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Can patients with mild post-operative hyponatraemia following elective arthroplasty be discharged safely? A large scale service evaluation suggests they can

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Can patients with mild post-operative hyponatraemia following elective arthroplasty be discharged safely? A large scale service evaluation suggests they can.

Abstract

Background: Post-operative hyponatraemia is common following arthroplasty. Clinical hyponatraemia guidelines lack detail on when treatment is necessary, and there is a paucity of literature to guide best practice.

Methods: Data were collected within retrospective service evaluations over two time periods in a single high throughput joint unit. The hospital's electronic database identified 1,000 patients who were admitted electively between February 2012 and June 2013 and again between November 2018 and April 2019 for primary total hip, total knee or uni-compartmental knee arthroplasty. Hyponatraemia and non-hyponatraemia groups were compared. Logistic regression analysis was used to identify independent predictors of post-operative hyponatraemia, length of stay (LOS), re-attendance or re-admission to hospital.

Results: Between 2012-13 and 2018-19, 32.1% and 25.7% of patients respectively developed post-operative hyponatraemia (serum sodium ($s[Na]$) ≤ 135 mmol/L). Those with post-operative hyponatraemia were significantly older, weighed less, were more comorbid and had lower pre-operative sodium. Multivariate analysis showed that increased age, knee surgery and lower pre-operative $s[Na]$ independently predicted post-operative hyponatraemia. Post-operative hyponatraemia did not independently predict LOS, re-attendance or re-admission to hospital, **within 90 days**, in either cohort.

Conclusion: Post-operative hyponatraemia is common and may be a marker of pre-operative vulnerability. In these cohorts, it was not independently associated with LOS, re-attendance or re-admission to hospital. We suggest that otherwise well patients with mild

hyponatraemia can be safely discharged earlier than is often the case and may not require extensive investigation. Further examination and research is required to develop a pre-operative approach to predict which patients will develop significant post-operative hyponatraemia.

Keywords: Hyponatraemia, Post-operative, Prevalence, Risk factors, Arthroplasty

Background

It is not yet clear to what extent hyponatraemia after surgery reflects an appropriate transient physiological response, and to what extent it reflects pre-existing physiological vulnerability. It is also unclear what risks (if any) accompany a minor, short-lived, self-limiting drop in serum sodium concentration ($s[Na]$). An accumulating body of evidence suggests that routine post-operative laboratory blood testing may not always be necessary and can perhaps be safely omitted in some settings¹⁻³. Hyponatraemia, defined here as a $s[Na] \leq 135$ mmol/L, is a common electrolyte disorder that, when encountered following surgery, often triggers a series of investigations and a prolonged hospital stay⁴⁺⁵. As enhanced recovery after surgery (ERAS) programmes become more popular, and the focus moves towards proactive and pragmatic perioperative care with shorter inpatient stays, there is a need to better identify those individuals who are likely to come to harm as a result of hyponatraemia, whilst minimising unnecessary tests for others who are likely to tolerate a small and short-lived drop in $s[Na]$ without complication⁶. Whilst thorough guidelines regarding identification and management of hyponatraemia exist and reference post-operative hyponatraemia, specific evidence and guidance related to the management of post-operative hyponatraemia in ERAS for arthroplasty is lacking⁷⁻⁹.

We conducted a large service evaluation of post-operative inpatient medical complications following arthroplasty in 2012-13. Adjustments have since been made to perioperative practices, and in order to reassess the needs of our patients prior to the rolling out of an ERAS programme, we re-assessed the incidence of hyponatraemia and associated factors. Here, we present large-scale data captured in an effort to establish: i) the incidence of, and risk factors associated with, hyponatraemia following elective primary Total Hip Arthroplasty (THA), Total Knee Arthroplasty (TKA) or Uni-Compartmental Knee Arthroplasty (UKA); and ii) associations between post-operative hyponatraemia and other post-operative complications.

