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Serum albumin: New thoughts on an old treatment

A study suggests guidelines are needed in BC to ensure more appropriate use of albumin.

ABSTRACT:

Background: **A review of serum albumin use in BC was undertaken to gain insight into why albumin is being used and to identify specialties using albumin most commonly.**

Methods: **All BC hospitals were invited to collect data on albumin use for 1 month to 3 months in 2003. A form completed for each order of albumin recorded the product ordered, the specialty of the ordering physician, the indication for use, and the patient's diagnosis and serum albumin level. Thirteen hospitals participated in the study, representing 89% of total provincial albumin use. Data were sent to the Provincial Blood Coordinating Office for analysis.**

Results: **The most common indications for albumin use were hypotension in hemodialysis (18.9%), volume replacement/expansion (15.0%), and hypoalbuminemia (14.8%), followed by plasmapheresis (6.3%), volume expansion after cardiac surgery (5.6%), and pump priming for cardiac surgery (5.3%). Nephrology was the specialty demonstrating the largest single proportion of provincial albumin use at 20.3%, followed by internal medicine (15.1%), general surgery (12.1%), and cardiac surgery (10.8%). Other specialties demonstrating moderate albumin use were anesthesiology (7.1%), gastroenterology (6.6%), and critical care medicine (5.9%). The relative proportion of albumin used by each specialty varied across the hospitals studied.**

Conclusions: **The interhospital differences in use suggest practice variations within BC, and the use of albumin for indications that literature-based guidelines in other jurisdictions have found unsupportable suggests some prescriptions are inappropriate. Practice variations could be minimized and albumin used more appropriately with the introduction of guidelines and education strategies regarding the use of albumin and other volume expanders.**

Background

In recent years the question of the appropriate use of human albumin has been of keen interest to clinicians and blood system funders. In British Columbia, no standardized guidelines exist for serum albumin use. There have been attempts in other jurisdictions to create such guidelines,[1-3] but controversy continues.[4,5]

In October 2002, the BC Ministry of Health Services, through the Provincial Blood Coordinating Office, invited a number of acute care physicians along with members of the BC Transfusion Medicine Advisory Group to serve on an Albumin Working Group. The group's mandate was to review the use of albumin in BC, to consider the applicability of alternatives, to recommend practice guidelines for the use of albumin, nonprotein colloid (e.g., pentastarch, hetastarch), and crystalloid (e.g., normal saline, Ringer lactate) solutions, and to develop a physician education strategy encouraging appropriate use of these products. As

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an initial step, a review of albumin use in BC was undertaken to gain insight into why albumin is being used and to identify specialties using albumin most commonly.

Why question utilization?

Data provided by Canadian Blood Services indicate that albumin use in BC grew by 5.5% between the fiscal years ending in 2001 and 2002, declined by 0.6% over the course of the next fiscal year, then grew 9.5% in the fiscal year ending in 2004. The associated changes in cost were 13.3%, 18.7%, and -0.5%, respectively, with the disproportion due to fluctuations in the price of albumin. The total cost to the province over the fiscal year ending in 2004 was $2.14 million. An equivalent amount of a lower-priced alternative, such as pentastarch (Pentaspan), costs approximately two-thirds as much as albumin, and normal saline costs even less. In view of the availability of lower-cost alternatives, consideration must be given to how albumin can be used most effectively to benefit our patients.

Albumin efficacy

Controversy surrounding the efficacy and potential harm of albumin use in a variety of clinical settings is long-standing. There have been numerous randomized controlled trials and meta-analyses examining this issue.[4-16] The most recent attempt to answer the question of efficacy and potential harm of using albumin versus normal saline is the Saline Versus Albumin Fluid Evaluation (SAFE) trial. This well-designed, randomized controlled trial published in the *New England Journal of Medicine* in 2004 found no significant difference in the relative risk of death after 28 days in 6997 critical care patients receiving either 4% albumin or normal saline for fluid resuscitation.[17]

This lack of demonstrable improvement in mortality with the use of albumin in fluid resuscitation, coupled with the availability of equally effective lower-cost alternatives, emphasizes the need for a published set of guidelines to ensure the safe, cost-effective use of albumin.

