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SPECIAL ARTICLE

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Fluid resuscitation in neonatal and pediatric hypovolemic shock: a Dutch Pediatric Society evidence-based clinical practice guideline

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Abstract *Objective:* To develop a clinical practice guideline that provides recommendations for the fluid, i.e. colloid or crystalloid, used for resuscitation in critically ill neonates and children up to the age of 18 years with hypovolemia. *Methods:* The guideline was developed through a comprehensive search and analysis of the pediatric literature. Recommendations were formulated by a national multidisciplinary committee involving all stakeholders in neonatal and pediatric intensive care and were based on research evidence from the literature and, in areas where the evidence was insufficient or lacking, on consensus after discussions in the committee. *Results:* Because of the lack of evidence in neonates and children, trials conducted in adults were considered. We found several recent meta-analyses that show excess mortality in albumin-treated groups, compared with crystalloid-treated groups, and one recent large randomized controlled trial that found evidence of no mortality difference. We found no evidence that synthetic colloids are superior to crystalloid solutions. *Conclusions:* Given the state of the evidence and taking all other considerations into account, the guideline-developing group and the multidisciplinary committee recommend that in neonates and children with hypovolemia the first-choice fluid for resuscitation should be isotonic saline.

Keywords Practice guideline · Systematic review · Shock · Fluid therapy · Crystalloid · Colloid · Albumin · Child

Introduction

Hypovolemia is the most common cause of circulatory failure in children. When inadequate tissue perfusion is not recognized and treated during a narrow window of opportunity, critical tissue hypoxia may develop, leading to a cascade of events resulting in multiple organ failure and death. For this reason the concept of early goal-directed therapy was introduced by Rivers [1]. The authors show that this concept provides significant benefits with respect to outcome in adult patients.

The first step in the treatment of hypovolemic shock is adequate fluid resuscitation with either a crystalloid or a colloid solution. Pediatric advanced life-support guide-

lines recommend up to 60 ml/kg fluid resuscitation during treatment of hypovolemic and septic shock [2]. For decades there has been controversy over the relative benefits of crystalloid versus colloid solutions for fluid resuscitation of hypovolemic patients [3]. Since the publication of two systematic reviews in 1998 in the *British Medical Journal* [4, 5] and the Cochrane Library [6, 7], the debate has intensified. These reviews of clinical trials conducted predominantly in adults consistently show an excess mortality of around 6% in critically ill patients who received human albumin solutions in comparison with patients who received a crystalloid.

In the Netherlands, the current uncertainty has resulted in the plea for a national evidence-based guideline in the pediatric age group. The goal of this guideline is to define the current optimal choice of fluid used for treatment of neonates and children with circulatory failure due to hypovolemia, and to attain more uniformity in clinical practice. Recently the final version of this guideline was issued; it is now recommended and endorsed by the Dutch Pediatric Society.

In this paper we describe the methods and results of this guideline developmental process, including (1) a survey questionnaire to assess pre-guideline volume replacement strategies on neonatal and pediatric intensive care units in the Netherlands; (2) a systematic review of all randomized controlled trials on fluid resuscitation in hypovolemic neonates and children; (3) all systematic reviews on fluid resuscitation in hypovolemic adults; (4) other considerations taken into account to reach consensus in our national committee; and (5) the final guideline recommendations.

Methods

Figure 1 outlines the guideline development process.

To develop this clinical practice guideline, we formed a guideline development group consisting of five members. A national multidisciplinary committee was formed comprising 29 members of all relevant disciplines and stakeholders (see Appendix).

As one of the goals of this guideline was to achieve more uniformity in clinical practice policy, we developed a questionnaire to first investigate the current Dutch pediatric practice of fluid solutions used for volume resuscitation. The questionnaire was sent to all directors of neonatal ($n = 10$) and pediatric intensive care units ($n = 8$) in the Netherlands.

Based on the results of this questionnaire, the following questions were formulated: (1) What type of fluid solution should be used for initial resuscitation of hypovolemia in neonates and children? (2) What is the optimal amount of fluid to be given and at what infusion rate? (3) What are the possible side effects related to each type of fluid, such as hypernatremia and peripheral edema?