Methods

Data were collected within retrospective service evaluations of inpatient complications and unplanned re-attendances at hospital in consecutive elective primary THA, TKA and UKA patients in a high-throughput elective primary joint unit. The evaluations were registered with the Healthcare Trust's Standards, Quality and Audit Department: 2012-13 reference number 4232 and 2018-19 reference number 5996. The hospital's electronic database was used to identify 1,000 patients who were admitted electively from 29th February 2012 until 25th June 2013 (2012-13) and from 26th November 2018 until 30th April 2019 (2018-19). Patients from 2012-13 were admitted under the care of a single surgeon. In comparison, for the second collection period, we broadened the remit to include all surgeons in the unit, only THA and TKA patients were included, and less data were collected, for example, medications and inpatient events were not recorded.

Perioperative Practices

All THAs were performed in the lateral decubitus position using the posterior approach using both cemented and cementless fixation although the majority of acetabulae were cementless. All TKAs were performed using a medial parapatellar approach without patellar resurfacing and again with both cemented and cementless fixation with the majority, unlike the rest of the UK being cementless¹⁰. All UKAs were performed using the medial Oxford uni-compartmental implant (Biomet, Warsaw, IN, USA) with the majority being cementless. Antimicrobial prophylaxis was administered according to the unit's policy. Between 2012 and 2018 antibiotic prophylaxis changed from 2 g of Flucloxacillin and 1.5 mg/kg of Gentamicin given intravenously prior to knife to skin, followed by three further intravenous doses of 2 g of Flucloxacillin at 6, 12 and 18 hours post-operatively, to Cefuroxime 1.5g with 1.5 mg/kg of Gentamicin given intravenously prior to knife to skin, followed by two further intravenous doses of 1.5 g of Cefuroxime at 8 and 16 hours post operatively. Patients with a history of penicillin allergy or methicillin-resistant *Staphylococcus aureus* (MRSA) received 10 mg/kg Teicoplanin and 1.5 mg/kg Gentamicin intravenously once only prior to knife to skin. For cemented components intravenous Gentamicin was not administered as the bone cement utilised contains Gentamicin. Tranexamic acid was only administered to patients deemed at high risk of bleeding, including those with rapidly progressive osteoarthritis during the first audit period but was more widely used in the second. Venous thromboembolism prophylaxis consisted of foot pumps for all combined with either Enoxaparin for 28 days or Aspirin for 6 weeks as per hospital guidelines and then surgeon preference. All high risk patients received Enoxaparin.

Routine practice during these time periods included checking of electrolytes on post-operative Day 1 and Day 2. Post-operative hyponatraemia was investigated and managed by the attending medical team in line with regional published guidelines¹¹.

Between 2012-2013 and 2018-2019 normal practice changed to include routine default holding of antihypertensive medications in the immediate post-operative period.

Data Collection

Written clinical notes and local/regional electronic databases (including regional radiology systems and regional Electronic Care Records) were interrogated during data collection capturing data including Emergency Department (ED) attendances and episodes of hospital re-admission **within 90 days**. Additional data were manually extracted from medical and nursing notes by trained research staff or assistants (nursing and medical staff).

Hyponatraemia was defined as a $s[Na] \leq 135$ mmol/L. This was further categorised as mild: 130 - 135 mmol/L; moderate: 125 - 129 mmol/L; or severe: <125 mmol/L [4].

When available, pre-operative results, measured on the day of surgery, were utilised. If not available, $s[Na]$ taken at pre-operative assessment were used. One patient in the 2012-13 group and three patients in the 2018-19 group did not have pre-operative results available.

