the last serum albumin level detection before its administration, all 74 patients with severe hypoproteinemia (serum albumin <20.0 g/L) had rational indications for using human serum albumin. Among 586 patients with serum albumin ≥35.0 g/L, 29.5% received human serum albumin and 12.1% had irrational indications for doing so. Nutritional support was the most common irrational indication (10.43%). Of 1,324 patients with serum albumin 20.0 to 35.0 g/L, 803 (40.5%) had irrational indications for receiving human serum albumin. Altogether, patients with serum albumin 20.0 to 35.0 g/L had the most irrational indications for using human serum albumin.

Data on enteral-parenteral nutritional support for using human serum albumin

As shown in Table 3, 51.9% of human serum albumin was used to treat severe hypoproteinemia (serum albumin <20.0 g/L) and for nutritional support. To analyze the nutritional support of patients using human serum albumin based on the last serum albumin level detection before its administration, rationality analysis of enteral and parenteral nutritional support was conducted for all 1984 patients using human serum albumin. A total of 982 patients (49.5%) had an NRS-2002 score >3, and 645 patients (32.5%) with NRS-
Table 2. Patient rational and irrational indication analysis

| Irrational indications                      | Total user ratio | Use amount ratio | Serum albumin (≥35.0 g/L) | Serum albumin (20.0–35.0 g/L) | Serum albumin (≤20.0 g/L) | Irrational nutritional support ratio |
|--------------------------------------------|------------------|------------------|---------------------------|-----------------------------|---------------------------|-------------------------------------|
| Hypoproteinemia (Serum albumin 20.0–35.0 g/L) | 30.0             | 20.83            | 1.41                      | 28.58                       | 0.0                       | 59.0                                |
| Nutritional support                        | 21.9             | 27.13            | 10.43                     | 11.44                       | 0.0                       | 16.6                                |
| Pleural effusion                           | 0.3              | 0.14             | 0.10                      | 0.15                        | 0.0                       | 40                                  |
| Peripheral edema                           | 0.2              | 0.40             | 0.0                       | 0.20                        | 0.0                       | 50                                  |
| Serious infection                          | 0.1              | 0.04             | 0.10                      | 0.0                         | 0.0                       | 100                                 |
| Postoperative wound healing                 | 0.1              | 0.05             | 0.0                       | 0.10                        | 0.0                       | 100                                 |
| Anemia                                     | 0.1              | 0.01             | 0.05                      | 0.0                         | 0.0                       | 100                                 |
| Pancreatitasis                              | 0.1              | 0.02             | 0.05                      | 0.0                         | 0.0                       | 0.0                                 |
| Rational indications                        |                  |                  |                           |                             |                           |                                     |
| Increased brain pressure                   | 23.0             | 38.87            | 8.01                      | 14.87                       | 0.10                      | 41.4                                |
| Expansion after cardiac surgery            | 13.1             | 6.54             | 7.06                      | 6.05                        | 0.0                       | 79.2                                |
| Edema or ascites induced by nephropathy     | 3.0              | 1.46             | 0.15                      | 1.71                        | 1.16                      | 5                                   |
| Severe hypoproteinemia                     | 2.3              | 1.63             | 0.0                       | 0.0                         | 2.32                      | 54.3                                |
| (Serum albumin ≤20.0 g/L)                  |                  |                  |                           |                             |                           |                                     |
| Edema or ascites induced by liver cirrhosis| 1.8              | 0.95             | 0.0                       | 1.66                        | 0.15                      | 83.3                                |
| Edema or ascites induced by liver cirrhosis|                  |                  |                           |                             |                           |                                     |
| Diuresis                                   | 1.2              | 0.27             | 0.50                      | 0.71                        | 0.0                       | 50                                  |
| Cardiac surgery                            | 1.0              | 0.62             | 0.60                      | 0.40                        | 0.0                       | 70                                  |
| Hyperbilirubinemia of newborn               | 0.9              | 0.07             | 0.81                      | 0.05                        | 0.0                       | 5.9                                 |
| Colloid osmotic pressure increase           | 0.5              | 0.57             | 0.15                      | 0.30                        | 0.0                       | 22.2                                |
| Paracentesis                               | 0.4              | 0.13             | 0.05                      | 0.30                        | 0.0                       | 71.4                                |
| Shock induced by hemorrhage, trauma, and burns| 0.2              | 0.13             | 0.0                       | 0.15                        | 0.0                       | 33.3                                |
| Hematodialysis                             | 0.1              | 0.01             | 0.05                      | 0.0                         | 0.0                       | 0.0                                 |
| Infectious shock                           | 0.1              | 0.14             | 0.0                       | 0.05                        | 0.0                       | 100                                 |
Table 3. Nutritional support of patients using human serum albumin