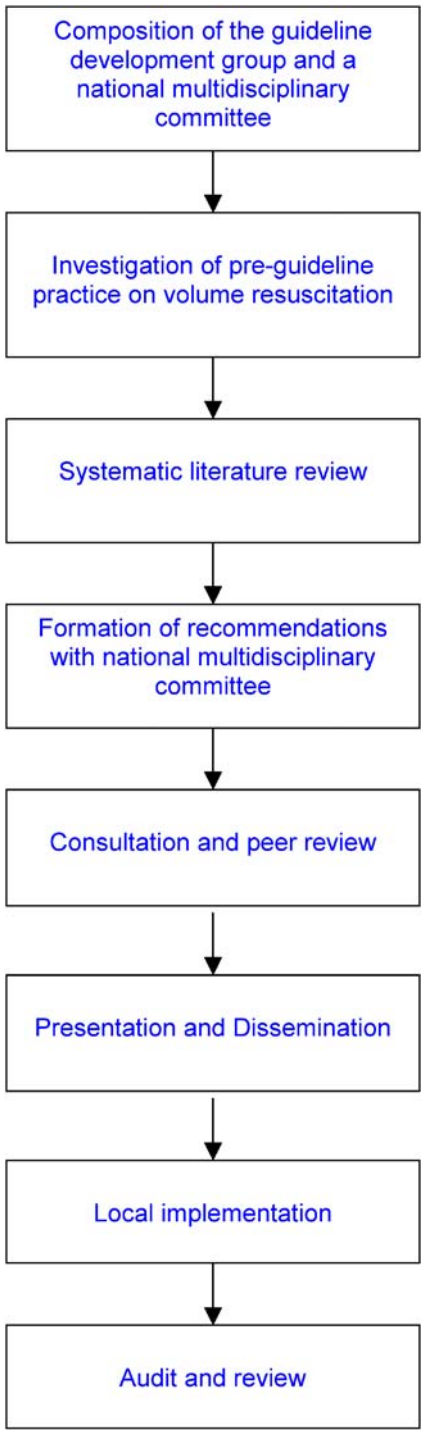

Fig. 1 Guideline development process

Studies were identified by sensitive computerized searches of Medline (1966–2000), Embase (1988–2000) and the Cochrane Library, with the help of a clinical librarian. In addition, reference lists of all available articles were reviewed to identify additional citations

not found in the computerized search. Studies written in English, French, German and Dutch were eligible for inclusion. We searched for guidelines, systematic reviews, meta-analyses and randomized controlled trials on volume resuscitation in critically ill neonates, children and adults with hypovolemia due to septic shock, trauma, dehydration, hemorrhage and post-cardiac surgery. With regard to question 2 we searched for studies comparing different volumes and rates of infusion in critically ill children. In October 2005 we repeated our literature search and looked for additional systematic reviews and randomized controlled trials in neonates and children. Studies were included only when they concerned clinically relevant outcomes, i.e. mortality and major morbidity such as pulmonary edema, length of stay in hospital, intraventricular hemorrhage or impaired neurodevelopment. Further details on the search strategy can be requested from the authors.

Each study was assessed independently for its methodological quality by two investigators using critical appraisal forms originally published in *JAMA* (http://ugi.usersguides.org/usersguides/hg/hh_start.asp). Disagreement between these raters was resolved by consensus. Each article was assigned a 'level of evidence' (Table 1), which in turn influenced the 'grade of recommendation' (Table 2). These grades of recommendation originate from the US Agency for Health Care Policy and Research [8].

The committee met on two separate occasions to formulate the final recommendations. In the event that there was not enough evidence or the evidence was of poor quality, the recommendations were based on consensus after discussion in the committee and finally by show of hands. The following 'other considerations' for reaching consensus were taken into account: (a) potential side effects of colloids and crystalloids, (b) current insight in pathophysiological mechanisms and their impact on the applicability of evidence from adults to children and neonates and (c) costs. All three aspects will be discussed below.

After a draft guideline was released it was piloted among end-users in the national multidisciplinary committee's hospital wards; feedback was received and included in the final version of the guideline. A comprehensive technical report can be obtained from the authors.