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The need for guidelines

Other districts have developed comprehensive guidelines using systematic, literature-based consensus methods. These guidelines identify numerous clinical situations that albumin should not be used for, including hypoalbuminemia, nutritional intervention, first-line volume expansion (either in post-operative or critically ill patients), hypotension in hemodialysis (unless sodium restriction is desired), and cardiac bypass pump priming.[1,2] When comparing these guidelines with the common indications for albumin use in BC, it is apparent that a large percentage of the albumin prescribed in the province is ordered in direct contradiction to these guidelines. Although there is controversy regarding appropriate use of albumin, the number of clinical indications falling within existing guidelines for use, or consideration of use, is limited. Albumin is recommended for postoperative liver resection patients with ascites, for nephritic syndrome, and for plasmapheresis. The use of albumin for spontaneous bacterial peritonitis in cirrhotic patients also has evidence in its favor.[10]

An additional incentive to develop guidelines governing albumin use is the potential for infectious disease transmission with the use of human-derived blood products. While rigorous donor screening and testing, coupled with the appropriate preparation of human albumin, can decrease the risk of disease transmission, the absolute risk is not zero. The albumin pasteurization process does not eliminate the risk of transmission of certain viruses such as hepatitis A and parvovirus.[18,19] Prion-transmitted diseases such as Creutzfeld-Jakob disease are also of concern because of the lack of knowledge regarding their transmissibility through blood products.[20,21]

With the inherent risk of disease transmission and the relatively high cost of albumin compared with equally efficacious alternatives, the use of this product in our province needs to be reviewed. The introduction of practice guidelines that ensure the appropriate use of albumin and the applicability of alternatives can then be considered.

BC Albumin Working Group: Prospective Study of Albumin Use in BC

INSTRUCTIONS TO TRANSFUSION SERVICE STAFF: For each order of albumin filled, please answer the following questions. If you have questions, please call the PBCO at 604-806-8840 or 1-866-508-5501. Thank you.

Hospital MoH Number and Hospital Name _____ **Initials of person completing this form:** _____

Patient chart number: _____ **Patient age:** _____

Date: _____ / _____ / 2003
(day) (month)

Product ordered (circle product name and write number of vials ordered):

Albumin 5%	Albumin 25%
_____ x 50 mL	_____ x 50 mL
_____ x 250 mL	_____ x 100 mL
_____ x 500 mL	

Name of ordering physician: _____

Specialty of ordering physician (place a checkmark beside response):

___ Anesthesiology
___ Cardiac Surgery
___ Emergency Medicine
___ Gastroenterology
___ General Surgery
___ Hematology
___ Internal Medicine
___ Nephrology
___ Neurology
___ Neurosurgery
___ Obstetrics and Gynecology
___ Orthopaedics
___ Pediatrics
___ Plastic Surgery
___ Other (specify):
_____

Patient's diagnosis:_____

Indication for use (place a checkmark beside the best response):

___ Cardiac Surgery: prime pump
___ Cardiac Surgery: postoperative volume expansion
___ Cerebral Ischemia/Closed Head Injury/Subarachnoid Hemorrhage
___ Diuretic Resistant Peripheral Edema/Ascites
___ Hemorrhagic Shock
___ Hepatic resection
___ Hepatorenal syndrome
___ Hyperbilirubinemia of newborn
___ Hypoalbuminemia
___ Hypoalbuminemia and malabsorption
___ Hypotension in Hemodialysis
___ Nephrotic Syndrome
___ Non-hemorrhagic Shock
___ Nutritional Intervention
___ Organ transplantation
___ Pancreatitis
___ Paracentesis and Ascites
___ Plasmapheresis
___ Prevention of Peripheral Edema/ Pulmonary Edema/Ascites
___ Thermal Injury
___ Volume Replacement/Expansion
___ Other (specify):
_____

Patient's most recent serum albumin level: _____ g/L

Figure 1. Albumin study form.

