Colloids versus Crystalloids in Fluid Resuscitation: An Analysis of Randomized Controlled Trials

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Background. Controversy about fluid therapy in resuscitation has existed since the 1960s. The difficulty could be that fluid behavior at the lung capillary membrane level may vary depending on the patient's particular pathology.

Methods. Mortality rates taken from randomized controlled trials were analyzed to compare colloidal and crystalloidal fluid for resuscitation efforts. We controlled for the underlying pathological process by categorizing subjects into three groups: (1) surgical stress, (2) hypovolemia, and (3) severe pulmonary failure. A cost-effectiveness analysis also was performed.

Results. No statistically significant differences in mortality rates were found. The cost of each life saved using crystalloids is $45.13, and the cost of each life saved using colloidal solutions is $1493.60.

Conclusions. Because there is no significant mortality-rate advantage to using colloids, and because the cost-effectiveness ratio for crystalloids is much lower than for colloids, it is concluded that crystalloids should always be used in resuscitation efforts.

Key words. Colloids, resuscitation, mortality, cost-effectiveness. *J Fam Pract 1991; 32:387-390.*

Controversy about fluid therapy in resuscitation has existed since the 1960s. The difficulty in predicting the effects of colloidal and crystalloidal fluids may be caused by the fact that fluid behavior at the lung capillary membrane level may vary depending on the patient's particular pathology.

Many laboratory and clinical studies addressing this topic have been reported in the past three decades. Some of them have shown advantages for crystalloids,[1–8] some have demonstrated advantages for colloids,[9–15] and still others have demonstrated no difference between the two.[16,17]

In evaluating the effectiveness of fluid resuscitation, several authors have studied a wide variety of physiologic variables and different physiologic endpoints. Surprisingly, mortality has not been the primary dependent measure. The sole exception is the work of Velanovich.[18] Velanovich used a meta-analytic approach and found that the overall treatment effect, when data from several studies were pooled, showed a 5.7% relative difference in mortality rates in favor of crystalloid therapy. He pooled data from randomized and nonrandomized clinical trials. His decision to include the nonrandomized study of Shoemaker et al[10] played a large role in his results.

The present article describes a data compilation from several randomized controlled clinical trials (Table 1), an analysis of mortality rates of different patient populations, and a cost-effectiveness analysis of different types of fluid therapy in resuscitation.

Material and Methods

To determine whether there is a difference between colloid and crystalloid fluid resuscitation, data from rigorously designed studies, ie, randomized clinical trials,[16,19–24] were pooled. Thereafter, mortality rates were analyzed by separating trials according to the severity of the underlying process of the patients. The following three groups were used:

1. Patients with surgical stress only (major operative procedures on the abdominal aorta). Patients in this group had no hypovolemic shock, no pulmonary failure, and no sepsis.
2. Injured patients, subject to surgical stress and presenting with hypovolemia.

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Table 1. Mortality Rates in Randomized Controlled Trials Comparing Colloidal and Crystalloidal Fluid Resuscitation Efforts

Group, by Severity of Underlying Process	Authors of Studies Analyzed	Colloid Therapy		Crystalloid Therapy	
		n	died	n	died
1 Surgical stress	Virgilio et al[16]	15	1	14	1
	Boutros et al[19]	7	0	17	2
2.1 Hypovolemic without complications	Lowe et al[20]	57	3	84	3
	Moss[21]	16	0	20	1
2.2 Hypovolemic with complications	Rackow et al[22]	18	11	8	6
	Lucas et al[23]	27	7	25	0
3 Pulmonary failure	Metildi et al[24]	20	12	26	13

3. Patients with established severe pulmonary failure (intrapulmonary shunt of greater than 20% and a roentgenogram of the chest demonstrating interstitial and intra-alveolar edema). Fluid therapy in these patients was administered after the diagnosis of pulmonary failure was made.