| Serum albumin level (g/L) | Number of cases | NRS-2002 scoring | Number of cases (%) | Type of nutritional support | Number of cases (%) | Irrational nutritional support (%) | Type of irrational nutritional support | Number of cases |
|--------------------------|-----------------|------------------|--------------------|-----------------------------|--------------------|-----------------------------------|----------------------------------------|----------------|
| ≥ 35.0                   | 586             | <3               | 357 (18.0)         | Enteral nutrition           | 9 (0.45)           | 176 (49.3)                        | Amino acids alone                      | 13             |
|                          |                 |                  |                    | Parenteral nutrition        | 18 (0.91)          |                                   | Fat emulsion alone                      | 106            |
|                          |                 |                  |                    | Enteral-parenteral nutrition | 235 (11.84)       |                                   | Human serum albumin alone               | 77             |
|                          |                 |                  |                    | No nutritional support      | 95 (4.79)          | False or missing NRS-2002 scoring |                                       | 117            |
| ≥ 3                      | 229             | (11.5)           | 15 (0.76)          | Enteral nutrition           | 15 (0.76)          | 84 (36.7)                         | Amino acids alone                      | 23             |
|                          |                 |                  |                    | Parenteral nutrition        | 16 (0.81)          |                                   | Fat emulsion alone                      | 29             |
|                          |                 |                  |                    | Enteral-parenteral nutrition | 163 (8.22)        |                                   | Human serum albumin alone               | 74             |
|                          |                 |                  |                    | No nutritional support      | 35 (1.76)          | False or missing NRS-2002 scoring |                                       | 0              |
| 20.0–35.0                | 1324            | <3               | 629 (31.7)         | Enteral nutrition           | 16 (0.81)          | 396 (63.0)                        | Amino acids alone                      | 36             |
|                          |                 |                  |                    | Parenteral nutrition        | 23 (1.16)          |                                   | Fat emulsion alone                      | 113            |
|                          |                 |                  |                    | Enteral-parenteral nutrition | 313 (15.78)       |                                   | Human serum albumin alone               | 373            |
|                          |                 |                  |                    | No nutritional support      | 277 (13.69)        | False or missing NRS-2002 scoring |                                       | 604            |
| ≥ 3                      | 695             | (35.0)           | 33 (1.66)          | Enteral nutrition           | 33 (1.66)          | 239 (34.4)                        | Amino acids alone                      | 64             |
|                          |                 |                  |                    | Parenteral nutrition        | 29 (1.46)          |                                   | Fat emulsion alone                      | 75             |
|                          |                 |                  |                    | Enteral-parenteral nutrition | 502 (25.30)       |                                   | Human serum albumin alone               | 223            |
|                          |                 |                  |                    | No nutritional support      | 131 (6.60)         | False or missing NRS-2002 scoring |                                       | 10             |
| ≤ 20.0                   | 74              | <3               | 16 (0.8)           | Enteral nutrition           | 0 (0.00)           | 11 (68.8)                         | Amino acids alone                      | 1              |
|                          |                 |                  |                    | Parenteral nutrition        | 1 (0.05)           |                                   | Fat emulsion alone                      | 1              |
|                          |                 |                  |                    | Enteral-parenteral nutrition | 2 (0.10)          |                                   | Human serum albumin alone               | 10             |

(continued)
2002 scores <3 and serum albumin <35.0 g/L met the standards for enteral and parenteral nutritional support. Therefore, 1627 patients (82%) required nutritional support, 745 (45.8%) had irrational nutritional support, and 694 (35%) received human serum albumin alone as nutritional support. Thus, irrational nutritional support was highly prevalent among patients in this study.

Discussion

Our findings show that 51.9% of human serum albumin given in the present study was used by patients receiving nutritional support and those with hypoproteinemia (serum albumin 20.0–35.0 g/L), and that a considerable number of patients received irrational nutritional support. As well as 940 patients receiving human serum albumin for rational nutritional support, 922 patients (46.5%) received irrational nutritional support.

