Fluid management: the pharmacoeconomic dimension

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Abstract

Cost is a key concern in fluid management. Relatively few data are available that address the comparative total costs of care between different fluid management regimens in particular clinical indications. Relevant costs of fluid-associated morbidity and mortality, including those incurred after intensive care unit or hospital discharge, also need to be considered in evaluating the cost–benefit ratios of administered fluids. Rigorously designed pharmacoeconomic studies are needed to delineate the costs and benefits of various approaches to fluid management.

Keywords: colloids, economics (medical), morbidity, mortality, serum albumin

The controversy surrounding choice of resuscitation fluid owes much of its intensity and longevity to economic concerns, yet reported pharmacoeconomic data comparing costs of various fluid regimens are remarkably limited. The expenditures for one fluid have typically been compared with those for another when cost data have been reported [1–3]. These data have rarely rigorously addressed the comparative total costs of care taking into account potential differences in outcomes such as morbidity, mortality and length of intensive care unit or hospital stay. Consequently, the available pharmacoeconomic evidence to date unfortunately fails to provide a solid foundation upon which to rest clinical decision-making.

It will ultimately be necessary to define cost–benefit ratios with specific reference to particular clinical indications and fluid management regimens. In one randomized control trial (RCT), for example, acute albumin administration in hospitalized cirrhotic patients with ascites significantly shortened hospital stay and reduced total costs of care by nearly 60% [4]. Chronic albumin administration on an outpatient basis, however, did not afford a similarly favourable cost–benefit ratio.

Albumin stands centre stage in the debate over fluid management costs. This natural colloid has been reported to account for a substantial fraction of the pharmacy budget at some hospitals. Some clinical investigations have failed to provide evidence of significant patient benefit associated with albumin administration [5–8]. Such lack of benefit coupled with the comparatively high unit dose cost of this colloid has often prompted calls for the abandonment of albumin in fluid management. The RCTs of albumin administration reported to date have nevertheless typically involved quite small numbers of patients and were accordingly statistically underpowered to detect differences in clinically relevant endpoints such as morbidity, mortality and length of stay.

HES = hydroxyethyl starch; RCT = randomized controlled trial.

Indeed, not a few studies have revealed significant differences favouring albumin in these clinically relevant endpoints. A recent RCT of patients with cirrhosis and spontaneous bacterial peritonitis has attracted considerable notice in this regard [9]. Both mortality and incidence of renal impairment were significantly reduced by albumin administration. The incidence of renal impairment or severe hyponatraemia in an earlier RCT of cirrhotic patients with tense ascites was significantly lower in patients treated by therapeutic paracentesis with versus without albumin infusion [10]. Development of either or both of these complications was significantly predictive of higher actuarial mortality rate.

Such differences favouring albumin are not restricted to cirrhosis. Addition of albumin to the priming solution in a RCT of patients undergoing cardiopulmonary bypass surgery was associated with a significant 34% reduction in mediastinal blood loss during the first 12 h postoperatively [11]. Furthermore, substitution of hydroxyethyl starch (HES) for albumin as the cardiopulmonary bypass priming fluid in a retrospective case–control study involving 288 patients, intended as a cost-saving measure, was associated with a dose-dependent increase in incidence of haemorrhage [12]. The US$3458 median unadjusted hospital cost associated with treatment of haemorrhage in these patients was far greater than the difference in cost between HES and albumin.

Hypovolaemic and septic shock, gastrointestinal surgery and hypoalbuminaemia are additional indications in which RCTs have provided evidence of significant benefit due to albumin administration. The incidence of pulmonary oedema, based upon radiographic evidence, was significantly four-fold greater for the saline than either the albumin or HES groups in a RCT of 26 patients with hypovolaemic and septic shock [13]. The severity of intestinal oedema during gastrointestinal surgery in a RCT of 18 patients was significantly less among recipients of albumin than of either Ringer's lactate or HES [14]. The total number of complications among 61 hypoalbuminaemic patients enrolled in a RCT of albumin supplementation was significantly greater by 136% in control than albumin patients, and the number of control patients experiencing complications was significantly greater by 44% [15]. Furthermore, the numbers of control patients developing septicaemia and pneumonia were significantly greater than those of the albumin group.

The unanswered question, of course, is the extent to which such differences in morbidity would affect the cost–benefit ratio of albumin. At a minimum, however, these differences suggest that, in certain indications and with certain administration regimens, the benefits of albumin may well justify its costs.

Another factor that needs to be considered is the time horizon for assessing total costs of care. Delayed morbidity and mortality occurring after discharge might contribute substantially to the total costs of care, although such added costs have seldom been addressed in clinical investigations thus far. In the RCT of Sort *et al* [9], for instance, the total hospital mortality rate for both the albumin and control groups together was 19%. An additional 13% of patients had, however, died by 3 months. Delayed severe persistent pruritus, most commonly manifested as pruritic crisis, has been reported in 32% of patients receiving extended HES treatment [16]. Such pruritus was encountered, on average, 25 days after commencement of treatment, and pruritus developed in the majority of patients after HES administration was discontinued. The repercussions of fluid therapy may extend to even longer time periods. In a renal transplantation study of 438 patients, for instance, intraoperative albumin administration was associated with a dose-dependent reduction in frequencies of delayed or absent perioperative graft function and a significantly higher graft survival rate at 1 year postoperatively [17]. Late morbidity and mortality after discharge from the intensive care unit or hospital can clearly impose additional costs that should be taken into account.

The current pharmacoeconomic picture of fluid management is very far from complete. There is little doubt that further studies are needed to establish the cost–benefit ratio of particular fluid administration regimens in specified clinical indications. The focus of such studies needs to be on the total costs of care.

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