Methods

All BC hospitals were invited to participate in the BC Albumin Working Group's Prospective Study of Albumin Use in BC. Data collection was scheduled from 15 April to 15 June 2003. Smaller facilities were encouraged to continue collecting until 15 July to provide a sufficient volume of data. Larger facilities received particular encouragement to participate. Hospitals unable to collect data for a full 2 months were allowed to collect for a shorter period, although a minimum of 1 month of data was sought from each site.

During the study period, all participating transfusion services completed a form for each order of albumin filled (see **Figure 1**). The form was designed to capture the product ordered, the specialty of the ordering physician, the indication for use, and the patient's diagnosis and serum albumin level. The form listed specialties that commonly order albumin and indications considered previously and presently as widely accepted reasons to use albumin. Some of these indications continue to be generally accepted while others are controversial or have fallen out of favor.

Completed forms were returned to the Provincial Blood Coordinating Office (PBCO) for data entry and analysis.

Ethics approval was not required for the study because the data were collected by the PBCO as part of its operating activities, which include monitoring and managing the utilization of blood and blood products in BC. The office's data collection activities have been approved in a privacy impact assessment by the BC Ministry of Health Services. No information identifying individual patients was collected for this study.

Results

Thirteen hospitals participated in the study, representing 89% of total provincial albumin use during the study period. The total albumin use quoted in the results refers to the 89% of provincial use we were able to capture. This high capture rate was important for examining provincial utilization practices and will aid in the development of workable guidelines.

Although the official data collection dates were 15 April to 15 June 2003, inclusive, 6 of the 13 sites collected data on different dates. One of the hospitals collected data from 23 April to 15 June, two collected from 1 May to 15 July, and three collected from 15 April to 15 July. Despite these differences, we believe that the data captured give us adequate insight into regional differences in use overall.

The proportion of albumin use captured at each hospital ranged from 85% to 100% (mean 97.6%, median 99.5%). Most hospitals had a system to ensure that albumin study forms were completed with each albumin

Table 1. Albumin use by indication.

Indication	% of total albumin use	% of 5% albumin use	% of 25% albumin use
Hypotension in hemodialysis	18.9%	0.2%	27.8%
Volume replacement/Expansion	15.0%	20.7%	12.3%
Hypoalbuminemia	14.8%	2.2%	20.7%
Indication not given	9.4%	11.6%	8.4%
Plasmapheresis	6.3%	19.7%	0
Cardiac surgery: Postoperative volume expansion	5.6%	10.2%	3.4%
Cardiac surgery: Prime pump	5.3%	8.0%	4.0%
Thermal injury	3.0%	0.6%	4.1%
Diuretic resistant peripheral edema/ Ascites	2.7%	0.4%	3.8%
Other	2.4%	2.9%	2.2%
Cerebral ischemia/Closed head injury/ Subarachnoid hemorrhage	2.3%	7.0%	0
Post-op, not specified	2.2%	6.2%	0.2%
Paracentesis and ascites	2.1%	0.1%	3.1%
Organ transplantation	2.0%	3.0%	1.5%
Nonhemorrhagic shock	1.8%	2.4%	1.6%
Prevention of peripheral edema/ Pulmonary edema/Ascites	1.6%	0.3%	2.2%
Hypovolemic and/or hemorrhagic shock	1.5%	2.5%	1.1%
Hepatic resection	1.1%	1.8%	0.7%
Nephrotic syndrome	0.7%	0.1%	1.0%
Pancreatitis	0.6%	0.1%	0.8%
Hypoalbuminemia and malabsorption	0.4%	0.1%	0.5%
Hepatorenal syndrome	0.3%	0	0.4%
Hemorrhagic shock	0.2%	0.1%	0.2%
Nutritional intervention	0.1%	0	0.1%

Percentages may not add to 100 due to rounding.