Statistical Analysis

Patients undergoing more than one surgery during the collection period were considered as different entries. All statistical analyses were carried out using SPSS for Windows (IBM, Version 26.0, Armonk, NY, USA) and all data were assessed for normality using the Shapiro-Wilk test. Chi-square analysis (or Fisher's Exact test as appropriate) and the Mann-Whitney U test were used to compare categorical and continuous variables, respectively, between those with and without post-operative hyponatraemia. The Kruskal Wallis test was used to compare $s[Na]$ between THA, TKA and UKA patients, since previous studies have found varying susceptibility to hyponatraemia by type of arthroplasty¹²⁺¹³. The Wilcoxin Signed-

Rank test was used to compare pre- and post-operative s[Na]. Logistic regression analysis was used to determine factors associated with hyponatraemia, LOS, re-attendance and re-admission. Variables which displayed $p < 0.1$ in univariate analysis for either cohort were added to the multivariate logistic regression model. Otherwise, statistical significance was set at the $p < 0.05$ level. More data were available for the 2012-13 group (manuscript under review), however, only variables which were available for both groups were used in these analyses.

Results

2012-13 cohort: A total of 1,015 patients underwent elective THA, TKA or UKA. Of these, one underwent non-arthroplasty surgery, one was a duplicate record and notes were not available for 13 patients, leaving 1,000 arthroplasties on 969 patients; any bilateral procedures were staged as opposed to simultaneous.

2018-19 cohort: A total of 994 patients underwent elective THA or TKA (1,000 arthroplasties); again any bilateral procedures were staged. Three patients did not have pre-operative s[Na] results and as such were removed from the analysis.

i) Incidence and predictors of post-operative hyponatraemia

In 2012-13, 32.1% of patients developed post-operative hyponatraemia. Of these 321 patients, 281 (87.5%) had mild, 37 (11.5%) had moderate, and 3 (0.9%) had severe hyponatraemia. In 2018-19, 25.7% developed post-operative hyponatraemia. Of these 256 patients, 233 (91.0%) had mild, 17 (6.6%) had moderate and 6 (2.3%) had severe hyponatraemia. Baseline characteristics and pre-operative variables are shown in Table 1. There were no significant differences in general anaesthetic, spinal block or peripheral block frequencies between those with and without post-operative hyponatraemia in either cohort (data not shown).

144 **Insert Table 1 here**

145 **Table 1 Title:** Pre-operative patient characteristics and comparison of those with and without post-
146 operative hyponatraemia

147 **Legend:** Median (IQR) used for continuous variables and n (%) used for categorical variables.

148 Multivariate analysis showed that increased age, knee surgery (as compared to hip surgery)
149 and lower pre-operative s[Na] independently predicted post-operative hyponatraemia
150 (Table 2).

151 **Insert Table 2 here**

152 **Table 2 Title:** Logistic regression analysis of factors associated with post-operative hyponatraemia
153 ($\text{Na} \leq 135 \text{ mmol/L}$) following elective primary hip and knee arthroplasty

154 The perioperative change in s[Na] by pre-operative hyponatraemia classification can be seen
155 in Figure 1.

156 **Insert Figure 1a.**

157 **Title:** 2012-13 - Mean change in serum sodium categorised by pre-operative sodium levels.

158 **Legend:** Number of patients within each group: Total= 999, Pre-op normal s[Na] = 930, Pre-
159 op Mild s[Na] = 64, Pre-op Moderate s[Na] = 5

160 **Insert Figure 1b.**

161 **Title:** 2018-19 - Mean change in serum sodium categorised by pre-operative sodium levels

162 **Legend:** Number of patients within each group: Total= 994, Pre-op normal s[Na] = 957, Pre-
163 op Mild s[Na] = 34, Pre-op Moderate s[Na] = 3

164 ii) Associations between post-operative hyponatraemia and other post-operative
165 complications

Patients with post-operative hyponatraemia had a significantly longer LOS compared to those who did not ($p < 0.001$) (Table 3). However, multivariate analysis, adjusting for: gender, age, height, weight, pre-operative s[Na], post-operative s[Na], ASA grade, type of surgery, pre-operative haemoglobin and post-operative fasting glucose – showed that post-operative s[Na] was not an independent predictor of LOS (2012-13; Odds ratio [OR] 1.44 (95% CI 0.74-2.80, p -value=0.286, 2018-19; OR 1.69, 95% CI 0.71-4.02, p -value= 0.236).