Results

Questionnaire

The response to the questionnaire was 10/10 (100%) of the neonatologists and 7/8 (88%) of the pediatric intensivists. First-choice fluid for volume resuscitation was in 50% a crystalloid and in 50% a colloid solution for both neonatologists and pediatric intensivists. The neonatologists used human albumin as a priority colloid, and the pediatric intensivists predominantly used a synthetic colloid, e.g. Gelofusine.

Literature

We did not identify any evidence-based guidelines on this topic. Our search for systematic reviews, meta-analyses

Table 1 Classification of evidence levels

1a	Evidence obtained from meta-analysis of randomized controlled trials
1b	Evidence obtained from at least one randomized controlled trial
2a	Evidence obtained from at least one well-designed controlled study without randomization
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study*
3	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies
4	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

* Refers to a situation in which implementation of an intervention is outside of the control of the investigators, but an opportunity exists to evaluate its effect

Table 2 Classification of grades of recommendations

A	Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing specific recommendation (Evidence levels 1a, 1b)
B	Requires the availability of well-conducted clinical studies but no randomized clinical trials on the topic of recommendation (Evidence levels 2a, 2b, 3)
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level 4)

Note: These classifications of types of evidence and the corresponding grades of recommendation originate from the US Agency for Health Care Policy and Research [8]

and randomized controlled trials identified 93 citations, of which 65 met the inclusion criteria. Twelve articles concerned children or neonates. Included systematic reviews and randomized trials are summarized in Table 3 and Table 4, respectively.

Question 1: What type of fluid solution should be used for initial resuscitation of hypovolemia?

Premature and full term neonates We identified one meta-analysis by Kirpalani, which was excluded because it does not analyze hypovolemic neonates separately [9]. We identified five randomized controlled trials [10–14]. Four studies did not meet our inclusion criteria: three focused on giving fluids prophylactically after birth [10–12] and one on giving albumin when there was hypoalbuminemia [13]. Only the study by So [14] met our inclusion criteria. The investigators undertook a randomized controlled trial to study the efficacy of a colloid (i.e. 5% albumin) versus a crystalloid (i.e. isotonic saline) in the treatment of 63 hypotensive preterm neonates. Outcomes, as assessed by the number of infants that died (RR 1.36; 95% CI 0.69–2.66), chronic lung disease (RR 0.48; 95% CI 0.13–1.87) or intraventricular hemorrhage (RR 1.52; 95% CI 0.91–4.87), did not differ significantly between the groups, but the wide confidence intervals indicate that the study was underpowered.

Older children Our search identified six randomized trials [15–20]. Four studies were excluded: one of them assessed albumin supplementation for hypoalbuminemia [16], another assessed hypertonic saline in neurotrauma [18], the third included children with severe malaria and metabolic acidosis, not hypovolemia per se [19], and the study by Ngo [17] used surrogate endpoints. Together with the recently published Wills trial [20], the Ngo study is the only large randomized controlled trial in children. We will briefly discuss the results of this trial, although it does not meet our inclusion criterion on clinical relevant outcomes.

Ngo performed a randomized, double-blind trial comparing the efficacy of four different fluid regimens (dextran 70, 3% gelatin, lactated Ringer's, and isotonic saline) in the initial management of dengue shock syndrome (DSS) in 222 children aged 1–15 years. The primary outcome measures were the initial pulse pressure recovery time and the occurrence of subsequent episodes of shock. Secondary outcome measures included the development of 'any complication' of fluid therapy. There were no deaths in any of the groups and there were no differences in the 'reshock' rate among the four groups. Six children had allergic reactions after colloid therapy (five received gelatin and one dextran), defined as fever and chills. One child in the gelatin group had severe epistaxis and another child in the dextran group a large hematoma at a site of minor trauma. In this study no clear benefits of any one of the four fluids in improving these surrogate endpoints could be demonstrated. Normal saline performed as well as the colloid solutions.