Table 2. Albumin use by specialty.

Specialty of ordering physician	% of total albumin use	Volume (g)	% of 5% albumin use	Volume (g)	% of 25% albumin use
Nephrology	20.3%	1127.5	4.6%	14350.0	27.5%
Internal medicine	15.1%	687.5	2.8%	10875.0	20.9%
General surgery	12.1%	5242.5	21.6%	3975.0	7.6%
Cardiac surgery	10.8%	4647.5	19.2%	3575.0	6.9%
Anesthesiology	7.1%	1800.0	7.4%	3650.0	7.0%
Gastroenterology	6.6%	175.0	0.7%	4850.0	9.3%
Neurology	5.9%	4250.0	17.5%	275.0	0.5%
Critical care	5.9%	200.0	0.8%	4275.0	8.2%
Hematology	4.3%	2362.5	9.7%	900.0	1.7%
Other	2.8%	275.0	1.1%	1862.5	3.6%
Resident	2.6%	1200.0	4.9%	775.0	1.5%
Pediatrics	2.0%	1157.5	4.8%	350.0	0.7%
Emergency medicine	1.4%	100.0	0.4%	1000.0	1.9%
General practice	1.2%	50.0	0.2%	900.0	1.7%
Neurosurgery	1.0%	637.5	2.6%	125.0	0.2%
Oncology	0.9%	342.5	1.4%	365.2	0.7%

Percentages may not add to 100 due to rounding.

order. However, there were some sites where some orders may have been made without filling out a study form.

Use by indication

Albumin use by indication as a percentage of all study participants is shown in **Table 1**. The most common indications for albumin use were hypotension in hemodialysis (18.9%), volume replacement/expansion (15%), and hypoalbuminemia (14.8%), followed by plasmapheresis (6.3%), volume expansion after cardiac surgery (5.6%), and pump priming for cardiac surgery (5.3%). No indication was given for 9.4% of total albumin use and 2.4% of indications were marked as "Other." The accuracy of the given clinical indication was estimated at 50% to 100% (mean 87.1%, median 92.5%), depending on the hospital site. Sites with high accuracy confirmed each indication with the ordering physician. Sites with lower accuracy occasionally relied on the interpretation of the blood bank technologist, nurse, or unit clerk. In some cases, the patient's diagnosis was taken as the indication, which is not always appropriate. Occasionally, the preprinted list of indications was not used and an indication was handwritten. These written indications were assessed and some were assigned to one of the preprinted indications. For example, handwritten indications of "severe ascites," "edema," "diuresis," "diuretic therapy," "fluid overload," "fluid retention," and "correction of peripheral edema" were combined and added to the preprinted indication "Diuretic resistant peripheral edema/ascites."

Use by specialty

The use of albumin by specialty of the ordering physician as a percentage of all study participants is shown in **Table 2**. Nephrology had the largest percentage of provincial albumin use at 20.3%, followed by internal medicine (15.1%), general surgery (12.1%), and cardiac surgery (10.8%). Other specialties with moderate albumin use were anesthesiology (7.1%), gastroenterology (6.6%), and critical care medicine (5.9%). The relative proportion of albumin use by each specialty varied across sites, as shown in **Table 3**. The accuracy of the physician specialty ranged from 70% to 100% (mean 94.4%, median 96.5%). These accuracy figures were estimates provided by the blood bank technologists who coordinated the study at their sites. Sites confident in their accuracy of physician specialty checked directly with the ordering physician. Occasionally, difficulty arose when interns or residents filled out the forms and their specialty was not clear. Any future study should ensure standardized reporting of the specialty and indication on the form and confirm these with the physician directly.

Table 3. Hospital variations in albumin use by specialty.

