OBJECTIVES:

Previous studies have shown that in children with severe malaria, resuscitation with albumin infusion results in a lower mortality than resuscitation with saline infusion. Whether the apparent benefit of albumin is due solely to its colloidal properties, and thus might also be achieved with other synthetic colloids, or due to the many other unique physiological properties of albumin is unknown. As albumin is costly and not readily available in Africa, examination of more affordable colloids is warranted. In order to inform the design of definitive phase III trials we compared volume expansion with Gelofusine (succinylated modified fluid gelatin 4% intravenous infusion) with albumin.

DESIGN:

This study was a phase II safety and efficacy study.

SETTING:

The study was conducted at Kilifi District Hospital, Kenya.

PARTICIPANTS:

The participants were children admitted with severe falciparum malaria (impaired consciousness or deep breathing), metabolic acidosis (base deficit > 8 mmol/l), and clinical features of shock.

INTERVENTIONS:

The interventions were volume resuscitation with either 4.5% human albumin solution or Gelofusine.

OUTCOME MEASURES:

Primary endpoints were the resolution of shock and acidosis; secondary endpoints were in-hospital mortality and adverse events including neurological sequelae.

RESULTS:

A total of 88 children were enrolled: 44 received Gelofusine and 44 received albumin. There was no significant difference in the resolution of shock or acidosis between the groups. Whilst no participant developed pulmonary oedema or fluid overload, fatal neurological events were more common in the group receiving gelatin-based intervention fluids. Mortality was lower in patients receiving albumin (1/44; 2.3%) than in those treated with Gelofusine (7/44; 16%) by intention to treat (Fisher’s exact test, p = 0.06), or 1/40 (2.5%) and 4/40 (10%), respectively, for those treated per protocol (p = 0.36). Meta-analysis of published trials to provide a summary estimate of the effect of albumin on mortality showed a pooled relative risk of death with albumin administration of 0.19 (95% confidence interval 0.06-0.59; p = 0.004 compared to other fluid boluses).
CONCLUSIONS:

In children with severe malaria, we have shown a consistent survival benefit of receiving albumin infusion compared to other resuscitation fluids, despite comparable effects on the resolution of acidosis and shock. The lack of similar mortality benefit from Gelofusine suggests that the mechanism may involve a specific neuroprotective effect of albumin, rather than solely the effect of the administered colloid. Further exploration of the benefits of albumin is warranted in larger clinical trials.