Insert Table 3 here

Table 3 Title: *Post-operative outcomes with comparison of those with and without post-operative hyponatraemia*

Legend: ** p -value comparing those with post-operative hyponatraemia ($Na \leq 135$ mmol/L) and those with normal sodium values ($Na > 135$ mmol/L) post-operatively.*

Differences in re-attendance at EDs, and/or re-admission within 90 days between those who had post-operative hyponatraemia and those who did not are shown in Table 3. Again, multivariate analysis, adjusting for: gender, age, height, weight, pre-operative sodium, post-operative sodium, ASA grade, type of surgery, pre-operative haemoglobin and post-operative fasting glucose – showed that post-operative sodium was not independently associated with re-attendance and/or re-admission within 90 days (Table 4). Further logistic regression analysis adjusting for the same variables aforementioned, but this time assessing post-operative hyponatremia as an ordinal variable (no hyponatraemia: >135 mmol/L, mild: 130 - 135 mmol/L or moderate and severe: <129 mmol/L), showed that the same variables remained significantly associated with re-attendance or re-admission following elective primary hip and knee arthroplasty (2012-13: gender, height, LOS; 2018-19: gender).

Insert Table 4 here

Table 4 Title: Logistic regression analysis of factors associated with re-attendance or re-admission following elective primary hip and knee arthroplasty

Legend: *Post-operative hyponatraemia as categorical variable; yes or no (reference).

Discussion

Main findings

Within our arthroplasty population post-operative hyponatraemia is common with around one-quarter (2018-19 data) to one-third (2012-13 data) of patients affected. It appears to be a marker of pre-operative vulnerability, as patients developing post-operative hyponatraemia following elective primary arthroplasty were significantly older, weighed less, were more comorbid and had lower pre-operative sodium concentrations. We have found that post-operative hyponatraemia does not independently predict LOS or re-attendance at ED, and/or re-admission to hospital within 90 days. This suggests that increased rates of re-attendance at ED, and/or re-admission to hospital within 90 days seen in people with post-operative hyponatraemia could be related to other reasons as opposed to being directly related to the post-operative hyponatraemia.

Regulation of sodium and water are multifaceted, and surgery may lead to a reduced s[Na] via several pathways. These likely include blood loss, inflammation, pain, vomiting, fever, positive pressure ventilation, anaesthesia and analgesia leading to the production of antidiuretic hormone (ADH), appropriately or inappropriately^{12,14-16}. Increasingly popular ERAS programmes concentrate assessments and interventions pre-operatively aiming to minimise post-operative inpatient stays and may reduce post-operative complications⁶⁺⁹. In addition, evidence is accumulating that suggests routine post-operative electrolyte testing is not necessary for all patients¹⁻³. Our finding that post-operative hyponatraemia is common but does not independently predict re-attendance at ED, and/or re-admission to hospital

213 within 90 days suggests that omitting routine post-operative electrolyte testing would leave
214 common, mild, post-operative hyponatraemia unrecognised but that this may be safe. We
215 acknowledge that patients captured here had their hyponatraemia recognised and, if
216 appropriate, managed according to local guidelines¹¹, and this may have affected outcome.

217 Recently published further analysis of the 2012-13 data showed that there were no
218 significant differences in re-attendance at emergency departments and/or re-admission
219 within 90 days between those who had post-operative hyponatraemia whilst in hospital
220 (39/217 = 18.0%) and those who did not (103/783 = 13.2%), or between those who were
221 discharged with hyponatraemia (18/108 = 16.7%) and those discharged with normal s[Na]
222 (124/880 = 14.1%).¹⁷

223 We have shown that whilst patients developing post-operative hyponatraemia tended to be
224 older, more comorbid and more anaemic, only age and lower pre-operative s[Na]
225 independently predicted post-operative hyponatraemia. As we move to better pre-
226 operative characterisation of perioperative risk, more accurate information will be required
227 to predict those who need post-operative laboratory testing. Electrolytes are tested to
228 assess problems other than hyponatraemia, acute kidney injury being the other main
229 example, so again more information is needed before we can accurately identify patients
230 likely to need post-operative laboratory testing.

