



# SCIENTIFIC REPORTS



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## Synthetic colloid resuscitation in severely injured patients: analysis of a nationwide trauma registry (TraumaRegister DGU)

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The purpose of this study was to investigate the efficacy and safety of synthetic colloid resuscitation among severely injured patients. Fluid resuscitation of trauma patients of a nationwide trauma registry was analysed between 2002 and 2015. Effects of synthetic colloid resuscitation in the pre-hospital setting and emergency department on renal failure, renal replacement therapy and multiple organ failure were analysed among patients with  $\geq 2$  days intensive care unit stay, and in-hospital mortality was analysed among all patients. 48,484 patients with mean age of 49 years and mean injury severity score of 23 points were included; 72.3% were male and 95.5% had blunt trauma. Risk-adjusted analyses revealed that patients receiving  $>1,000$  ml synthetic colloids experienced an increase of renal failure and renal replacement therapy rates (OR 1.42 and 1.32, respectively, both  $p \leq 0.006$ ). Any synthetic colloid use was associated with an increased risk of multiple organ failure ( $p < 0.001$ ), but there was no effect on hospital mortality ( $p = 0.594$ ). Between 2002 and 2015 usage of synthetic colloids dropped, likewise did total fluid intake and usage of blood products. The data from this analysis suggests that synthetic colloid resuscitation provides no beneficial effects and might be harmful in patients with severe trauma.

**Purpose.** Synthetic colloid infusion solutions have been developed to increase haemodynamic stabilization effectively and economically. One of the most frequently used synthetic colloid worldwide is hydroxyethyl starch (HES)<sup>1</sup>. Concerns about the use of starches grew after three multicentre randomised controlled trials (RCTs) found that HES was associated with a higher risk of acute kidney injury and bleeding in patients with sepsis or critical illness<sup>2</sup> and more deaths in patients with sepsis<sup>3,4</sup> when compared with crystalloids. The trials prompted the German Federal Institute for Drugs and Medical Devices to ask the European Medicines Agency (EMA) to review the use of HES in 2012. The EMA committee recommended suspending all use of HES. However, after the United Kingdom unilaterally removed HES from the shelves, a second EMA review was triggered. A second assessment committee confirmed that HES solutions must not be used in critically ill patients or those with sepsis and burn injuries but allowed their continued use in patients with hypovolaemia due to acute blood loss within the first 24 hours after elective surgery or trauma<sup>5</sup>. This decision was based on “some reassurance that the risks of mortality and renal injury in surgical and trauma patients may be lower than those in critically ill and [septic] patients”<sup>6</sup>. However, there is only one small prospective RCT in trauma patients<sup>7,8</sup>. In general, published studies on synthetic colloid resuscitation in the trauma population have methodological weaknesses due to low sample sizes, limited observation periods, incomparable study groups, missing control groups, inconsistent definitions and study endpoints with low clinical relevance<sup>5,7,9–14</sup>. Moreover, in early 2017 the US based patient advocacy group Public Citizen filed a petition with the U.S. Food and Drug Administration (FDA) requesting that the

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