Specialty of ordering physician	Proportion of each hospital's total albumin use												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Anesthesiology	3.2%	0	0	0	0	0	42.3%	0%	0.8%	0	0.6%	0	8.4%
Cardiac surgery	8.2%	0	0	0	0	0	0.7%	5.6%	4.3%	0	14.9%	0	24.8%
Critical care	1.8%	7.0%	0	0	0	0	0	0	13.5%	0	1.9%	10.7%	4.0%
Emergency medicine	0.9%	0	0	8.7%	0	0	0	11.1%	0.1%	0	0	0	3.5%
Gastroenterology	0.9%	0	0	8.7%	0	0	5.0%	0	9.2%	58.2%	1.2%	35.3%	5.6%
General practice	0	0	3.1%	8.7%	27.1%	0	2.8%	0	0	5.5%	0	0	0.1%
General surgery	0.1%	0	0	0	2.3%	23.9%	6.2%	0	9.7%	0	4.3%	20.3%	23.5%
Hematology	0	0	0	0	0	0	1.4%	0	0	0	0	12.8%	11.4%
Internal medicine	0.2%	10.9%	96.3%	56.5%	70.6%	65.2%	0.4%	47.2%	22.4%	0	12.4%	7.5%	7.9%
Nephrology	3.5%	80.5%	0	0	0	10.9%	0	0	36.9%	24.9%	0	2.1%	1.8%
Neurology	10.3%	0	0	0	0	0	37.7%	0	0.4%	0	54.0%	6.4%	4.3%
Neurosurgery	0	0.8%	0	0	0	0	0	36.1%	0	0	0	0	1.5%
Oncology	12.8%	0	0	0	0	0	0	0	0	0	0	0	0
Pediatrics	25.7%	0	0.6%	17.4%	0	0	0	0	0	0.3%	0	0	0
Resident	28.8%	0	0	0	0	0	0	0	0	0	1.9%	0	1.3%
Other	3.7%	0.8%	0	0	0	0	3.6%	0	2.9%	11.1%	8.8%	4.8%	1.9%

Percentages may not add to 100 due to rounding.

Implications of results

The baseline data collected on albumin use in British Columbia will be used by the Albumin Working Group to consider the development of practice guidelines and to target any subsequent educational interventions. Although no attempt was made to assess the appropriateness of albumin use, either in terms of clinical indication or dosage, albumin is evidently being used for indications that the literature-based guidelines referred to earlier have found unsupportable. For example, hypoalbuminemia, volume replacement/expansion, hypotension in hemodialysis, and cardiac bypass pump priming together accounted for 54% of use. Some of this use may have been warranted, but a considerable portion of it probably was not.

Albumin is evidently being used for indications that the literature-based guidelines referred to earlier have found unsupportable.

This is not surprising, given that other investigators have reported a high degree of inappropriate albumin prescription at their institutions. An evaluation of albumin use at 53 hospitals in the United States found that albumin was inappropriately prescribed for 57.8% of adult patients and 52.2% of pediatric patients.[22] Another US multicentre observational study found that 62% of funds spent on albumin and nonprotein colloid therapy was for inappropriate administrations.[2] A similar study in Spain found that 77% of the cost of albumin was associated with inappropriate use.[23]

The interhospital variations in the pattern of albumin use within BC also merit further investigation. While the discrepancies undoubtedly partly reflect differences in patient populations and in surgical services offered by each facility, they also suggest practice variations that require the introduction of guidelines and educational strategies regarding the use of albumin and other volume expanders.

Conclusions

The results of a study undertaken to assess the present pattern of albumin utilization in BC suggest that albumin is in widespread use for indications that literature-based guidelines in other jurisdictions have found unsupportable. The major specialty users are nephrology, internal medicine, general surgery, and cardiac surgery, although notable interhospital variations exist. Through the generation and implementation of guidelines, we hope that albumin can be used more appropriately and these differences can be minimized.

Albumin is expensive compared with colloid and crystalloid alternatives and is not without risk to patients. For volume expansion, there are equally efficacious alternatives. There is controversy in the literature with respect to the benefits and risks. However, it is our belief that albumin should be reserved for specific, evidence-supported uses.

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Competing interests

None declared.

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