

Choice of fluid for resuscitation of septic shock

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Objectives: To determine current practice in choice of fluid resuscitation in children following publication of a systematic review that demonstrated a higher mortality in patients treated with human albumin solution.

Methods: A descriptive telephone and postal questionnaire survey directed at the on call paediatric registrar, lead clinician for paediatrics and the paediatric pharmacist at each of 33 hospitals within the Greater London area. The study was coordinated by the Paediatric Intensive Care Unit at St Mary's Hospital, London. The questionnaire was designed to assess whether a protocol/guidelines existed for resuscitation fluid in children with septic shock; whether the participants were aware of the systematic review and if so, had it changed clinical practice. The word "protocol" was used in its broadest sense to include guideline and policy.

Results: 11 hospitals had guidelines for fluid resuscitation of septic shock in children. These varied greatly: only three gave clear instructions of which fluid to use and how to use it. Choice of fluid varied widely and there was wide discrepancy between consultant's and registrar's choice of fluid. The systematic review had led to a change in policy in two thirds of respondents.

Conclusion: It is apparent that few paediatric departments have a written protocol or guidelines for the management of septic shock that is accessible to all those concerned in the acute treatment of seriously ill children. The systematic review into choice of fluid has had an impact on clinical practice with no data regarding whether this is in the patient's best interests.

The choice of resuscitation fluid in adults and children has been a subject for controversy for many years. A systematic review by the Cochrane Injuries Group Albumin Reviewers published in 1998 in the *British Medical Journal* added to this debate by suggesting that patients treated with human albumin solution (HAS) for its various indications (hypovolaemia, hypoalbuminaemia, and burns) may have a 6% increased risk of death compared with those treated with crystalloid solutions.¹ This systematic review did not include any trials that compared the use of HAS with crystalloid in children with sepsis. HAS is extensively used in the resuscitation of seriously ill children.

Clinical experience with use of 4.5% HAS as first line resuscitation fluid in paediatric septic shock, indicates that it is an effective treatment, with evidence to suggest that its use, along with other therapeutic modalities is associated with a reduction in mortality (Levin M *et al*, and the Meningococcal Study Group, Proceedings of the 2nd annual Meeting of the Royal College of Paediatrics and Child Health, York, 1998). While these are anecdotal data, there is no evidence that HAS is associated with harm in this condition. In addition, 4.5% HAS is recommended by the Acute Life Support Group as initial resuscitation fluid in children with septic shock.²

Meningococcal septicaemia is now the most common infectious disease cause of death in UK children.^{3–4} Meningococcal septicaemia causes a profound capillary leak syndrome together with myocardial dysfunction and multisystem failure.⁵

The authors of the systematic review felt that HAS use in critically ill patients should be urgently reviewed. But where has this left the practising clinician in the emergency management of the child with septic shock?

AIM

We postulated that there would be a change in practice regarding the use of 4.5% HAS in the initial management of children with septic shock following publication of the

systematic review. Our aim was to ascertain whether district general hospitals had a policy, guidelines or a protocol regarding the type of fluid to be used in resuscitation, and if so, whether these and clinical practice had been influenced by the systematic review.

METHODS

Thirty three district general hospitals with paediatric units were randomly selected within the Greater London area. A telephone and postal survey was conducted between August 1998 and February 1999, with a consultant paediatrician, the on call paediatric registrar and the paediatric pharmacist in each hospital. Six questions were asked, and a copy of the current protocol for the management of septic shock was requested:

- (1) Do you have a policy/protocol/guidelines regarding the choice of fluid in the resuscitation of children with septic shock?
- (2) What is your current practice regarding the choice of fluid in the resuscitation of children with septic shock?
- (3) Are you aware of the Cochrane Injuries Group Albumin Reviewers' systematic review?
- (4) If so, has it changed hospital policy/guidelines/protocol and practice regarding the use of 4.5% HAS?
- (5) Is 4.5% HAS freely available in your hospital?
- (6) Is cost an issue?

RESULTS

Only 11 of the 33 hospitals had any specific policy, guideline or protocol for the management of septic shock in children. These were examined in terms of specific advice on type and quantity of fluid to be given:

The guidance varied a great deal in presentation, from a single paragraph to being part of a 25 page general book of guidelines in paediatrics.

Of the 11:

- three gave clear instructions of which fluid to use and how to use it; two of the three stated the use of 4.5% HAS for resuscitation in meningococcal disease
- three were protocols specifically for meningococcal disease, two of which stated the use of 4.5% HAS, the third was non-specific regarding choice of fluid
- one was a non-specific protocol regarding fluid resuscitation in children with clear instructions not to use HAS
- one was a protocol for bacterial meningitis only, with guidelines on fluid restriction. This was part of a protocol booklet, which did not contain any guidelines on the management of shock in children
- one was a resuscitation table, with no advice on choice of fluid
- one was a protocol for the management of septic shock, advising use of 0.9% saline
- one was a table of intravenous rehydration guidelines, suggesting the use of 4.5% HAS in cases of shock.

