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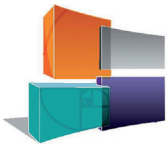

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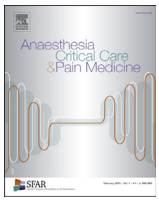

Original article

A comparison of balanced and unbalanced crystalloid solutions in surgery patient outcomes

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ABSTRACT

Introduction: The objective of this study was to evaluate adverse patient outcomes associated with the choice of intravenous fluid administered during general anaesthesia.
Methods: This study was a retrospective chart review of vascular surgery patients at a Canadian tertiary care hospital. Patients were separated into three groups: those who were intraoperatively administered normal saline (NS), balanced crystalloids, or a combination of both solutions. Multivariate analysis was performed to determine association between volume of each fluid type administered and adverse outcomes including in-hospital mortality, prolonged intensive care unit admission, vasopressor requirement, ventilator requirement, hemodialysis requirement, and a composite endpoint of any of these adverse events occurring.
Results: Overall, 796 vascular surgery patients were included in the analysis. There were 425 patients who received balanced crystalloids, 158 patients who received NS, and 213 patients received both balanced crystalloids and NS. Groups were similar in age ($P = 0.06$), but varied in gender ($P < 0.001$) and overall health (ASA ≥ 2; $P = 0.027$). The most common adverse event was ventilator requirement (NS: 27.9%, balanced: 7.5%, both: 38.0%; $P < 0.001$). Mortality was lowest in the group that received balanced fluids (NS: 12.0%, balanced: 5.9%, both: 10.8%; $P = 0.018$). Patients who were administered NS or both fluids were more likely to reach the composite endpoint than patients receiving balanced crystalloid alone.
Conclusion: The administration of an unbalanced crystalloid solution was associated with poor patient outcomes in our study population.

1. Introduction

The use of crystalloid solutions are essential for the provision of anaesthesia, resuscitation, and acute care to patients, but the choice of which crystalloid fluid to use remains a matter of debate [1,2]. The recent focus on hydroxyl ethyl starches as volume replacement solutions has resulted in many questions regarding the use of crystalloid fluids unanswered, such as the benefit of using "balanced" crystalloids over classic "unbalanced" fluids like normal saline (NS) [3,4]. Balanced crystalloids are similar to NS in that they contain sodium and chloride as their primary electrolytes, but they differ through the addition of a buffering compound in order to "balance" the solution closer to physiological pH [5]. Common types of balanced solutions include Ringer's Lactate and Normosol. However, due to a lack of available data, there are no accepted standards or guidelines regarding their use and hence their administration is highly variable, relying mostly on physician preference [6].

It is unclear whether the choice of crystalloid is associated with a difference in adverse patient outcomes such as mortality, extended length of stay in the Intensive Care Unit (ICU), and other markers of poor patient condition such as post-operative vasopressor requirement, ventilator support, and renal replacement therapy. Previous investigations have demonstrated that the intraoperative infusion of modest volumes of NS is associated with the development of hyperchloraemic metabolic acidosis [7–10],

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increased blood product use [4,9,11], hyperkalemia [10,12], and a potentially higher risk of renal injury and need for renal replacement therapy [13,14].

In addition, recent data has indicated that the choice of crystalloid fluid used may have greater impact on patient outcomes than previously appreciated. Some investigations have found higher in-hospital morbidity in patients receiving NS as opposed to balanced crystalloids in major abdominal surgery [4], and a higher mortality in septic patients who are fluid resuscitated with NS in the ICU [6]. Post-operative hyperchloraemia itself has been associated with an increased risk of in-hospital mortality [15]. Another investigation highlighted a more rapid recovery from systemic inflammatory response syndrome and reduction in inflammation with the use of balanced intravenous (IV) fluids [16]. While these studies establish the importance of crystalloid choice in some clinical settings, the impact of crystalloid therapy and its association with adverse patient outcomes remains poorly understood.

Vascular surgery patients represent a surgical population at high risk for adverse events, and peri-operative medical management in this population can be challenging [17]. The objective of this investigation was to compare the impact of crystalloid fluid therapy choice in a vascular surgery population undergoing general anaesthesia. We hypothesized that the use of an unbalanced IV fluid during a vascular surgery procedure would be associated with a higher rate of adverse patient outcomes.

