

Introduction of guidelines for the use of albumin and the effect on albumin prescribing practices in British Columbia

Although the amount of albumin being used for appropriate indications has increased since provincial guidelines were introduced, the majority of orders for albumin continue to be for inappropriate indications.

ABSTRACT:

Background: Albumin is a human blood product associated with risks to patients and subject to supply shortfalls. It is expensive compared with synthetic colloid and crystalloid alternatives. An audit performed in 2003 found that albumin was being used for a wide variety of indications in British Columbia, many of which were not supported by the literature. Based on these results, evidence-based guidelines for albumin use were developed and released in October 2007. The guidelines specified “Indications for which albumin may be used” and “Indications for which albumin should not be used.” The audit was repeated in 2009 to determine if the introduction of guidelines had any effect on albumin prescribing practices in BC.

Methods: Nine of the 13 hospitals audited in 2003 were audited again in 2009. Transfusion medicine technologists in participating hospitals recorded the specialty of the ordering physician and the indication for

albumin use for each order filled during both audit periods.

Results: The three most common clinical entities requiring albumin reported in 2009 are listed as appropriate indications for this blood product in the provincial guidelines. In stark contrast, the most common clinical entities requiring albumin reported in 2003 are listed as inappropriate in the guidelines. However, along with this improvement in prescribing practice, the 2009 audit also shows that many clinicians are still using albumin for indications that are not supported by the literature. The major users of albumin continue to be cardiac surgery and internal medicine, particularly hematology and nephrology.

Conclusions: While some progress has been made, continuing education is required to encourage clinicians to follow evidence-based guidelines and ensure that albumin is prescribed for patients who are most likely to benefit.

Background

Albumin has historically been used for a wide variety of indications. However, prescribing albumin for many of these indications is not supported by current evidence or is controversial or

Dr King is a staff anesthesiologist at Royal Jubilee Hospital and Victoria General Hospital in Victoria, BC, and a clinical instructor in the Department of Anesthesiology, Pharmacology, and Therapeutics at the University of British Columbia. Dr Roland is a staff hematopathologist at Vancouver General Hospital in Vancouver, BC. She is also an assistant professor in the Department of Pathology and Laboratory Medicine at UBC. Ms Selin is manager of utilization management for the British Columbia Provincial Blood Coordinating Office in Vancouver. Dr Chipperfield is regional medical leader for Blood Transfusion Medicine, Vancouver Coastal Health, and a staff hematopathologist at Vancouver General Hospital. She is also an assistant professor in the Department of Pathology and Laboratory Medicine at UBC. Dr Morrison is medical director of Transfusion Medicine for Fraser Health and chair of the Transfusion Medicine Advisory Committee of BC. He is also an assistant professor in the Department of Pathology at UBC.

This article has been peer reviewed.

only weakly supported by the available literature.¹⁻⁴ Standardized use of albumin is necessary to ensure maximal benefit to patients while minimizing unnecessary exposure to blood products and their associated risks (allergic reactions, circulatory overload, and transmission of bloodborne infectious agents). At \$2.60 per gram (Canadian dollars),⁵ albumin is substantially more expensive than the alternatives, which include crystalloids (such as normal saline or Ringer lactate) and synthetic colloids (such as the hydroxymethyl starches), entailing a significant financial burden for a product of questionable clinical benefit.

In 2003, the BC Transfusion Medicine Advisory Group (TMAG) audited albumin prescribing practices in British Columbia and found that albumin was being used for indications that were considered unsupported by literature-based guidelines in other jurisdictions.⁶ In 2004, the SAFE study,⁷ a randomized controlled trial of albumin versus normal saline for fluid resuscitation in critical care patients, found no significant difference between the two groups with respect to 28-day mortality, duration of mechanical ventilation, or hospital length of stay. These studies provided the stimulus for the development of the Guidelines for Albumin Use in Adults in British Columbia, a joint effort of the BC Provincial Blood Coordinating Office, TMAG, and a group of acute care physicians. The guidelines⁸ were released in October 2007 and are available online at www.pbco.ca.

