Journal of the Formosan Medical Association (2014) 113, 429–435

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

New 6% hydroxyethyl starch 130/0.4 does not increase blood loss during major abdominal surgery—A randomized, controlled trial☆

Ming-Hui Hung [a,b,†], Conghua Zou [c,†], Feng-Sheng Lin [a], Chen-Jung Lin [a], Kuang-Cheng Chan [a,b,*], Yanqing Chen [c,**]

[a] Department of Anesthesiology, National Taiwan University Hospital, Taipei, Taiwan
[b] Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan
[c] Department of Anesthesiology, Fujian Provincial Hospital, Fuzhou, China

Received 29 May 2012; received in revised form 30 July 2012; accepted 1 August 2012

KEYWORDS
abdominal surgery;
blood coagulation;
fluid therapy;
hydroxyethyl starch;
tissue perfusion

Background/Purpose: Ideal fluid management during surgery still poses a clinical dilemma gauging the benefits and adverse effects. This randomized controlled trial compared the tissue perfusion and coagulation profiles under clinically equivalent hydroxyethyl starch (HES 130/0.4) and lactated Ringer's solution (LR).

Methods: Eighty-four patients undergoing major abdominal surgery were randomized to receive either HES or LR. Tissue perfusion parameters using heart rate, arterial blood pressure, central venous pressure, cardiac index, stroke volume index, and central venous oxygen saturation were measured at T0 (baseline), T1 (start of surgery), T2 (1 hour after start of surgery), and T3 (end of surgery). Coagulation parameters using thrombelastography (TEG) were measured at T0 (baseline), T4 (after 15 mL/kg fluid transfused), and T5 (24 hours after baseline).

Results: The total amount of fluid administrated was 1547.9 ± 424.0 mL in HES group and 2303.1 ± 1033.7 mL in LR group ($p < 0.001$). The parameters of tissue perfusion and TEG did not differ significantly between groups at any time point except for a transient decrease in clot

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

☆ This research is attributed to Department of Anesthesiology, National Taiwan University Hospital and Department of Anesthesiology, Fujian Provincial Hospital.

* Corresponding author. Department of Anesthesiology, National Taiwan University Hospital, 7, Chung-Shan South Road, Taipei 10002, Taiwan.

** Corresponding author. Department of Anesthesiology, Fujian Provincial Hospital, 134, East Road, Fuzhou, Fujian Province, China.
E-mail addresses: jkjchan@gmail.com (K.-C. Chan), sxd605@21cn.com (Y. Chen).

† These authors contributed equally to the results of this study as first authors.

http://dx.doi.org/10.1016/j.jfma.2012.08.002

kinetic and clot strength at T4 for HES group. There was no significant difference in blood loss and consumption of blood products between the two fluids.
Conclusion: HES 130/0.4 is a more efficient intravascular volume expander to maintain tissue perfusion than conventional crystalloid. Transient hypocoagulability induced by HES 130/0.4 does not warrant excessive blood loss and blood transfusion.

Introduction

Perioperative fluid management for intravascular volume deficits has been, and still is, the focus of much debate in perioperative medicine.[1] The debate has primarily focused on the choice of the ideal fluid therapy with either crystalloid or colloid, or with either liberal or restrictive amount of fluid.[2–5] Large-volume crystalloid resuscitation is associated with an increase in tissue edema, which further jeopardizes tissue perfusion locally.[6] On the contrary, adverse effects of colloid therapy, such as anaphylaxis and hemostatic impairment, are of concern.[7]

In a major abdominal surgery, patients commonly suffer from absolute or relative intravascular volume deficits because of preoperative fasting, gastrointestinal preparation, perioperative bleeding, exposure evaporation, third-space losses, and vasodilation after general anesthesia.[8] Hypovolemia during surgery has been associated with intraoperative hemodynamic instability and tissue and/or organ hypoperfusion. Therefore, adequate restoration of intravascular volume is important to fulfill the nutritive role of the circulation and to have beneficial outcomes on both morbidity and mortality.

However, the optimal strategy remains controversial and uncertain, and mostly depends on the dogma and belief of the caring physician in spite of fluid therapy recommendations.[8] Recently, a new generation of hydroxyethyl starch (HES) preparation (Voluven®, 6% HES 130/0.4, Fresenius Kabi GmbH, Bad Homburg, Germany) was introduced. It has a lower mean molecular weight (130,000 Da), a lower degree of molar substitution (0.4), and a narrower molecular distribution profile; therefore, it is expected to have less hemostatic interference than other HES preparations.[1,9] However, interference with blood coagulation is still the main obstacle to its adoption in perioperative fluid management, especially in major surgery with potentially significant bleeding and fluid shift.[9] Therefore, this study was designed to assess the efficacy of this new HES preparation on tissue perfusion and coagulation in patients undergoing major abdominal surgery, compared to that of lactated Ringer's solution (LR), by the concept of goal-directed fluid management.[10,11]

Patients and methods

The study protocol was approved by our Research Ethics Committees, and 84 adult patients undergoing elective major abdominal surgery were included with their written informed consent. Inclusion criteria for participation in the study were loss of more than 500 mL blood during surgery and admission to an intensive care unit after the surgery. Patients with cardiac insufficiency (New York Heart Association class III–IV), renal impairment (serum creatinine >1.5 mg/dL), altered liver function (aspartate aminotransferase >40 U/L, alanine aminotransferase >40 U/L, or serum total bilirubin >2 mg/dL), preoperative anemia (hemoglobin <10 g/dL), preoperative coagulation abnormalities (platelet count $<100000/\mu L$; international normalized ratio >1.5), and known allergy to HES were excluded from the study.

Anesthesia was induced with thiopental (4–6 mg/kg) and fentanyl (3 μg/kg). Neuromuscular blockade was achieved with cisatracurium (0.2 mg/kg). Anesthesia was maintained by incremental doses of fentanyl, cisatracurium, and 1–2% isoflurane titrated accordingly. Mechanical ventilation was performed in all patients to maintain arterial oxygen saturation of $>95\%$ and end expiratory carbon dioxide concentration between 35 and 40 mmHg. Perioperative hemodynamic monitoring included continuous measurement of electrocardiogram, arterial blood pressure, and central venous pressure (CVP). Warming blanket device and fluid warmers were used to keep patients normothermic ($>36.0^{\circ}C$). The patients were managed perioperatively by anesthesiologists who were not involved in the study and process of randomization.

Patients were randomly assigned to two groups by using computer-generated random numbers. In HES group, patients received intravenous infusion of 0.6% HES 130/0.4 throughout the operation and, in LR group, LR was administered. Fluid was given to maintain a predefined target of mean arterial blood pressure (MAP) between 65 and 90 mmHg or CVP between 8 and 12 mmHg. Vasopressor or inotropic agents were added when volume administration was not effective in maintaining the predefined target blood pressure for 5 minutes.[10,11] Maximum allowed doses for HES and LR infusion were 15 and 45 mL/kg, respectively, which should be followed by other crystalloid infusion (e.g., 0.9% saline or 5% glucose water) if necessary. Packed red blood cell (RBC) was transfused when hemoglobin level dropped below 8 g/dL. At the end of surgery, endotracheal tube was removed at the discretion of the caring anesthesiologist. All patients were sent to the intensive care unit and mechanical ventilation continued if necessary. Intravenous morphine was used for postoperative pain management for patients who requested patient-controlled analgesia (PCA) prior to surgery. Those without consent for PCA received intravenous fentanyl infusion titrated as required in the intensive care unit.

Measurement of tissue perfusion

Tissue perfusion parameters were obtained by an uncalibrated arterial pressure-based cardiac output monitor