In healthy adults, around 20% to 30% of hepatocytes are involved in the production of human serum albumin and 10 to 15 g of serum albumin is released into the blood circulation system daily. Serum albumin has an effective half-life of 12 to 19 days and is metabolized by muscle, the liver, and kidneys. Normal serum albumin levels are maintained at 35.0 to 55.0 g/L.\(^1\,^2\,^2\)

According to the Chinese Society of Parenteral and Enteral Nutrition 2008 (CSPEN 2008), when patients have severe ascites, pleural effusion, and edema but lack accurate BMI values, their serum albumin levels (ALB) can be used to replace BMI evaluation criteria. When ALB < 30 g/L, the NRS-2002 score is 3.\(^3\,^2\,^3\)

However, besides changes in ALB synthesis and degradation, reduced ALB levels may be attributed to the disease state such as fluid loss and inflammatory responses.\(^1\,^0\)

Therefore, use of the ALB level as an alternative means of evaluating the nutritional...
status was found to be inappropriate.\textsuperscript{24} The irrational use of human serum albumin for hypoproteinemia and nutritional support has been observed in China\textsuperscript{19-21} and other countries.\textsuperscript{22,23} Although CFDA human serum albumin instructions for use suggest that human serum albumin is suitable for the prevention and treatment of hypoproteinemia, UHC guidelines for the use of albumin, nonprotein colloid, and crystalloid solutions indicate that this is an example of an irrational application.\textsuperscript{16} For patients needing nutritional support, human serum albumin is only recommended in those unable to receive enteral feeding and who have very low serum albumin levels ($<20.0\, \text{g/L}$), severe diarrhea ($>2\, \text{L/d}$), or ineffective oligopeptide treatment.\textsuperscript{14} Similarly, other recommendations list low serum albumin levels ($>25\, \text{g/L}$), hypoproteinemia without hypotension, edema, and malnutrition as irrational indications for using human serum albumin,\textsuperscript{12} while another study suggests that patients with severe hypoproteinemia ($<20\, \text{g/L}$) should be allowed to use human serum albumin.\textsuperscript{14}

Clinically, it is widely believed that patients with low serum albumin require human serum albumin as nutritional supplementation to increase levels. However, there is currently no reliable evidence-based data to support its use as protein supplementation. Typical enteral nutritional support involves oral and tube feeding, although total parenteral nutritional support is used if the gastrointestinal tract is dysfunctional. Partial parenteral nutritional support is typically used in combination with enteral nutritional support if the gastrointestinal tract is partially functional. The channels for parenteral nutritional support include a central venous catheter, peripherally inserted central catheter, venous puncture, and venous port access, and multiple nutritional drugs are available for enteral and parenteral nutritional support dependent on the disease and means of

Example of drug delivery. However, because of a lack of knowledge on nutritional drugs, many clinicians focus on the treatment of disease and neglect nutritional support despite the fact that many evidence-based medical findings show that normalized and rational enteral and parenteral nutritional support improves the therapeutic effect and reduces medical costs.

Although human serum albumin can be used for encephalopathy and fluid resuscitation, it is not the optimal choice. Compared with human serum albumin, some plasma dilatants such as succinylated gelatin, polypeptide, and hydroxyethyl starch are more accessible with lower costs.\textsuperscript{2} Human serum albumin should therefore only used as a substitute when non-protein colloid use is not permitted, particularly because there is no evidence to suggest that it has better effects than standard colloidal solutions.\textsuperscript{25} This study found that human serum albumin was widely used to treat peripheral edema, pancreatitis, pleural effusion, and serious infections, all of which are irrational applications. Therefore, we suggest that the clinical application of human serum albumin should be strictly controlled under rational circumstances to reduce treatment costs and avoid wasting medical resources.

This study focused on the rationality analysis of human albumin application and nutritional support in China at a single medical center to demonstrate the current situation. It also discussed the optimization of human albumin as nutritional support. Drawn from this survey, the irrational applications of human serum albumin in a single department mainly concentrate in one or two irrational indications. Because of the insufficient knowledge and training, many clinical practitioners have the incorrect prescribing habits to cause the irrational use of human serum albumin and enteral-parenteral nutritional support. In the future, the supervision and approval system for the rational use of
human serum albumin is urgent to be established to restrict the clinical application of human serum albumin. In addition, it is very necessary to implement the enteral-parenteral nutritional support-related training for clinical practitioners to standardize the nutritional support and NRS-2002 scoring. For limitations, this study only focuses on the single center and patients using human albumin. In this survey, the human serum albumin specification published by CFDA is involved as the evaluative criteria, which is different from the human serum albumin guidelines in the USA and Europe, including Italy.\(^1\)\(^2\)\(^3\) In the future plan, the multicentric human albumin application rationality will be analyzed by cooperation with multiple large medical institutions. Also, patients without the use of human albumin will be involved in the future research to provide more evidences for the rational use of human albumin and nutritional support.

