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Predictors and outcome impact of perioperative serum sodium changes in a high-risk population

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Editor's key points

- Fluctuations in plasma sodium concentration are common during the perioperative period.
- The authors studied the epidemiology of these changes in patients undergoing non-cardiac surgery lasting >1 h.
- Decreases and especially increases in plasma sodium were associated with increased mortality risk.
- Studies are needed to investigate causality and the value of better control of plasma sodium concentration.

Background. The perioperative period may be associated with a marked neurohumoral stress response, significant fluid losses, and varied fluid replacement regimes. Acute changes in serum sodium concentration are therefore common, but predictors and outcomes of these changes have not been investigated in a large surgical population.

Methods. We carried out a retrospective cohort analysis of 27 068 in-patient non-cardiac surgical procedures in a tertiary teaching hospital setting. Data on preoperative conditions, perioperative events, hospital length of stay, and mortality were collected, along with preoperative and postoperative serum sodium measurements up to 7 days after surgery. Logistic regression was used to investigate the association between sodium changes and mortality, and to identify clinical characteristics associated with a deviation from baseline sodium >5 mmol litre^{-1}.

Results. Changes in sodium concentration >5 mmol litre^{-1} were associated with increased mortality risk (adjusted odds ratio 1.49 for a decrease, 3.02 for an increase). Factors independently associated with a perioperative decrease in serum sodium concentration >5 mmol litre^{-1} included age >60, diabetes mellitus, and the use of patient-controlled opioid analgesia. Factors associated with a similar increase were preoperative oxygen dependency, mechanical ventilation, central nervous system depression, non-elective surgery, and major operative haemorrhage.

Conclusions. Maximum deviation from preoperative serum sodium value is associated with increased hospital mortality in patients undergoing in-patient non-cardiac surgery. Specific preoperative and perioperative factors are associated with significant serum sodium changes.

Keywords: hospital mortality; perioperative period; sodium

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Disorders of plasma sodium concentration are common in hospitalized patients and are associated with increased hospital stay, resource utilization, and mortality. Surgical patients may be particularly vulnerable, since the perioperative period is often characterized by a vigorous neurohumoral stress response, significant fluid losses, and widely varying fluid replacement regimes. Previous studies have reported hospital outcomes associated with dysnatraemias present on admission, in specific medical or surgical subspecialities, in intensive care, or in mixed medical–surgical populations without reference to the perioperative period.[1–7] Only two studies have focused exclusively on perioperative patients. Leung and colleagues[6] reported increased mortality in patients with preoperative hyponatraemia using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP), and McCausland and colleagues[7] described similar outcomes in dysnatraemic patients after orthopaedic surgery. No previous study has investigated perioperative sodium changes.

While small changes are commonplace and may typically reflect measurement artifact or diurnal variation,[8–10] large changes are often associated with endocrine or iatrogenic factors. These can be harmful in themselves, by inducing osmotic disequilibrium and cerebral dysfunction,[11 12] or may reflect an underlying impairment of sodium and water homeostasis that predicts adverse outcomes independently of prevention or treatment. However, both predictors and outcomes of marked changes remain poorly characterized, and the possibility remains that intervention to minimize sodium fluctuations may be beneficial. Hence, we investigated a large cohort of patients undergoing intermediate and major in-patient surgery to identify clinical correlates of

moderate-to-severe sodium changes, and to quantify any associated increase in mortality. We speculated that knowledge of these factors, and closer attention to electrolyte monitoring and fluid therapy in patients at increased risk, might attenuate any associated increase in mortality.

Methods

With local research ethics committee approval, we extracted anonymized electronic records of 31 206 in-patient surgical procedures lasting more than 1 h at Cambridge University Hospitals between January 1, 1996, and December 31, 2005. This encompassed all specialities with the exception of cardiothoracic surgery. Hospital length of stay and mortality were obtained from the hospital's administrative database, while information on co-morbidities, important preoperative conditions, and perioperative events was available from a perioperative audit database, as recorded during each procedure by the attending anaesthetist.