Initial choices of fluid ranged between a non-specific instruction for colloid or crystalloid, normal saline, 4.5% HAS, Haemaccel or Gelofusine. Gelofusine was advocated in one protocol in both children and infants.

Initial fluid boluses to be given ranged from no clear instruction to 10 to 20 ml/kg, the commonest being 20 ml/kg. There were few specific instructions on when to call a senior staff member, when to inform anaesthetists, and when, for example to start inotropes.

The six questions asked of the consultant, the on call registrar and the pharmacist elicited the following answers:

(1) Do you have a protocol or guidelines regarding the choice of fluid in the resuscitation of septic shock? (table 1)

- 23 of 33 consultants (70%) said they had a protocol, but only eight of their registrars knew of its existence
- five registrars said a protocol existed when their consultants had said that one did not.
- 11 (33%) sent their protocols, which showed wide variability; only two were specific for the resuscitation of septic shock, with little agreement about the choice and volume of fluid to be given.
- five were in the process of being written or rewritten; two were using the St Mary's protocol for meningococcal disease,⁶ and one used the Advanced Paediatric Life Support protocol.²

(2) On being asked their current policy regarding the choice of fluid in the resuscitation of children with septic shock:

- 23 (70%) consultants use 0.9% NaCl as first line therapy, except in the case of meningococcal disease where six of them use 4.5% HAS; eight use 4.5% HAS with all sepsis, two didn't know what their protocol suggested
- 21 (64%) registrars use 0.9% NaCl as first line fluid therapy
- 12 (36%) registrars use 4.5% HAS as first line fluid therapy
- 11 (33%) registrars gave a different answer from their consultants for their fluid of choice for resuscitation

(3) On being asked whether they were aware of the systematic review:

- All consultants were aware
- 32 of 33 registrars were aware
- 77% of pharmacists were aware

(4) And, if so, has it changed hospital policy and practice regarding the use of 4.5% HAS?

- 21 consultants (64%) have changed their policy; however six of their registrars weren't aware that policy had changed
- 20 registrars (61%) said yes
- four registrars didn't know whether hospital policy had changed or not

Table 1 Is there a protocol or guideline regarding the choice of fluid in the resuscitation of septic shock in your hospital?

Protocol/Guideline	Yes	No	Don't know	Total
Consultant	23	9	1	33
Registrar	13	19	1	33
Pharmacist	3	7	9	19

- Most consultants and registrars were now using 0.9% NaCl instead of 4.5% HAS first line; with a small increase in the use of Gelofusine and fresh frozen plasma

(5) Is 4.5% HAS freely available in your hospital?

The availability of HAS was restricted in 11 of 33 hospitals.

(6) Is cost an issue?

In three of the 33 units (10%) the use of HAS was restricted because of financial considerations.

DISCUSSION

This audit examined current practice in the management of children with septic shock, and whether this had been influenced by publication of the systemic review by the Cochrane Injuries Group Albumin Reviewers.¹ The publication of this review has understandably caused enormous concern and confusion among clinicians concerning the use of 4.5% HAS, which seems to have led to changes in the resuscitation policy regarding children with septic shock. The consequences of these changes in resuscitation policy, and the confusion in general, are yet to be determined, but there has been a documented reduction in the use of HAS.⁷ It is unfortunate that the interpretation, by clinicians, of a systematic review of the use of HAS may have an enormous and potentially adverse influence concerning clinical practice, yet there is little, or nothing in the way of published data to either support or refute this change in practice in children with septic shock. The Cochrane Injuries Group Albumin Reviewers did not investigate the issue of the use of HAS in children with septic shock, presumably because no such data exist. However, clinicians treating this group have wrongly extrapolated the results of the systematic review and changed their practice accordingly, with unpredictable and possibly deleterious results.

For patients with shock of any aetiology, treatment of the underlying cause is mandatory. Rapid intravascular volume expansion guided by clinical examination and urine output is frequently adequate to restore organ perfusion and blood pressure in children with shock. In paediatric septic shock, Carcillo *et al* showed that rapid fluid resuscitation, using volumes in excess of 40 ml/kg in the first hour after presentation, was associated with an improvement in mortality, with no increase in the risk of pulmonary oedema.⁸

The type of fluid used for resuscitation of patients with shock is subject to ongoing debate with arguments that include: type of fluid lost; maintenance of plasma oncotic pressure; risk of infection and cost. Studies have repeatedly shown that less than 25% of administered crystalloid solutions remain within the intravascular space and the remainder rapidly and freely fills the interstitial and intracellular fluid spaces.⁹⁻¹¹ This means that approximately four times the volume of crystalloid solution would be required to have the equivalent volume enhancing effect of a substance that remained within the intravascular compartment.