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References
1. Evans TW. Review article: albumin as a drug–biological effects of albumin unrelated to oncotic pressure. *Aliment Pharmacol Ther* 2002; 16: 6–11.
2. Mendez CM, McClain CJ and Marsano LS. Albumin therapy in clinical practice. *Nutr Clin Pract* 2005; 20: 314–320.
3. Quinlan GJ, Martin GS and Evans TW. Albumin: Biochemical properties and therapeutic potential. *Hepatology* 2005; 41: 1211–1219.
4. Bernardi M, Ricci CS and Zaccherini G. Role of human albumin in the management of complications of liver cirrhosis. *J Clin Exp Hepatol* 2014; 4: 302–311.
5. Fletcher AG Jr, Gimbel NS and Riegel C. Parenteral nutrition with human serum albumin as the source of protein in the early post-operative period. *Surg Gynecol Obstet* 1950; 90: 151–154.
6. Zheng ZH, Zhang LJ, Liu WX, et al. Predictors of survival in Chinese patients with lupus nephritis. *Lupus* 2012; 21: 1049–1056.
7. Katalinic L, Premuzic V, Basic-Jukic N, et al. Hypoproteinemia as a factor in assessing malnutrition and predicting survival on hemodialysis. *J Artif Organs* 2019; 22: 230–236.
8. Feinberg J, Nielsen EE, Korang SK, et al. Nutrition support in hospitalised adults at nutritional risk. *Cochrane Database Syst Rev* 2017; 5: CD011598.
9. Annic B, Nina KB, Pascal T, et al. Individualised nutritional support in medical inpatients – a practical guideline. *Swiss Med Wkly* 2020; 150: 9.
10. Erstad BL. Serum albumin levels: who needs them? *Ann Pharmacother* 2020: 1060028020959348.
11. Equator Network Guideline. https://www.equator-network.org/ (2020, accessed 10 November 2020).
12. Liumbruno G, Bennardello F, Lattanzio A, et al. Recommendations for the use of albumin and immunoglobulins. *Blood Transfus* 2009; 7: 216–234.
13. Caraceni P, Angeli P, Prati D, et al. AISF-SIMTI position paper: the appropriate use of albumin in patients with liver cirrhosis. *Blood Transfus* 2016; 14: 8–22.
14. Fukui H, Saito H, Ueno Y, et al. Evidence-based clinical practice guidelines for liver cirrhosis 2015. *J Gastroenterol* 2016; 51: 629–650.
15. Adapted from UHC guidelines for the use of albumin, nonprotein colloid, and crystalloid solutions, May 2000. http://medi-guide.med itool.cn/ymtpdf/6060BD6C-30DE-A612-
16. Prescribing information. Instructions for human albumin. Tonglu Biopharmaceutical Inc. May 2020.

17. Kreymann KG, Berger MM, Deutz NEP, et al. ESPEN guidelines on enteral nutrition: intensive care. Z Gastroent 2006; 44: 685–697.

18. Singer P, Berger MM, Van Den Berghe G, et al. ESPEN guidelines on parenteral nutrition: intensive care. Clin Nutr 2009; 28: 387–400.

19. Compher CW, Boullata JI, Braunschweig CL, et al. Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients, 2009. J Parenter Enter Nutr 2009; 33: 255–259.

20. Kondrup J, Allison SP, Elia M, et al. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003; 22: 415–421.

21. Huhmann MB and August DA. Review of American Society for Parenteral and Enteral Nutrition (ASPEN) clinical guidelines for nutrition support in cancer patients: nutrition screening and assessment. Nutr Clin Pract 2008; 23: 182–188.

22. Fanali G, Di Masi A, Trezza V, et al. Human serum albumin: From bench to bedside. Mol Aspects Med 2012; 33: 209–290.

23. Chinese Medical Association. Clinical diagnosis and treatment guide for parenteral and enteral nutrition support in China. Beijing: People’s Medical Publishing, 2006, pp.16–20.

24. McClave SA, Taylor BE and Martindale RG. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P. E.N.) (vol 40, p. 159, 2016). J Parenter Enter Nutr 2016; 40: 1200.

25. Bederson JB, Sander Connolly Jr E, Hunt Batjer H, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a special writing group of the stroke council, American Heart Association (vol 40, p. 994, 2009). Stroke 2009; 40: E518.