Given that numerous studies have shown that albumin is used inappropriately most of the time,⁹⁻¹¹ it was hoped that the introduction of locally developed guidelines would result in a change in prescribing practices. There were early indications that this might be the case: in the calendar year following release of the guidelines,

the amount of albumin issued to BC hospitals by the Canadian Blood Services decreased by 9.7%, while albumin use across Canada (excluding Quebec) rose by 3.6% (oral communication with J. Unrau, hospital liaison specialist, Canadian Blood Services BC and Yukon, 2 December 2011).

men's Health Centre of BC was excluded because the 2007 guidelines are for adult patients only, and most of the albumin at that site is used for pediatric patients.

The hospital transfusion services at all sites were asked to complete a form for each albumin order filled dur-

Albumin has been shown to have uncertain or no benefit over conventional intravenous fluids for many of the indications for which it is most commonly used, yet the overall use of albumin continues to rise in Canada.

In order to examine the effect that the introduction of guidelines for the use of albumin has had on BC prescribing practices, we performed another province-wide audit of albumin use in 2009. We hypothesized that the proportion of albumin used inappropriately (i.e., for indications not named in the guidelines or those categorized in the guidelines as "Indications for which albumin should not be used") would decrease compared with the baseline established in 2003.

Methods

After the study design was approved by the research ethics board and institutional review board of each participating site, the audit began.

Twelve of the thirteen hospitals that participated in the original 2003 audit were asked to participate in the 2009 audit. The Children's and Wo-

men's Health Centre of BC was excluded because the 2007 guidelines are for adult patients only, and most of the albumin at that site is used for pediatric patients. The hospital transfusion services at all sites were asked to complete a form for each albumin order filled during the study period: 1 October to 1 December 2009. The form included fields for the hospital, the type and amount of albumin ordered, the specialty of the ordering physician or service, and the clinical indication for the product. To participate, hospitals were required to collect data for at least 1 month, and were then asked to collect data for a full 2 months.

At the end of the study period, the anonymized completed forms were returned to the Provincial Blood Coordinating Office for entry into a database and further analysis. The specialty of the ordering physician and indications for use were then compared with data from the 2003 audit, which were reorganized to include only the hospitals that participated in both audits.

Finally, transfusion medicine directors and chief technologists at each

site were asked to describe how the Guidelines for Albumin Use in Adults in British Columbia document was distributed within their respective hospitals and whether additional education about the Guidelines was provided.

Results

Nine hospitals in four of BC's five health regions agreed to participate in the study. All hospitals began data collection on 1 October 2009. Eight hospitals collected data for 2 months, and

one hospital collected data for 1 month. A total of 315 forms were received. Eight of the hospitals reported a capture rate of 90% to 100% of their albumin use; one hospital reported capture of approximately 50% of use. As this hospital accounted for less than 2% of provincial albumin use and for only 1% of the albumin used in the study, the incomplete data capture does not affect the conclusions.

The total amount of albumin ordered during the 2009 audit was 67 277.5 grams versus 47 032.3 grams for the same hospitals during the 2003 audit. Because hospitals collected for different lengths of time in the first study, these amounts are not directly comparable. The amounts can, however, be used as denominators for determining the proportion of appropriate albumin use in each year.

Use by indication

The indications for albumin use according to the guidelines are shown in **Table 1**. The 2003 values have been reformulated to include only the hospitals that participated in both studies. Indications have been divided into three categories: (1) Appropriate use (i.e., indications are listed in the 2007 guidelines under the heading "Indications for which albumin may be used"); (2) Inappropriate use—specified (i.e., indications are listed in the guidelines under the heading "Indications for which albumin should not be used"); (3) Inappropriate use—not specified (i.e., indications are not specifically mentioned in the guidelines because no evidence supporting the use of albumin for them exists).

The amount of albumin used in 2009 considered to be appropriate according to the 2007 guidelines increased by nearly 35% when compared with the amount used in 2003. Indeed, the top three indications in 2009 were all considered appropriate:

Table 1. Appropriateness of albumin use by indication according to guidelines, 2003 vs 2009.