Albumin is a plasma protein that provides approximately 80% of the intravascular colloid oncotic pressure in normal subjects. It has a molecular weight of 69 000 and is relatively impermeable to the vascular membrane under normal conditions. This capillary barrier is disrupted in sepsis and trauma.

However, in these conditions, the intravascular half life of albumin is 24 hours, with haemodynamic improvement persisting up to 36 hours after administration.¹² In addition to its relatively large molecular size, albumin has the additional advantage that it is a physiological molecule with many other functions.

Maintenance of plasma colloid oncotic pressure seems to be important in the control of normal organ function. Clinical studies in critically ill adults have found strong correlation between decreased plasma colloid oncotic pressure and an increased pulmonary wedge pressure and the subsequent development and severity of pulmonary oedema.^{13 14}

Unfortunately, there are no data to suggest that the noted increase in the use of crystalloid solutions for resuscitation of children with septic shock is safe, while the data on which the Cochrane Injuries Group Albumin Reviewers based their conclusion are completely lacking with regard to children with septic shock. Unless the noted change in practice in fluid resuscitation in children with septic shock is accompanied by a careful audit of outcome to ensure that harm is not being done, children may be being put at risk by clinicians wrongly interpreting statistical data.

In addition, it is disconcerting that relatively few paediatric departments have any written guidelines for the management of septic shock that is accessible to all those concerned in the acute treatment of seriously ill children. It may be that no protocol existed because there are no data to suggest one fluid is better than another. However, management of septic shock does not only entail fluid resuscitation and lack of a clear management protocol or guidelines for children with septic shock may be a cause for concern.

The discrepancy between paediatric trainees and consultants in their responses suggests poor communication within the paediatric department concerned, and may be a source of confusion when faced with an acute clinical scenario.

The findings of our study are disturbing given that meningococcal disease, the commonest cause of septic shock in childhood, has become the most important cause of childhood mortality from infection in the United Kingdom.

The continuing confusion regarding the choice of fluid for resuscitation of children with septic shock should prompt a formal review of current practice and an attempt to gather data regarding which is the optimal fluid to use for this indication.

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Contributors

Dr Sparrow helped design the questionnaire, gather the data and write the manuscript. Dr Hedderley helped design the questionnaire and gather the data. Dr Nadel helped design the questionnaire and write the manuscript.

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REFERENCES

- 1 **Cochrane Injuries Group Albumin Reviewers.** Human albumin administration in critically ill patients: systematic review of randomised controlled trials. *BMJ* 1998;**317**: 235–40.
- 2 **The Advanced Life Support Group.** *Advanced paediatric life support*. 3rd edn. London: BMJ Publishing Group, 2001.
- 3 **Platt M.** Child health statistical review. *Arch Dis Child* 1997;**77**:542–8.
- 4 **Anon.** 1995 *Communicable disease statistics*. London: Office of National Statistics, 1997.
- 5 **Nadel S, Habibi P, Levin M.** Management of acute meningococcal disease in childhood. In: Cartwright K, ed. *Meningococcal disease*. Chichester: Wiley, 1995:207–43.
- 6 **Pollard A, Britto J, Nadel S, et al.** Emergency management of meningococcal disease. *Arch Dis Child* 1999;**80**:290–7.
- 7 **Roberts I, Edwards P, McLelland B.** More on albumin. Use of human albumin in UK fell substantially when systematic review was published. *BMJ* 1999;**318**:1214–15.
- 8 **Carcillo JA, Davis AL, Zaritsky A.** Role of early fluid resuscitation in pediatric septic shock. *JAMA* 1991;**266**:1242–5.
- 9 **Rackow EC, Falk JL, Fein IA, et al.** Fluid resuscitation in circulatory shock: a comparison of the cardiorespiratory effects of albumin, hetastarch, and saline solutions in patients with hypovolemic and septic shock. *Crit Care Med* 1983;**11**:839–50.
- 10 **Griffel MI, Kaufman BS.** Pharmacology of colloids and crystalloids. *Crit Care Clin* 1992;**8**:235–53.
- 11 **Shires GT, Williams J, Brown F.** Acute changes in extracellular fluids associated with major surgical procedures. *Ann Surg* 1961;**154**:803.
- 12 **Rothschild MA, Bauman A, Yalow RS, et al.** Tissue distribution of I-131 labelled human serum albumin following intravenous administration. *J Clin Invest* 1955;**34**:1354.
- 13 **Rackow EC, Fein IA, Siegel J.** The relationship of the colloid osmotic-pulmonary artery wedge pressure gradient to pulmonary edema and mortality in critically ill patients. *Chest* 1982;**82**:433–7.
- 14 **Morissette M, Weil MH, Shubin H.** Reduction in colloid osmotic pressure associated with fatal progression of cardiopulmonary failure. *Crit Care Med* 1975;**3**:115–17.