A laboratory database provided measurements of serum sodium concentration, including the latest preoperative value as baseline (no earlier than 14 days before operation), and all values in the first 7 days after surgery. The highest and lowest sodium values in the first 7 postoperative days were then compared with baseline to define the following mutually exclusive categories for analysis: no change >5 mmol litre^{-1}; decrease >5 mmol litre^{-1}; increase >5 mmol litre^{-1}; both increase and decrease >5 mmol litre^{-1}.

Obstetric and paediatric patients (under age 13) were excluded from the study population, as were those missing either preoperative or postoperative sodium measurements, and those without complete data on preoperative conditions and perioperative events. Only the first surgical procedure carried out during an admission was studied.

The above exclusions ensured that we studied a high-risk cohort, since all had surgery involving more than 1 h of operating time, and all had both preoperative and postoperative sodium measurements. Preoperative measurement in particular would suggest co-morbidity, major surgery, or both. We were unable to collect data on perioperative fluids from the records obtained.

Statistical analysis

Summary statistics was computed for baseline characteristics and outcomes of the cohort. Hospital admissions were fitted in a multivariate logistic regression model to investigate the association between maximum change in sodium concentration and hospital mortality. The model was adjusted for co-morbidities and other relevant confounders, and also for possible correlation between admissions of the same patient. Odds ratios (ORs) were adjusted using the floating absolute risk method to allow comparison between potential confounders, rather than only comparison of each with its absence.[13] Multivariate logistic regression was also used to identify co-morbidities and conditions associated with large changes in sodium (>5 mmol litre^{-1}).

All models were adjusted by the number of postoperative sodium measurements, to minimize bias related to clinical acuity, and by calendar year to allow for differences in clinical practice over time. Forward selection procedures were used to obtain the most parsimonious model using likelihood ratio tests. All analyses were performed using Stata (version 10.1), and significance was set at 5%.

Results

Study population

Complete data were available for 16 216 admissions (14 942 patients). Exclusions are shown in Supplementary Figure S1, the largest number resulting from missing values for physician-entered preoperative and perioperative variables. Baseline characteristics and outcomes are given in Table 1. In 86.2% of admissions, at least one significant preoperative condition was present; in 45.8%, ASA physical status was assessed as III or higher. The most prevalent co-morbidities included hypertension (29.4%), malignancy (16.1%), ischaemic heart disease (15.3%), and obesity (11.9%). There were 632 hospital deaths, corresponding to a mortality of 3.9%.

Sodium changes and hospital mortality

Associations between perioperative changes in sodium concentration and hospital mortality are shown in Figure 1. A deviation from the preoperative value of >5 mmol litre^{-1} in either direction was associated with a higher risk of death than patients with smaller changes. This was strongest with increases, which carried three times the risk [adjusted OR 3.02; 95% confidence interval (CI) 2.52–3.62] of those with small or no change. Decreases in sodium increased mortality by about 50% (OR 1.49; 95% CI 1.21–1.83). When preoperative sodium concentration was normal, the relationships were more pronounced, with ORs of 3.49 and 1.62 for increases and decreases, respectively.

Clinical correlates of large sodium changes

Figures 2 and 3 show the results of multivariate logistic regression investigating clinical correlates of large perioperative decreases and increases, respectively. Figure 2 shows that those more likely to have a large decrease in sodium concentration were older (>60 yr, OR 1.34), and had procedures of longer duration (OR 1.30). Those with diabetes (OR 1.30) or liver disease (undergoing transplant, OR 1.74), who were mechanically ventilated (OR 1.41) or receiving oxygen (OR 1.55), and who used patient-controlled analgesia in the postoperative period (OR 1.21), were all more likely to have a large decrease in sodium than those who were not. Major urological and renal procedures were also associated with this risk (OR 1.35), compared with a reference group comprising all in-patient laparoscopic operations. Obesity appeared to be protective against large decreases (OR 0.80).

Figure 3 shows the adjusted clinical correlates of large sodium increases. These also included longer operations (OR 2.31), and preoperative ventilation (OR 1.65) or oxygen (OR