Indication	2003	2009	2003 vs 2009 % difference	2009
	% of total albumin used	% of total albumin used		Number of orders
Appropriate use				
Cardiac surgery: postoperative volume expansion	8.37	16.85	+8.48	11
Hepatic resection	1.57	8.68	+7.11	16
Nephrotic syndrome	0.69	1.74	+1.04	10
Paracentesis and ascites	2.60	13.26	+10.66	26
Plasmapheresis	7.12	15.76	+8.64	10
Thermal injury	1.44	0.07	-1.36	1
Total	21.79	56.36	+34.57	74 (23.5%)
Inappropriate use—specified				
Cardiac surgery: pump prime	6.17	0	-6.17	0
Cerebral ischemia/closed head injury/subarachnoid hemorrhage	3.64	1.13	-2.51	5
Hypoalbuminemia	10.95	2.34	-8.61	18
Hypoalbuminemia and malabsorption	0.53	1.69	+1.16	6
Hypotension in hemodialysis	10.37	6.43	-3.94	26
Nutritional intervention	0.05	0.76	+0.71	2
Volume replacement/expansion	16.35	11.13	-5.22	67
Total	41.89	23.58	-18.41	124 (39.4%)
Inappropriate use—not specified				
Diuretic resistant peripheral edema/ascites	1.54	1.06	-0.48	7
Hepatorenal syndrome	0.43	0.59	+0.17	1
Organ transplantation	3.22	2.68	-0.54	6
Other	22.71	5.40	-23.48	42
Pancreatitis	0.53	0.52	-0.01	2
Prevention of peripheral edema/ascites	1.46	8.86	+7.40	50
Renal failure	0.27	1.04	+0.77	9
Total	36.33	20.15	-16.18	117 (37.1%)

(1) postoperative volume expansion for cardiac surgery; (2) plasmapheresis; and (3) paracentesis and ascites. However, the majority of orders submitted for albumin in 2009 were still for “inappropriate” indications and only 23.5% of all orders in 2009 were for appropriate indications.

Use by specialty

The specialties of the physicians who ordered albumin are shown in **Table 2**. The only major change from 2003 was a large increase in use by internal medicine. However, this is almost completely offset by a large decrease in use by nephrology, and the changes may be the result of coding the same practitioners differently. As in 2003, the major users of albumin were internal medicine, cardiac surgery, general surgery, and hematology. However, it is important to note that cardiac surgery use moved from primarily inappropriate use in 2003 (cardiac surgery: pump prime) to appropriate use in 2009.

Educational survey

Seven of the nine hospitals completed the survey about disseminating the 2007 albumin guidelines and providing additional education. Five sites distributed the guidelines via hard copy, one site distributed the guidelines via e-mail, and one site distributed the guidelines via multiple methods (e-mail, hard copy, posted on intranet, and integrated into a preprinted order form). Two hospitals distributed the guidelines to all physicians, three hospitals distributed only to the specialties that typically use albumin, one hospital only to nephrologists and intensivists, and another hospital only to nephrologists. Two hospitals provided additional education about the guidelines: one held grand rounds for all physicians and the other held resident rounds.

Table 2. Comparison of albumin use by specialty, 2003 vs 2009.

Specialty	2003	2009	2003 vs 2009 % difference
	% of total albumin used	% of total albumin used	
Anesthesiology	10.90	2.27	-8.63
Cardiac surgery	14.78	20.25	+5.47
Cardiology	0.16	0.06	-0.10
Critical care	3.24	2.24	-1.00
Emergency medicine	2.18	0.07	-2.10
Gastroenterology	5.05	2.12	-2.93
General practice	0.74	1.86	+1.12
General surgery	14.51	18.01	+3.50
Hematology	6.30	13.58	+7.28
Infectious diseases	0.05	0.15	+0.10
Internal medicine	11.67	31.44	+19.77
Nephrology	17.28	3.05	-14.23
Neurology	7.95	1.10	-6.85
Neurosurgery	1.62	1.04	-0.58
Obstetrics and gynecology	0.37	0.52	+0.15
Oncology	0.01	0.07	+0.06
Orthopaedics	0.05	0.07	+0.02
Other	1.76	0.15	-1.61
Resident*	0.85	0.15	-0.70
Respiratory	0.05	1.25	+1.19
Vascular	0.48	0.56	+0.08
Total	100.00	100.00	

*This category contains physicians-in-training whose specialty is unclear.

Conclusions

Albumin has been shown to have uncertain or no benefit over conventional intravenous fluids for many of the indications for which it is most commonly used, yet the overall use of albumin continues to rise in Canada. The amount of albumin issued to Canadian hospitals (excluding Quebec) grew 51.8% between 2003 and 2009 (oral communication with J. Unrau, hospital liaison specialist, Canadian Blood Services BC and Yukon, 2 December 2011).

