Evidence Update

Trauma Series

August 2003

Does albumin reduce mortality in critically ill people?

There is no evidence that albumin administration reduces the risk of death in critically ill patients with hypovolaemia, burns or hypoalbuminaemia.

Inclusion criteria

Types of studies:

All randomised controlled trials of human albumin or plasma protein fraction (PPF) administration (albumin/ PPF versus no albumin/PPF, or a crystalloid solution).

Types of participants:

Critically ill patients with hypovolaemia, burns or hypoproteinaemia. Trials involving patients receiving pre-operative volume loading or haemodilution, and trials of albumin administration during paracentesis were excluded.

Types of intervention:

Human albumin solution or plasma protein fraction (PPF).

Types of outcome measures:

The principal outcome measure was mortality from all causes assessed at the end of the follow up period scheduled for each trial.

Results

- 32 trials met the inclusion criteria and reported death as an outcome. Sixteen were adequately concealed.
- There were 177 deaths among 1519 trial participants.
- For each patient category the risk of death in the albumin treated group was higher than in the comparison group.
- For hypovolaemia the relative risk of death following albumin administration was 1.46 (95% confidence interval 0.97 to 2.22), for burns the relative risk was 2.40 (1.11 to 5.19), and for hypoalbuminaemia the relative risk was 1.38 (0.94 to 2.03).
- Overall, the risk of death in patients receiving albumin was 14% compared to 9% in the control groups, an increase in the risk of death of 5% (2% to 8%). These data suggest that for every 20 critically ill patients treated with albumin there is one additional death.





Adapted from The Albumin Reviewers (Alderson P, Bunn F, Lefebvre C, Li Wan Po A, Li L, Roberts I, Schierhout G). Human albumin solution for resuscitation and volume expansion in critically ill patients (Cochrane Review). In: The Cochrane Library, Issue 3, 2003. Oxford: Update Software.