Table 3 Summary of included systematic reviews comparing the effect of any fluid solution with other fluid solutions

Study	Year	Age group	Intervention	Comparison	Outcomes	Adequate search strategy	Quality assessment of RCTs	Description of articles	Focused clinical question	Description of selection procedure of RCTs	Description of data extraction	Valid statistical pooling	Assessment of heterogeneity	RR (95% CI)[a]	Level of evidence
Velanovich [24]	1989	Adult	Colloid	Crystalloid	Death	No	No	Yes	Yes	No	No	Yes	No	NG	NA
Bisonni [21]	1991	Adult	Colloid	Crystalloid	Death	No	No	No	Yes	No	No	No	No	NG	NA
Schierhout [5]	1998	Adult	Colloid	Crystalloid	Death	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1.52 (1.08-2.13)	1a
Choi [23]	1999	Adult	Colloid	Crystalloid	Death, pulmonary edema	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	0.86 (0.63-1.17)	1a
Bunn [22]	2000	Adult	Colloid	Colloid	Death	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	0.99 (0.69-1.42)	1a
Alderson [7]	2002	Adult	Albumin	No albumin	Death	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1.46 (0.97-2.22)	1a

NG, not given; NA, not applicable
[a] Mortality RR in hypovolemic patients

Table 4 Summary of included pediatric randomized trials comparing the effect of any fluid solution with other fluid solutions, and the recent SAFE trial

Study	Year	Age group	No of patients	Inter-vention	Comparison	Outcome	Adequate random-ization	Sufficient follow-up	Blinding of patients	Blinding of treatment	Blinding of effect assessment	Patients prognostic equal	Equal concomitant treatment	RR (95% CI) mortality	Level of evidence
Boldt [15]	1993	Child	30	Albumin	HES	Death, pulmonary edema	Yes	No	No	No	No	No	No	No deaths and no pulmonary edema occurred	1b
So [14]	1997	Child	63	Albumin	Crystalloid	Death, CLD*, IVH**	Yes	Yes	No	No	Yes	Yes	Yes	1.36 (0.69–2.66)	1b
SAFE Study Investi-gators [26]	2004	Adult	6997	Albumin	Isotonic saline	Death	Yes	Yes	Yes	Yes	Yes	Yes	Yes	0.99 (0.91–1.09)	1b
Wills [20]	2005	Child	512	Ringer's lactate or 6% dextran 70 (a colloid) or 6% hydroxyethyl starch (a colloid)		No. of of days in hospital	Yes	Yes	Yes	Yes	Yes	Yes	Not stated	Not given	1b

* CLD = chronic lung disease
** IVH = intraventricular hemorrhage

Boldt conducted a randomized study in 30 children less than 3 years of age undergoing cardiac surgery [15]. They were randomly assigned to receive albumin or low-molecular-weight hydroxyethyl starch solution (6% LMW-HES). No deaths occurred and none of the children had signs of pulmonary edema, but the wide confidence intervals indicate that the study was underpowered.

Recently, Wills conducted a large randomized controlled trial in 512 children with dengue shock syndrome, comparing three resuscitation fluids; Ringer's lactate, 6% dextran 70 and 6% hydroxyethyl starch [20]. A total of 383 children with moderately severe shock were randomly assigned to receive one of the three fluids and 129 children with severe shock to receive one of the colloids. The primary outcome was the requirement for supplemental intervention with rescue colloid. Secondary outcome measures were 'time taken to achieve initial and sustained cardiovascular stability' and 'number of days in hospital'. The relative risk of a requirement for rescue colloid was 1.08 (95% CI 0.78–1.47) among children with moderate shock who received Ringer's lactate as opposed to either of the colloid solutions. There were no differences in the time to final cardiovascular stability or the number of days in the hospital.

Adults Because of the lack of randomized controlled trials in children, we included trials conducted in critically ill adults. We found seven meta-analyses [4–7, 21–25] The systematic review by Wilkes was excluded because it did not analyze hypovolemic patients separately [25]. Recently a large randomized controlled trial, the Saline versus Albumin Fluid Evaluation (SAFE) Study, was published [26]. Because of poor methodological quality we will not discuss the two older systematic reviews that compare colloids with crystalloids in fluid resuscitation here [21, 24]. Instead, the results of the remaining four reviews and the SAFE Study will be discussed below.

