

UK Critical Care Research Forum

Small volume resuscitation **W**ith albumin in **I**ntensive care: **S**tudy of **H**aematological effects (**SWISH**)

Jonathan Bannard-Smith

Central Manchester University Hospitals, UK

Rinaldo Bellomo

Austin Health & ANZICS Research Centre, Melbourne, Australia

Background

- **Fluid bolus therapy (FBT) is common in critically ill patients.**
- **Safety issues with FBT**
 - Fluid type- artificial and/or natural colloids
 - Sodium and chloride content
 - Contribution to positive fluid balance



Background

ORIGINAL ARTICLE

A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

The SAFE Study Investigators*

- “In conclusion, our study provides evidence that **albumin and saline** should be considered **clinically equivalent** treatments for **intravascular volume resuscitation** in a heterogeneous population of patients in the ICU.”
- In first 48 hours those receiving albumin had:
 - Less fluid delivered ($P < 0.001$)
 - Less positive fluid balance ($P < 0.001$)

N Engl J Med 2004;350:2247-56.

Background

EFFECT OF INTRAVENOUS ALBUMIN ON RENAL IMPAIRMENT AND MORTALITY IN PATIENTS WITH CIRRHOSIS AND SPONTANEOUS BACTERIAL PERITONITIS

PAU SORT, M.D., MIQUEL NAVASA, M.D., VICENTE ARROYO, M.D., XAVIER ALDEGUER, M.D., RAMON PLANAS, M.D., LUIS RUIZ-DEL-ARBOL, M.D., LLUIS CASTELLS, M.D., VICTOR VARGAS, M.D., GERMÁN SORIANO, M.D., MÓNICA GUEVARA, M.D., PERE GINÈS, M.D., AND JOAN RODÉS, M.D.

TABLE 2. CLINICAL OUTCOME ACCORDING TO THE ASSIGNED TREATMENT.*

OUTCOME VARIABLE	CEFOTAXIME (N=63)	CEFOTAXIME PLUS ALBUMIN (N=63)	P VALUE
Resolution of infection — no. (%)†	59 (94)	62 (98)	0.36
Duration of antibiotic therapy — days	6±1	5±1	0.48
Paracentesis for ascites after resolution of infection — no. (%)‡	16 (25)	14 (22)	0.83
Hospital stay — days	13±1	14±1	0.48
Renal impairment — no. (%)	21 (33)	6 (10)	0.002
Death — no. (%)			
In hospital§	18 (29)	6 (10)	0.01
At three months¶	26 (41)	14 (22)	0.03

N Engl J Med 1999;341:403-9.

Background

Research

Open Access

Small-volume resuscitation with hyperoncotic albumin: a systematic review of randomized clinical trials

Matthias Jacob¹, Daniel Chappell¹, Peter Conzen¹, Mahlon M Wilkes², Bernhard F Becker³ and Markus Rehm¹

- Hyperoncotic HAS is suitable for FBT
- Potential benefits: less morbidity, renal failure, oedema
- No evidence of harm
- Further trials of hyperoncotic HAS required

11 out of 20 studies authored by J Boldt

Critical Care 2008, 12:R34

Research questions

For intensive care patients receiving 4% versus 20% albumin for fluid bolus therapy:

- What are the differences in FBT delivered? (volume, Cl⁻, Na⁺)
- Is it feasible to collect and compare data on thromboelastography? (**SWISH**)
- Is it feasible to collect and compare other physiological data commonly scrutinised during FBT? (**SWIPE**)

Pilot data

- **Retrospective study of ICU patients receiving 20% v 4% albumin as FBT**
 - 202 patients Apr 2012 – Mar 2013
 - Australian metropolitan tertiary ICU
 - Differences in FBT delivered
 - Physiological outcomes at 1,2 & 4 hrs