Two years after the introduction of evidence-based guidelines for albu-

min use in BC, the results are both heartening and discouraging. On the positive side, the total amount of albumin being used for appropriate indications has risen dramatically, from 22% to 56%. The top three indications are now in the appropriate category, in contrast to 2003 when the top three indications were in the inappropriate category. This could be interpreted as evidence that practice is changing toward more evidence-based use of albumin.

However, looking at the number of orders received for each indication in the 2009 audit, it is discouraging

to see that 39.4% of orders were for indications specifically listed in the guidelines as “Indications for which albumin should not be used” and an additional 37.1% of orders were for indications that were inappropriate, although they were not specifically named in the guidelines. It should be

ical education strategies require frequent reinforcement to continue altering practice.¹²

In summary, the introduction of evidence-based guidelines in British Columbia has led to mixed results. Although the amount of albumin being used for appropriate indications

Although the amount of albumin being used for appropriate indications has increased since the introduction of provincial guidelines, the majority of orders for albumin continue to be for inappropriate indications.

noted that this is a “best-case scenario,” as the ordering clinicians were given the benefit of the doubt when the data were analyzed. For example, the indication “hepatic resection” was considered appropriate even though the actual indication in the guidelines is “post-operative liver resection patients with concomitant ascites.”

The apparently suboptimal impact of the albumin guidelines may have been due to ineffective strategies for implementation or dissemination of the information. The delay between the 2007 release of the guidelines and the 2009 audit may mean that a temporary improvement in albumin use was not captured: there are hints of this in a 9.7% decrease in the amount of albumin issued to BC hospitals in 2008 followed by a 0.8% increase in 2009 (oral communication with J. Unrau, hospital liaison specialist, Canadian Blood Services BC and Yukon, 2 December 2011). It is known that clin-

ical education strategies require frequent reinforcement to continue altering practice.¹²

has increased since the introduction of provincial guidelines, the majority of orders for albumin continue to be for inappropriate indications, thus highlighting the importance of continuing education regarding the costs and risks of albumin use and the need to follow evidence-based guidelines.

Competing interests

None declared.

Acknowledgments

The authors would like to acknowledge the technical and medical staff of all the hospital transfusion services who contributed data. As well, the authors acknowledge the support and counsel of the BC Transfusion Medicine Advisory Group members in the planning of both audits and in the development of albumin guidelines. Finally, thanks go to the staff of the BC Provincial Blood Coordinating Office for their help with study design, data entry, data analysis, and manuscript preparation.

References

1. Boldt J. Use of albumin: An update. *Brit J Anaesth* 2010;104:276-284.
2. Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev* 2007;(3):CD000567.
3. Alderson P, Bunn F, Lefebvre C, et al.; Albumin Reviewers. Human albumin solution for resuscitation and volume expansion in critically ill patients. *Cochrane Database Syst Rev* 2004;(4):CD001208.
4. Fan E, Stewart TE. Albumin in critical care: SAFE, but worth its salt? *Crit Care* 2004;8:297-299.
5. Canadian Blood Services. 2010–2011 Plasma protein products price list. 2010.
6. Fan C, Phillips K, Selin S. Serum albumin: New thoughts on an old treatment. *BCM J* 2005;47:438-444.
7. Finfer S, Bellomo R, Boyce N, et al; SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the ICU. *N Engl J Med* 2004;350:2247-2256.
8. BC Provincial Blood Coordinating Office and BC Ministry of Health. Guidelines for albumin use in adults in British Columbia. Released October 2007. www.pbco.ca/images/UM/Albumin/guidelines%20for%20albumin%20use%20in%20bc%20%28oct%202007%29.pdf.
9. Yim J, Vermeulen L, Erstad B, et al. Albumin and nonprotein colloid solution use in US academic health centers. *Arch Intern Med* 1995;155:2450-2455.
10. Tanzi M, Gardner M, Megallas M, et al. Evaluation of the appropriate use of albumin in adult and pediatric patients. *Am J Health Syst Pharm* 2003;60:1330-1335.
11. Tarin Remohi MJ, Sanchez Arcos A, Santos Ramos B, et al. Costs related to inappropriate use of albumin in Spain. *Ann Pharmacother* 2000;34:1198-1205.
12. Tinmouth A. Reducing the amount of blood transfused by changing clinicians' transfusion practices. *Transfusion* 2007;47(suppl2):132S-136S. **BCMJ**