All four remaining systematic reviews are of good methodological quality (Table 3). The reviews by Alderson and Schierhout comparing colloids with crystalloids both show a 6% increase in mortality in the group receiving albumin [5, 6].

The meta-analysis by Choi [23] observed no difference between crystalloid and colloid resuscitation with respect to pulmonary edema [pooled RR 0.84 (0.25–2.45)] and mortality [pooled RR 0.86 (0.63–1.17)]. However, the power of the aggregated data was insufficient to detect small but potentially clinically important differences. Subgroup analysis showed a statistically significant reduction in mortality rate in trauma in favor of crystalloid resuscitation (RR 0.39, 95% CI 0.17–0.89).

The meta-analysis by Bunn did not show evidence that one colloid solution is more effective or safe than any other: albumin vs. HES: RR 1.17 (0.91–1.50), albumin vs gelatin: RR 0.99 (0.69–1.42) [22]. Again, in this study the confidence intervals are wide and the results do not exclude clinically relevant differences among colloids.

The SAFE Study investigators conducted a large randomized controlled trial in adult patients who had been admitted to the ICU and required fluid administration to maintain or increase intravascular volume [26]. A total of 6,997 patients were randomly assigned to receive 4% albumin or isotonic saline. The relative mortality risk among patients assigned to receive albumin compared with those assigned saline was 0.99 (95% CI 0.91–1.09). The authors conclude that there is evidence of no difference in mortality rate.

It is possible that there are certain subgroups where either colloids or crystalloids are more effective. These four meta-analyses comprised different patient categories, namely trauma, hypoalbuminemia, hypovolemia, sepsis, burns, and cardiopulmonary surgery. There was no evidence of advantage of colloids over crystalloids in any of these different indication subgroups, although in most cases the results were inconclusive because of lack of statistical power. Especially in patients after trauma or burns, albumin appeared to be associated with increased mortality and increased ventilator requirement. In trauma patients, the relative mortality rates when comparing albumin and saline were between 0.98 and 5.88. The SAFE Study included post-hoc subgroup analyses. The relative risk of death in the albumin group compared with patients in the saline group was 1.36 (95% CI 0.99–1.87) for trauma patients, 0.87 (95% CI 0.74–1.02) for patients with sepsis and 0.93 (95% CI 0.61–1.41) for patients with respiratory distress syndrome. It must, however, be noted that in large studies such subgroup differences frequently occur by chance, and common wisdom holds that hypotheses generated in this manner should be evaluated in specifically designed and appropriately powered future studies.

Question 2: What is the optimal amount to give and at what infusion rate?

We identified only one study by Carcillo about the role of early and rapid fluid resuscitation in children with septic shock [27]. Included were 34 children (median age 13.5 months) with septic shock who all required vasopressor and/ or inotropic support. Therapeutic decisions were left to the attending staff in this observational study. At 1 h and 6 h, respectively, group 1 ($n = 14$) received 11 ± 6 and 71 ± 29 ml/kg (mean $\pm$ SD) of fluid; group 2 ($n = 11$) received 32 ± 5 and 108 ± 54 ml/kg of fluid; and group 3 ($n = 9$) received 69 ± 19 and 117 ± 29 ml/kg of fluid. Fluids used were 5% albumin, fresh frozen plasma, cryoprecipitate, isotonic saline and lactated Ringer's solution. Details on which patient received which fluid were not given in the paper. Survival in group 3 (8 of 9 patients) was significantly better than in group 1 (6 of 14 patients) or group 2 (4 of 11 patients). The authors concluded that rapid fluid resuscitation in excess of 40 ml/kg in the first hour following emergency department presentation of children with septic shock is associated with improved survival. However, since the treatment groups were assigned non-randomly and the choice of treatment was based on clinical criteria that were determined by individual physicians, and since no adjustments were made for co-interventions like the use of inotropics, these observations cannot prove cause and effect. *Level of evidence: 2b.*

There is no evidence in children and neonates with hypovolemia not caused by septic shock about the optimal volume to be used and the velocity of fluid resuscitation. The efficacy of fluid replacement depends on the existing microvascular pressures, the compliance of the interstitial space and the permeability of the microvascular barrier. Hence both the volume and velocity of fluid resuscitation should be determined individually.