In all studies, subjects were randomized into groups receiving either colloidal or crystalloidal treatment. The proportion of subjects receiving colloidal treatment, however, was not exactly .5 (Table 1). This is because in two studies, the probability of a subject receiving colloidal therapy was not .5. In the study by Boutros et al[19] there were 26 subjects randomized (with equal probability) into three groups. Two of these groups received crystalloid solutions (one group received normal saline, the other, Ringer's lactate solution). In the same way, Rackow et al[22] randomized subjects into three groups. Two of these groups received colloids (one received albumin, the other, hetastarch).

Chi-square tests were used to determine whether differences in mortality rates among colloid and crystalloid subgroups were statistically significant.

Cost-effectiveness analysis was performed using a commercially available computer program called SMLTREE.[25]

Fluid cost estimates were obtained locally. At Oklahoma Memorial Hospital, the cost of 1 g of albumin was $5.00 and the cost of 1 L of Ringer's lactate solution was $5.95.

Results

When all the trials were pooled, the mortality rate for crystalloid therapy was 13.4%, and the mortality rate for colloid therapy was 21.25% (P was not significant at .01 level). Thereafter, mortality rates were compared between colloid and crystalloid therapy subgroups. This method of comparison was done for each of the three patient groups described previously (surgical stress, hypovolemic status, and pulmonary failure). The results are displayed in Figure 1. Significant differences were not found between colloid and crystalloid therapy in any of the patient groups.

Furthermore, in order to test whether the severity of the underlying process played an important role, group 2 was subcategorized into group 2.1, hypovolemic status, or shock without sepsis, or pulmonary failure; and group 2.2, serious hypovolemic shock with complications such as sepsis or pulmonary failure. Fluid therapy in these patients was administered before complications developed.

Afterward, colloid and crystalloid subgroups were analyzed for these patients. The results are displayed in Figure 2. There were no significant differences between the colloidal mortality rate and the crystalloidal mortality rate for either group 2.1 or group 2.2.

For clinical trial studies in which the criterion for the end of the resuscitation period was clearly stated, data for our cost-effectiveness analysis were pooled (Table 2). The per-patient intake of fluids in the resuscitation period averaged 4.70 L for the colloid group and 6.57 L for the crystalloid group. The per-patient average amount of albumin used in the colloid group was 229.77 g. There-

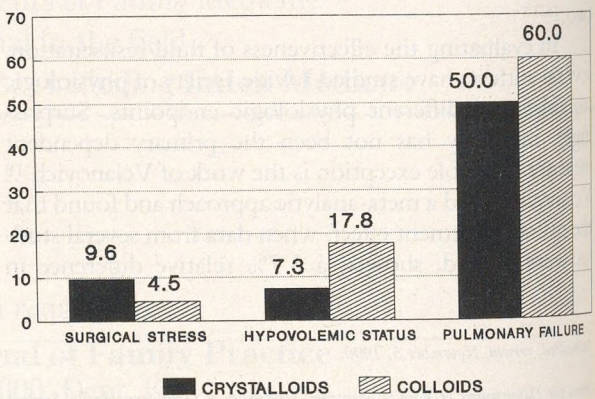

Figure 1. Combined mortality rates by diagnostic group for crystalloid and colloid resuscitation therapy.

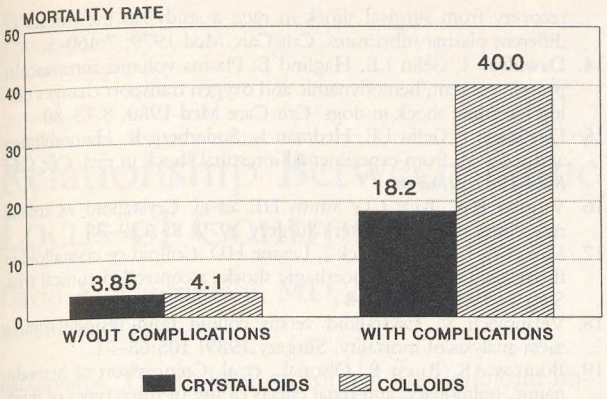

Figure 2. Combined mortality rates in patients with and without complications receiving crystalloid and colloid resuscitation treatments. Those patients with complications represent more severe cases before treatment.

fore, the per-patient crystalloidal therapy cost was estimated to have been $39.09; the estimate for the per-patient colloidal therapy cost was $1176.21. For crystalloidal therapy, the cost-effectiveness ratio is $45.13 per life saved; for colloidal therapy, the cost-effectiveness ratio is $1493.60 per life saved.