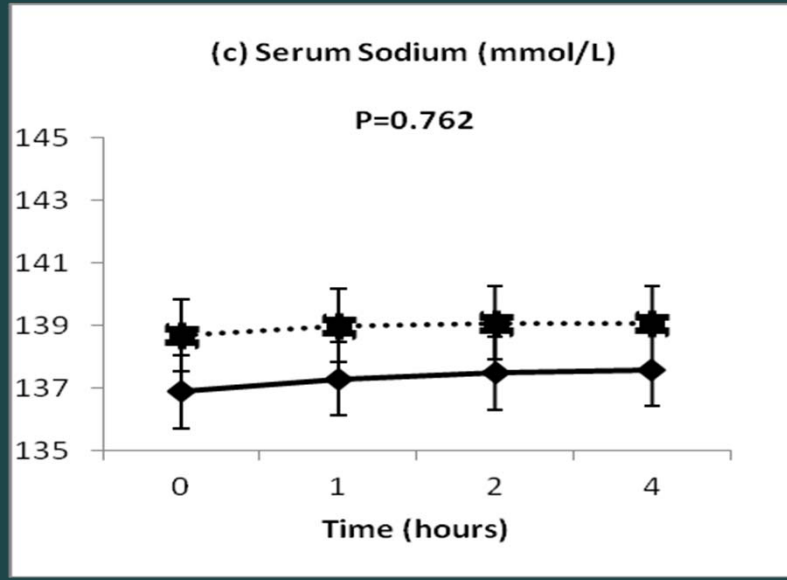
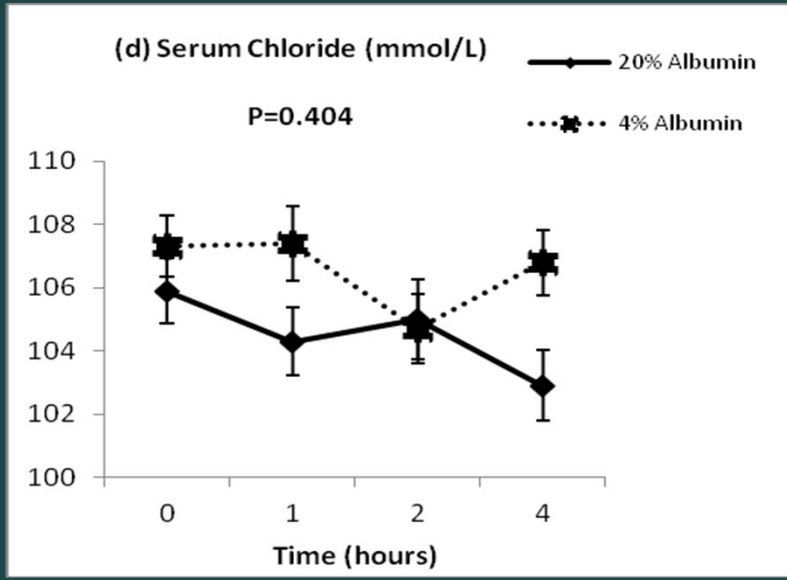
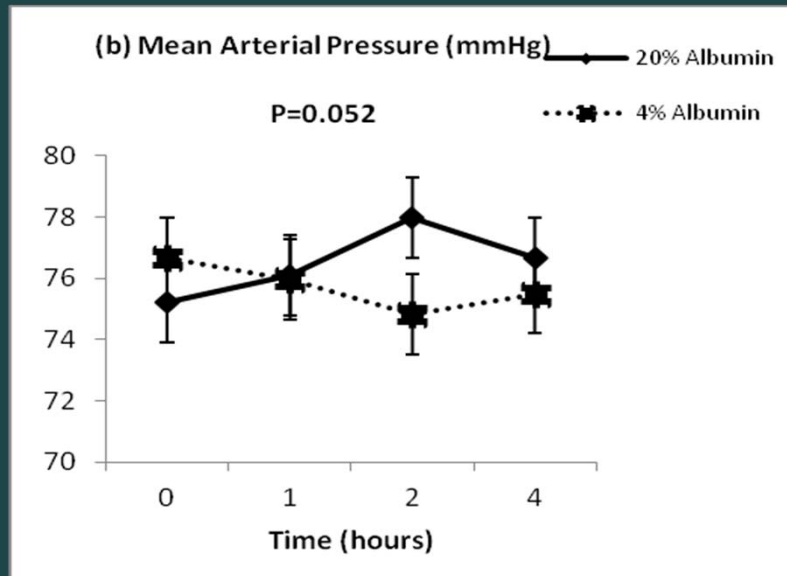
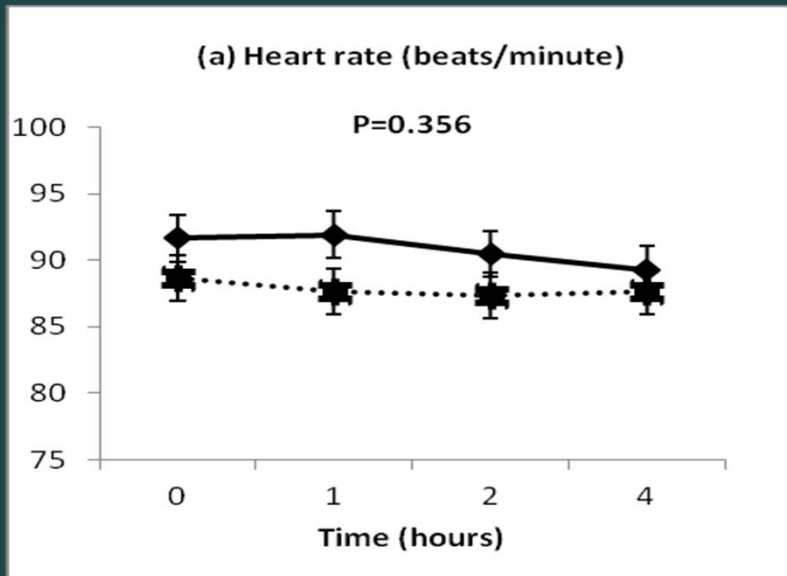
Bannard-Smith et al. Crit Care Resus 2015; 17(2): 122-8