231 Our findings are in keeping with the current literature. Post-operative hyponatraemia
232 usually occurs as a syndrome of inappropriate antidiuretic hormone secretion with an
233 estimated duration of 2-3 days⁷. As a result, a small short lived post-operative drop in s[Na]
234 may be due to a normal physiological response to trauma with duration less than 48 hours⁷.
235 Hyponatraemia may also, as we have shown, indicate underlying physiological
236 vulnerabilities, being associated in the literature with increasing age, comorbidity and
237 polypharmacy^{12,18-22}. Low pre-operative sodium is associated with negative outcomes after

surgery, suggesting that both the hyponatraemia itself and the negative outcomes may reflect underlying vulnerabilities²³⁻²⁵.

In contrast to our findings, Leung et al. (2012), in their database study, showed that pre-operative hyponatraemia ($s[Na] < 135$ mmol/L) predicted longer LOS and increased risk of post-operative complications and 30-day mortality²³. Abola et al. (2018) found that pre-operative hyponatraemia was associated with longer LOS and greater risk of reoperation²⁴. Additionally, McCausland et al. (2014) stated that dysnatraemia (hyper or hyponatraemia) is relatively common in the hospitalised orthopaedic population and is associated with greater LOS and 30-day mortality²⁶. It could be argued that our elective lower limb arthroplasty patient population studied are significantly different to those studied in the above papers (Leung et al studied all major surgery, Abola et al. studied upper limb arthroplasty and McCausland et al. studied all major orthopaedic surgery).

Other findings

In keeping with our finding that knee surgery independently predicted post-operative hyponatraemia (2018-19 data only), Sah (2014) reported that TKA patients may be more susceptible to developing post-operative hyponatraemia compared to THA patients¹³. However, Hennrikus et al. (2015) found that THA patients had an increased risk of developing post-operative hyponatraemia compared to TKA patients¹⁴.

Limitations

The main limitation of this report is that other relevant laboratory analyses and specific treatments administered for post-operative hyponatraemia (e.g. fluid restriction vs fluid

administration) are not described. We cannot say for example how many patients were fluid restricted or what the average daily fluid intake was for patients post-operatively.

Over both study periods the total numbers of patients with moderate, and specifically severe hyponatraemia are low (moderate: n=54, severe: n=9). The authors have made a number of conclusions regarding hyponatraemia as a whole; any results comparing subgroups of hyponatraemia need to be read taking these small numbers into consideration.

This data is from a single centre, however, the description of two large patient cohorts and the inclusion in the latter of all surgeons arguably enhances generalisability.

Conclusion

Post-operative hyponatraemia is common following elective arthroplasty, and is not independently associated with re-attendance and/or re-admission to hospital within 90 days. We suggest that otherwise well patients with mild (s[Na] 130 - 135 mmol/L) hyponatraemia can safely be discharged and followed up in the community. It is important to note that this is an observational finding, and studies directly comparing prolonged inpatient management to early discharge with community care would be preferable. Furthermore, it would be desirable to undertake research to ascertain a pre-operative model to predict which patients will develop significant post-operative hyponatraemia.

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381 **Other**

382 Oxford Uni-compartmental Knee Replacement

383 Responsible Manufacturer:

384 Biomet UK Limited

385 Waterton Industrial Estate

386 Bridgend

387	CF31 3XA
388	United Kingdom
389	
390	SPSS for Windows Version 26.0
391	IBM Headquarters
392	Armonk
393	NY
394	USA
395	