Question 3: What are the possible side effects related to the type of fluid used, such as hypernatremia and peripheral edema?

Hypernatremia Hypernatremia is thought by some to play a role in the development of intraventricular hemorrhage in neonates. There is a concern that by giving isotonic saline hypernatremia will be induced, because of a diminished renal sodium clearance potential in the first week of life. One of the outcomes assessed in the study by So was the serum sodium concentration [14]. The investigators included 63 hypotensive premature infants, randomly assigned to receiving a colloid or crystalloid solution. They could not find a significant difference in mean sodium concentration, or the rate of intraventricular hemorrhage or mortality, between the two groups. This lack of difference observed may be partly due to small numbers of patients. Furthermore, in most countries 5% albumin contains almost the same amount of sodium as isotonic saline (145 mmol/l vs. 154 mmol/l).

Peripheral edema Both the use of colloids and crystalloids is accompanied by the occurrence of peripheral edema [16, 28–31]. More important to know is how quickly such edema can be mobilized and whether there are any clinically relevant consequences. In our sensitive searches for evidence, no studies that give answers to these questions could be found.

Other considerations taken into account at the consensus meeting

Pathophysiology and applicability of the evidence from adults in neonates and children

If the alveolo-capillary membrane is intact, the lungs are well protected against a drop of colloid osmotic pressure (or hypoalbuminemia); if the membrane is damaged, the infusion of colloid aimed at increasing the colloid osmotic pressure is illusive, since the colloids leak into the interstitium and could even amplify the pulmonary and peripheral edema.

Table 5 The guideline's recommendations

1.	In neonates and children with hypovolemia the first-choice fluid for initial resuscitation is isotonic saline (Grade A)*
2.	When large amounts of fluids are required (e.g. sepsis), it is possible to use a synthetic colloid because of its longer duration in the circulation (Grade C)
3.	The initial fluid volume should be 10–20 ml/kg and repeated doses should be based on individual clinical response (Grade C)

* In adults there is grade A evidence. For reasons described in this paper this evidence is thought to be applicable to neonates and children.

Although most of the evidence in this field comes from studies in critically ill adults, the results of these investigations do not differ from those studies that have been conducted in critically ill neonates and children; there is just more information on adults. All studies fail to show an advantage of colloids over crystalloids when survival rates are considered. In addition, there is no clear evidence whether colloids or crystalloids confer benefit in certain subgroups of patients with shock, i.e. septic, hemorrhagic or hypovolemic. The reported increased mortality rate due to the use of albumin could be explained by the distribution of albumin across the capillary membrane, a process that is accelerated in critically ill patients [32]. Increased leakage of colloids into the extra vascular spaces might reduce the oncotic pressure difference across the capillary wall, making edema more likely. Yet, given the results of the SAFE Study, this mechanism may exist, but it may be less important in clinical practice than we thought previously. Although the distribution of body fluids in the neonate differs from that in adults, there is currently no reason to believe – either from pathophysiological theory or empirical evidence – that once a capillary leak exists, albumin would be beneficial in children.

It is, however, possible that in contrast to albumin, which is a small molecule (60 kDa), synthetic colloids with larger molecules (HES, 200 kDa) do not leak into the interstitial space. Yet, so far there is no evidence that some colloids are more effective or safer than others, when clinically relevant outcomes are considered.

Isotonic saline is distributed equally throughout the extracellular space. Because the extracellular fluid is one-fourth intravascular and three-fourths interstitial, only one-fourth of the infusate remains intravascular. For this reason some members of the multidisciplinary consensus group believed that it might be more efficient to use a synthetic colloid after initial crystalloids in patients with refractory hypovolemia and significant hemodynamic problems (e.g. those with severe sepsis). However, the SAFE Study showed that the ratio of the volume needed to maintain stable circulation of albumin to the same volume of isotonic saline administered was only 1.4. Again, we currently have no reason to believe that this ratio would be different in neonates and children.