2. Materials and methods

2.1. Study design and patient population

This is a historical cohort study of consecutive patients who required a vascular surgery procedure under general anaesthesia at a Canadian tertiary referral center. All patients 16 years of age or older who were intubated for a vascular surgery procedure over a three-year period were eligible. Study participants were identified through the patient admission/discharge/transfer system (STAR v.15) and the Anaesthesia electronic information management system (Saturn; Dräger Medical, Telford, PA, USA). Patients in cardiac arrest before intubation were excluded. We analyzed all patients with a complete record of pre- and intraoperative administration of IV fluids; any patients with missing elements in their fluid record were excluded from the study. This study was approved by the Institutional Research Ethics Board and performed in adherence to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational cohort studies [18].

2.2. Data collection

Patient age, gender, booking level, procedure type, vasopressor requirement, in-hospital mortality, and the type and volume of crystalloid fluid administered were collected from the electronic databases. The remaining variables (patient comorbidities, hemodialysis requirement, ventilator requirement, and ICU length of stay) were extracted from the medical record using a standardized abstraction form. The types of crystalloid fluid used at our institution were either balanced (i.e., Ringer's Lactate or Normosol-R [Hospira, Lake Forest, IL]) or unbalanced (i.e., NS). Assessments of patient comorbidities such as diabetes, chronic obstructive pulmonary disease, obesity, and their American Society of Anaesthesiology (ASA) physical status classification came from pre-procedure medical assessment forms documented by the anaesthesia team. A Microsoft Access (2003) database was created for data collation by one of the co-investigators.

To minimize risk of bias, all information was abstracted without modification from each of the databases accessed for this study. Database quality control procedures were present in each database to ensure accurate and reliable data entry. The sample size for this study was dependent on the number of vascular surgery patients requiring ETI that were captured in the two databases included in the study, thus we did not perform a power analysis.

2.3. Outcome measurements

The primary outcome of interest was a composite endpoint that consisted of any of the following outcomes occurring while in hospital post-surgery: in-hospital mortality, defined as mortality occurring within 30 days of ETI; the need for any post-operative mechanical ventilation; the need for any post-operative vasopressor therapy; extended ICU length of stay, defined as greater than 14 consecutive days; and the need for hemodialysis post-operatively, given that the patient did not require hemodialysis pre-operatively. As secondary outcomes, we assessed the study population for in-hospital mortality, extended ICU length of stay, and post-operative requirement for mechanical ventilation, vasopressor therapy, and hemodialysis.

2.4. Statistical analysis

Outcomes were stratified between those patients who received only a balanced fluid, those that received an unbalanced fluid, and those that received both balanced and unbalanced crystalloid fluids. Continuous variables were compared using *t*-test procedures where the assumption of normality was reasonable, and non-parametric statistics were used otherwise. Testing for categorical data was done using Fisher's Exact Test. All tests were two-sided, and a *P*-value of less than 0.05 was considered statistically significant.

To assess for associations of both the type and volume of fluid given with the primary and secondary outcomes, a series of logistic regression models were performed. Possible confounding variables were selected a priori based on existing knowledge and expert opinion. We controlled for the following confounders: age, gender, ASA score, urgency of procedure (Emergency: within two hours; Urgent: within 24 hours; Scheduled: greater than 24 hours or done on an outpatient basis), procedure type (Major: AAA repair, amputations, embolectomy; Bypass: central or peripheral bypass graft; Angioplasty: angioplasty or endarterectomy; Minor: vein stripping or soft tissue operation; Other: device insertion, or procedure that did not fit into any of the above groups), volume of packed red blood cells, platelets, and plasma given during the procedure. We also controlled for patient comorbidities including history of congestive heart failure (CHF), history of chronic renal failure (CRF), history of myocardial infarction (MI), and history of stroke since these are associated with peri-operative cardiac risk [19].

We defined the effect size of giving a "unit" of volume of each crystalloid type included in the study to be 500 ml in the logistic regression model. The volume per unit of platelets, pRBCs, and plasma were defined to be 350 ml, 280 ml, and 250 ml, respectively, in keeping with Canadian Blood Services standard average volumes. To assess for goodness-of-fit of the models we report the Hosmer-Le Cessie test result with a *P*-value of greater than 0.05 as a satisfactory fit. To assess for multicollinearity, we calculated the variance-inflation factor (VIF) for all of the fitted models. We considered a VIF of less than 2.5 to indicate that the predictor variables were not highly correlated.

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