Pilot data

Characteristics of Albumin FBT :

- Median volume: 4% = **500ml** ; 20% = **100ml** (P<0.0001).
- Sodium given: **70 mmol** vs. **10mmol** (P<0.0001).
- Chloride given: **64 mmol** vs. **2 mmol** (P<0.0001).

Bannard-Smith et al. Crit Care Resus 2015; 17(2): 122-8



Pilot data

Patient characteristics

- Sicker patients received 20% albumin
 - More liver disease & need for RRT
 - Higher crude mortality (18.8% vs. 6.6%)
 - No difference in mortality after risk adjustment [OR 1.21 (0.69-5.21) P=0.22]

Key findings

- 20% HAS group received
 - 5 times less volume,
 - 7 times less sodium and
 - 30 times less chloride
 - Trend toward a greater MAP effect

The proposed study

- **Investigator-initiated, multi-centre RCT**
 - Open label
 - Permuted blocks of varying size
- **20% (intervention) versus 4% (control) HAS for FBT**
 - Used for 48 hours after randomisation
 - Physiological data at baseline, 1,2 and 4 hours post each FBT episode.

The proposed study

- **Inclusion criteria?**

- Within 24hrs of ICU admission
- Age >18 years
- Treating clinician deems FBT necessary
- Presence of at least one of:
 - heart rate >100
 - systolic BP <90 mmHg
 - MAP <65 mmHg
 - PPV or SVV >12 %
 - Cardiac index <2.2 L/min/m²
 - Urine output <20 ml/hr
 - Lactate >2 mmol/L
 - Capillary refill >3 secs
 - CVP <8 mmHg.
 - Increasing need for vasopressors

- **Exclusion criteria?**

- Confirmed or suspected pregnancy
- Patients with TBI
- Active bleeding
- Haemoglobin <70 g/L
- Death expected <24hrs

The proposed study

- **Duration & follow-up**
 - 48 hours of intervention/control
 - ICU & Hosp discharge
 - 90 day follow-up
- **Outcomes**
 - Fluid delivered (volume & electrolyte load)
 - % Change in TEG data (**SWISH**)
 - Change in physiological data (**SWIPE**)
 - ICU/Hosp/90day outcomes

The proposed study

- **Sample size?**

- 40 patients (**SWISH**) - Manchester
- 200 patients (**SWIPE**) – All centres

- **Timeline?**

- Recruitment in Manchester: 2 pts/month
- Study period: 20-24 months

The proposed study analysis

- **Analysis plan**

- Repeated measures (dependent on distribution)
- Kaplan-Meier: in-hospital mortality and rate of discharge home.
- Logistic regression for baseline imbalances.
- Intention-to-treat for all analyses.

- **Estimated costs**

- Consumables: £240 per fluid bolus
- Research nurse: £150 per patient
- Overall estimate: £20,000

Details of study team

UK

Elaine Coughlan

Jonathan Bannard-Smith

Australia

Neil Glassford

Johan Mårtensson

Glen Eastwood

Michael Bailey

Rinaldo Bellomo

Current status

- **Protocol & sponsor in place**
- **Research nurses & fellow**
- **Funding applied for**
 - Commercial producer of albumin
 - ESICM research award
 - ???others...

Aim of presentation at UKCCRF

- **Advice on securing funding?**
 - Not commercially important
 - Widespread shortage of albumin
- **Validity of design?**
 - ?blinding
- **Other questions/comments?**