Costs

Colloid solutions are much more expensive than crystalloid solutions: 1 l of albumin currently costs around 140 Euro (152 US$), 1 l of HES costs 25 Euro (27 US$) and 1 l of isotonic saline costs 1.5 Euro (1.6 US$).

The committee's recommendations

As colloids are biological products with a potential infection hazard or a risk of anaphylactic reaction and because they are much more expensive than crystalloids, it was felt by the national multidisciplinary committee that their benefits over crystalloids should be proved before they were used. Given the state of the evidence and taking all other considerations into account, the guideline-developing group and the national multidisciplinary committee recommend that in neonates and children with hypovolemia the first-choice fluid for initial resuscitation should be isotonic saline. When large amounts of fluids are required (e.g. in sepsis), it is possible to use a synthetic colloid because of its longer duration in the circulation. The initial fluid volume should be 10–20 ml/kg, with repeated doses based on individual clinical response (Table 5).

Discussion

In adult patients the current volume of evidence on the solutions of choice for fluid resuscitation of hypovolemic patients is large, consistently showing no advantage of colloids over crystalloids. Despite this, several surveys have shown that this evidence has not changed clinical practice: the majority of physicians still use colloid products [33–35]. More interestingly, most physicians could not state reasons for choosing between products [34]. To bridge this apparent gap between the evidence and actual clinical practice, guidelines may be needed [36, 37]. Clinical practice guidelines are seen as powerful tools to achieve effective and efficient care, but have been demonstrated to be effective only if there is sufficient rigor in their method of development [38]. Having completed a rigorous and objective synthesis of the evidence base, the guideline-development group must make what is essentially a subjective judgment on the

recommendations that can validly be made on the basis of the available evidence [39]. Subjective judgment risks the reintroduction of bias into the process. However, in high-quality guideline-development processes this is not the judgment of one individual but of a carefully composed multidisciplinary group. An additional safeguard here is the requirement for the guideline-development group to present clearly the evidence on which the recommendation is based, and to make the link between the evidence and the recommendations explicit, explaining how the evidence was interpreted [39]. Thus, the summarized research evidence is only one factor in clinical guidelines, and the 'other considerations' are just as important in reaching consensus on the recommendations. This holds especially when there is insufficient research evidence. Therefore, these 'other considerations' should be clearly presented in any guideline or its technical report [40].

Before the present guideline was developed there was controversy in the Netherlands about the fluid of choice for volume replacement; about 50% of neonatologists and pediatric intensivists used colloids. We found that in children the volume and quality of the available research evidence is limited. The final recommendations are largely based on the 'other considerations', in this case the potential side effects of colloids and crystalloids, current insight into pathophysiological mechanisms and their impact on the applicability of evidence from adults to children and neonates, and costs. We involved 29 stakeholders in Dutch neonatal and pediatric intensive care practice to formulate the recommendations and unanimously decided that isotonic saline should be the first choice, because it is equally effective, safe and up to 100 times cheaper than albumin. We realize that in other settings and countries the 'other considerations' may play a different role and have a different bearing on decision making. As the process of development of this guideline was explicit, pediatric intensivists and neonatologists outside the Netherlands may make their own recommendations based on the information we have assembled.

We believe that the introduction of this nationwide guideline for fluid resuscitation may contribute to an optimal, cost-effective universal treatment strategy in pediatric patients with imminent circulatory failure.

Conclusion

Given the state of the evidence and taking other relevant considerations into account, the guideline-developing group and the Dutch national multidisciplinary committee recommend that in neonates and children with hypovolemia the first-choice fluid for resuscitation should be isotonic saline.

This guideline will be updated in July 2008

Appendix: National Multidisciplinary Committee

Neonatologists

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Others

M. Hemmink, nurse, neonatology; D. Tol, nurse, intensive care; T.W.J. Schulpen, MD, PhD, Director, Quality Office, Dutch Pediatric Society; C.R. Lincke, MD, PhD, Chair of the Society's Guideline Development Committee, Dutch Pediatric Society

None of the members of the study group or the national multidisciplinary committee had any connections with the pharmaceutical industry or had otherwise any financial interest in the final recommendations.

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