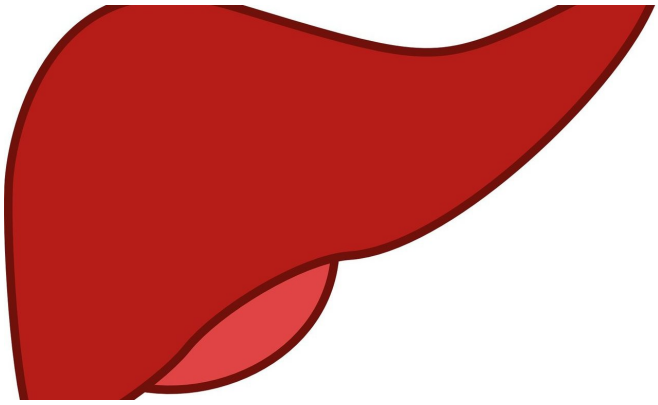
Albumin provides no benefit to hospitalized patients with advanced liver disease

3 March 2021



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Daily infusions of albumin provide no significant health benefit to patients hospitalised with advanced liver disease, over and above 'standard care', finds a large-scale multicentre trial led by UCL researchers.

Albumin is a protein made in the liver that prevents fluid leaking from the bloodstream to other body tissues and carries various substances throughout the body, such as hormones or enzymes. In people with liver disease, low albumin levels are associated with an increased risk of death among hospitalised patients who have cirrhosis, and laboratory studies have shown albumin to have an anti-inflammatory effect. Therefore, albumin infusions are considered the best fluid for patients with cirrhosis and are an integral part of clinical care.

Explaining the ATTIRE trial, Principal Investigator, Professor Alastair O'Brien (UCL Division of Medicine) said: "Acutely hospitalised patients with cirrhosis are very ill; infection and increased systemic inflammation lead to very high rates of death in those affected.

"Albumin infusions have been used with great enthusiasm by liver specialists for 70 years, are widely believed to be the best at reducing abnormal fluid build-up caused by cirrhosis and preclinical studies support an anti-inflammatory role. However, albumin is considerably more expensive than other fluids, shortages in production do occur and, crucially, confirmatory large-scale clinical trials to support use are lacking.

"To establish a better evidence base, we examined whether increasing a serum albumin level of 30 g/L or greater in these patients with repeated daily infusions of human albumin solution, compared with standard UK albumin use, would reduce the incidences of infection, kidney dysfunction, and death."

In the ATTIRE trial, published in the *New England Journal of Medicine*, 777 patients hospitalised with acute decompensated liver cirrhosis, were randomly placed in one of two groups. The trial was conducted across 35 UK sites and alcohol was the primary cause of cirrhosis in 90% of patients.

In the experimental arm of the study, known as the 'targeted albumin group', 380 patients were given daily infusions of human albumin solution to raise the concentration in the blood to 30 grams of albumin per litre or greater, for up to 14 days or until discharge.

In the other group, 397 patients were given 'standard care', which could include albumin infusions for draining ascites (fluid in the abdomen) or renal failure, for up to 14 days or until discharge. Standard care varies per patient, is based on a clinician's judgement, and the levels of albumin prescribed are far lower than the study's experimental arm.

The targeted albumin group received about 10 times more albumin and serum albumin levels rose to 30 grams per litre or greater within three days in

this group, whereas levels remained at 25 grams per litre or lower in the standard care group. To establish if the targeted albumin treatment had worked, the trial's primary end point was; infection, renal failure or death between days 3 and 15 after initiation of treatment.

Findings

In the targeted albumin group, 113 of 380 patients (29.7%) developed one of the primary end points: infection, renal dysfunction or death. In the standard care group it was 120 of 397 patients (30.2%). Across all hospitalised patients one third (32.3%) had died within six months of initiating treatment.

Researchers concluded there is no evidence of benefit for targeted albumin. In addition, more severe or life-threatening serious adverse events (i.e. pulmonary edema or ascites) occurred in those patients in the targeted albumin group.

Professor O'Brien, also Clinical Director of the UCL Comprehensive Clinical Trials Unit, added: "Our large, high quality, randomised trial showed no benefit for targeted albumin infusions and those given higher doses, in fact, had more serious adverse events. These data strongly support both the need to abandon the use of this costly therapy, and a reappraisal of our understanding of this complex condition. Finally, the high mortality in these patients does not appear to have changed in 20 years. This calls for a renewed focus on preventing the major causes of liver disease, excessive alcohol consumption and obesity."

Liver cirrhosis

Liver disease is the fifth commonest cause of death in the UK and the only one of the top 10 currently rising, predominantly as a consequence of excess alcohol consumption and increasing levels of obesity.

Around 70,000 people are admitted every year to hospitals in England with liver disease, and of those approximately 22,000 admissions are alcoholic liver disease and this figure continues to rise.

It is estimated that around 9,000 people die from cirrhosis in the UK each year. Average survival for people with decompensated (advanced) cirrhosis is two years. A common cause of death is infection as patients have a weakened immune system, yet no effective strategy exists to improve this.

The condition places a high demand on the health service with frequent admissions to hospital for management of ascites (abnormal fluid build-up in the abdomen) and other complications such as internal bleeding and brain complications such as encephalopathy.

Researchers from the UCL Institute for Liver and Digestive Health, the UCL Comprehensive Clinical Trials Unit, and the UCL Division of Medicine, played a part in this trial.

More information: Louise China, Nick Freemantle, Ewan Forrest, Yiannis Kallis, Stephen Ryder, Gavin Wright, Andrew Portal, Natalia Becares Salles, Derek Gilroy, and Alastair O'Brien, for the ATTIRE Trial Investigators, 'A Randomized Trial of Albumin Infusions in Hospitalized Patients with Cirrhosis' *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2022166

Provided by University College London