Discussion

In resuscitation research, study results are frequently dependent on the design and conditions of the experiment and the underlying pathological process. Increased microvascular permeability to albumin and protein macromolecules has been extensively documented and underlies the concern that colloidal solutions may be harmful or ineffective in clinical disorders.

Robin et al[26] demonstrated that in septic patients the concentration of solutes (such as albumin, globulin, and dextran) was similar in both pulmonary edema fluid and plasma. The authors concluded that permeability to macromolecules was increased in sepsis. Lung-lymph models have thus been used to show increased microvascular permeability in laboratory animals following intravenous injection of *Escherichia coli* endotoxin[27] and live *Pseudomonas* bacteria.[28] Haupt concluded that "the concern that resuscitations with colloidal fluids might be detrimental in conditions associated with increased microvascular permeability to macromolecules is valid."[29]

On the other hand, when microvascular permeability was normal, Tranbaugh et al[30] found no increment of extravascular lung water after hemodilution with crystalloidal solutions in severe hypovolemic shock. They concluded that lung contusion or sepsis are the primary determinants of interstitial fluid accumulation.

Our results are consistent with these trials. In patients presumably without altered microvascular permeability (group 1 and group 2.1), outcomes are independent of the kind of fluids used. The overall mortality rate in group 1 was higher than the mortality rate in group 2.1, and this difference could be explained by the average age in group 1 (mean age = 60) being higher than the average age in group 2.1 (mean age = 30).

In cases with definitely altered microvascular permeability (group 3), or in patients who were developing microvascular permeability alterations (group 2.2), colloidal treatment groups showed even higher mortality rates than crystalloidal treatment groups, but the difference was not enough to reach statistical significance. Therefore, colloids failed to show superiority over crystalloids, regardless of the severity of the underlying process.

Colloids could have a partial extravascular distribution that increases pulmonary edema (capillary leak syndrome). This could explain the lack of expected improvement for this type of therapy. In addition, there are clinical data indicating deleterious effects of albumin resuscitation on renal function,[31] cardiac function,[3] and coagulation.[32] There is also a small but definite incidence of serious allergic reactions[33] when colloids are used. Our results encourage the use of crystalloids in all cases.

Table 2. Albumin and Fluid Required for Resuscitation in Randomized Controlled Studies Included in Meta-analysis

Study Authors	Criterion	Colloid Therapy		Crystalloid Therapy Fluid (L)
		Albumin (g)	Fluid (L)	
Moss et al[21]	Clinical signs of satisfactory volume expansion	400	8	8
Lowe et al[20]	To restore vital signs	213	5.87	5.37
Virgilio et al[16]	Hemodynamic endpoints	170	3.40	8.40
Rackow et al[22]	Hemodynamic endpoints	136.1	1.55	4.52
Average		229.77	4.70	6.57

Furthermore, cost-effectiveness analysis showed that using crystalloids cost $45.13 per life saved as compared with using colloidal solutions at a cost of $1493.60 per life saved.

In choosing among feasible alternatives, the physician and the health policy analyst should consider some means of evaluation that compares the relative cost and effectiveness of these competing strategies. One appropriate measure is the cost to effectiveness ratio, which, in this case, could express how many additional patients' survival can be "bought" for each additional dollar expended. Since colloids cost more than crystalloids and are no more effective, the colloid strategy in fluid resuscitation can be rejected from further consideration.

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