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	udy	albumin n/N	Control n/N		Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl
	hypovolaemia Boldt 1993	0/15	0/15			0.0	Not estimable
	Boutros 1979	0/7	2/17	4	•	2.1	0.45 [0.02, 8.34]
×	Gallagher 1985	0/5	0/5			0.0	Not estimable
	Grundmann 1982	1/14	0/6	4	•	● 0.9	1.40 [0.06, 30.23]
	Lowe 1977	3/57	3/84			- 3.3	1.47 [0.31, 7.05]
	Lucas 1978	7/27	0/25			→ 0.7	13.93 [0.84, 231.94]
×	Nielsen 1985	0/13	0/13			0.0	Not estimable
×	Pockaj 1994	0/54	0/53			0.0	Not estimable
×	Prien 1990	0/6	0/6			0.0	Not estimable
	Rackow 1983	6/9	6/8		_	8.8	0.89 [0.48, 1.64]
	Shah 1977	2/9	3/11	-		3.7	0.81 [0.17, 3.87]
	So 1997	7/32	5/31			7.0	1.36 [0.48, 3.82]
	Tollofsrud 1995	0/10	1/10	4		2.1	0.33 [0.02, 7.32]
	Virgilio 1979	1/15	1/14	4		→ 1.4	0.93 [0.06, 13.54]
	Woittiez 1998	8/15	4/16		4	5.3	2.13 [0.81, 5.64]
	Woods 1993	1/37	0/32			→ 0.7	2.61 [0.11, 61.81]
	Zetterstrom 1981a	0/15	1/15	4		2.1	0.33 [0.01, 7.58]
	Zetterstrom 1981b	2/9	0/9			→ 0.7	5.00 [0.27, 91.52]
	st for overall effect=1.79 p=	are=9.45 df=12 p=0. 0.07	0041				
	burns Goodwin 1983	:0.07 11/40	3/39			→ 4.2	3.57 [1.08, 11.85]
	burns Goodwin 1983 Greenhalgh 1995	:0.07 11 / 40 7 / 34	3/39 3/36			4.0	2.47 [0.69, 8.79]
	burns Goodwin 1983	:0.07 11/40	3/39	4	•	•	
02 Sui	burns Goodwin 1983 Greenhalgh 1995	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2	3/39 3/36 2/7 8/82	4		4.0	2.47 [0.69, 8.79]
02 Sul Tes	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for overall effect=2.22 p= hypoalbuminaemia	11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03	3/39 3/36 2/7 8/82 933	4		4.0 2.8 11.0	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19]
02 Sul Tes	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squi st for ov erall effect=2.22 p= hypoalbuminaemia Bland 1973	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50	3/39 3/36 2/7 933 8/82 12/50	4		4.0 2.8 11.0 16.5	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62]
02 Sul Tes	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for ov erall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50 4/14	3/39 3/36 2/7 933 8/82 12/50 1/13	4			2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06]
02 Sul Tes	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for ov erall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50 4/14 6/34	3/39 3/36 2/7 8/82 933 12/50 1/13 4/33	4		4.0 2.8 11.0 16.5 1.4 5.6	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70]
02 Sul Tes	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for ov erall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50 4/14 6/34 7/18	3/39 3/36 2/7 8/82 933 12/50 1/13 4/33 6/22			4.0 2.8 11.0 16.5 1.4 5.6 7.4	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49]
02 Sul Tes	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for ov erall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116	3/39 3/36 2/7 8/82 933 12/50 1/13 4/33 6/22 6/103			4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56]
Sul Ter Ter	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for ov erail effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994 Greenough 1993	0.07 11/40 7/34 1/7 19/81 are=2.45 df = 2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116 6/20	3/39 3/36 2/7 8/82 12/50 1/13 4/33 6/22 6/103 4/20	4		4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8 5.5	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56] 1.50 [0.50, 4.52]
Sul Ter Ter	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squ st for ov erail effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994 Greenough 1993 Kanarek 1992	0.07 11/40 7/34 1/7 19/81 are=2.45 df = 2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116 6/20 3/12	3/39 3/36 2/7 8/82 12/50 1/13 4/33 6/22 6/103 4/20 2/12	4		4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8 5.5 2.8	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56] 1.50 [0.50, 4.52] 1.50 [0.30, 7.43]
Sul Ter Ter	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squi st for overall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994 Greenough 1993 Kanarek 1992 Nilsson 1980	0.07 11/40 7/34 1/7 19/81 are=2.45 df = 2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116 6/20 3/12 1/29	3/39 3/36 2/7 8/82 12/50 1/13 4/33 6/22 6/103 4/20 2/12 0/30			4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8 5.5 − 2.8 0.7	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56] 1.50 [0.50, 4.52] 1.50 [0.30, 7.43] 3.10 [0.13, 73.15]
Sul Ter Ter	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squi st for overall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994 Greenough 1993 Kanarek 1992 Nilsson 1980 Rubin 1997	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116 6/20 3/12 1/29 2/16	3/39 3/36 2/7 8/82 12/50 1/13 4/33 6/22 6/103 4/20 2/12 0/30 1/15	<		4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8 5.5 − 2.8 0.7 + 1.4	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56] 1.50 [0.50, 4.52] 1.50 [0.30, 7.43] 3.10 [0.13, 73.15] 1.88 [0.19, 18.60]
Sul Ter Ter	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squi st for overall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994 Greenough 1993 Kanarek 1992 Nilsson 1980	0.07 11/40 7/34 1/7 19/81 are=2.45 df = 2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116 6/20 3/12 1/29	3/39 3/36 2/7 8/82 12/50 1/13 4/33 6/22 6/103 4/20 2/12 0/30	<		4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8 5.5 − 2.8 0.7	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56] 1.50 [0.50, 4.52] 1.50 [0.30, 7.43] 3.10 [0.13, 73.15]
02 Sul Tes 03	burns Goodwin 1983 Greenhalgh 1995 Jelenko 1978 btotal (95% CI) st for heterogeneity chi-squi st for overall effect=2.22 p= hypoalbuminaemia Bland 1973 Bland 1976 Brown 1988 Foley 1990 Golub 1994 Greenough 1993 Kanarek 1992 Nilsson 1980 Rubin 1997	0.07 11/40 7/34 1/7 19/81 are=2.45 df=2 p=0.2 0.03 9/50 4/14 6/34 7/18 12/116 6/20 3/12 1/29 2/16 0/15 50/324 are=3.94 df=8 p=0.8	3/39 3/36 2/7 933 8/82 12/50 1/13 4/33 6/22 6/103 4/20 2/12 0/30 1/15 0/15 36/313			4.0 2.8 11.0 16.5 1.4 5.6 7.4 8.8 5.5 − 2.8 0.7 + 1.4	2.47 [0.69, 8.79] 0.50 [0.06, 4.33] 2.40 [1.11, 5.19] 0.75 [0.35, 1.62] 3.71 [0.47, 29.06] 1.46 [0.45, 4.70] 1.43 [0.58, 3.49] 1.78 [0.69, 4.56] 1.50 [0.50, 4.52] 1.50 [0.30, 7.43] 3.10 [0.13, 73.15] 1.88 [0.19, 18.60]

Reviewer's conclusions

Implications for practice:

It would seem reasonable to conclude clinicians considering using human albumin in critically ill patients should review their policies.

Implications for research:

A strong argument could be made that albumin should not be used outside the context of a properly concealed and otherwise rigorously conducted randomised controlled trial with mortality as the end point. Until such data become available, there is also a case for a review of the licensed indications for albumin use.

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