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Is postoperative hyponatremia a real threat for total hip and knee arthroplasty surgery?

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Abstract

Postoperative hyponatremia (POH) is thought to be a fearsome complication of orthopedic surgery. Primary aim of this cohort study was to evaluate the incidence of POH and its clinical relevance in elective surgery, outlining differences between total knee arthroplasty (TKA) and total hip arthroplasty, looking for the presence of any risk factor commonly related to POH.

Four hundred two patients that underwent total hip arthroplasty and total knee arthroplasty performed between 2016 and 2017 were retrospectively examined. Serum electrolytes, hemoglobin, hematocrit, glucose, and creatinine were evaluated preoperatively and at day 0-I-II from surgery. Age, sex, body mass index, comorbidities, drugs, surgery data, transfusions, postoperative symptoms, and length of stay (LOS) were determined. All surgeries were performed by the same equipe. Patients had the same perioperative management, excluded those that took thiazides, already at risk of POH.

Patients were divided in 2 groups: group A, patients with normal postoperative natremia (294 patients) and group B, patients who developed POH (108, 26.9%); 66.7% of these developed POH within 24 hours postoperatively. In group B mean postoperative natremia was 133.38 (127.78–134.85) mmol/L. Two patients (1.8%) developed moderate hyponatremia, no severe hyponatremia was documented. Type of surgery, operation time, LOS, and presence of postoperative symptoms did not show statistically significant differences within groups. At multivariate logistic analysis chronic use of thiazides was the only variable associated to a decreased risk of developing POH (OR = 0.39; $P = .03$). Hemoglobin postoperative values (OR = 1.22; $P = .03$), the need of postoperative transfusion (OR = 2.50; $P = .02$) and diabetes (OR = 2.70; $P = .01$) were associated to an increased risk of POH.

Although 26.9% of our patients exhibited POH, the onset of this disorder had no implication on postoperative symptoms and on LOS. Diabetes and transfusion are factors most often associated to POH.

Abbreviations: AUC = area under curve, LOS = length of stay, POH = postoperative hyponatremia, ROC = receiver operating characteristic curves, THA = total hip arthroplasty, TKA = total knee arthroplasty.

Keywords: arthroplasty, hip, hyponatremia, knee, orthopaedic, replacement, surgery

1. Introduction

Hyponatremia is the most common electrolyte disorder in hospitalized patients.[1] It is defined as a serum sodium concentration < 135 mmol/L, calculated by the formula: serum $[Na^+$ (mmol/L)] + 2.4 × [serum glucose (mg/dL) – 100]/100.[2,3] Based on serum sodium levels, hyponatremia could be mild [130 ≥ Na^+ (mmol/L) ≤ 134], moderate [125 ≥ Na^+ (mmol/L) ≤ 129], severe [Na^+ (mmol/L) ≤ 124]. Usually mild hyponatremia is asymptomatic, but in moderate and severe hyponatremia patients could develop many symptoms: nausea, headache, agitation, disorientation, lethargy, confusion, ataxia, falls to the ground, tremors, seizures, delirium, focal neurological deficits, coma, pseudobulbar palsy, Cheyne–Stokes breath, and death[3]. In patients undergoing surgery, slight symptoms are often confused with normal postoperative course. Postoperative hyponatremia (POH) is also associated with a greater risk of wound infections and perioperative systemic major complications such as pneumonia and coronary disease.[4] These conditions can cause prolonged hospitalization with increase in health costs and risk of short term death. Orthopedic patients are particularly at risk of developing POH because of the fragility, the fracture, the comorbidities, the multiple pharmacological therapies, the perioperative fluid restrictions, the surgery.[1,5–8]

Only few studies have examined the development of hyponatremia after primary hip and knee arthroplasties. Patients undergoing these surgeries are extremely different than those fractured: they are younger, healthier and with less pharmacological therapies, undergoing elective surgery, usually without ongoing electrolytic disorders. The success of fast track joint

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replacement surgery is strongly related to the absence of post-operative complications. Primary aims of this cohort study were to evaluate the incidence of POH and its differences between total knee arthroplasty (TKA) and total hip arthroplasty (THA), its impact on time of hospitalization and the presence of any risk factor commonly related to POH.

2. Methods

We retrospectively examined our electronic database about consecutive hip and knee replacement performed between 2016 and 2017 in Policlinico Umberto I University Hospital (Rome, Italy). According to the Italian regulation on retrospective observational studies, a notification to the Ethical Committee was done. Informed consent regarding the collection and analysis of the data related to the surgery was obtained from all the individual participants included in the study. All patients were part of a fast track program. Inclusion criteria were primary osteoarthritis of hip and knee, absence of pre-operative electrolyte disorders. Exclusion criteria was age > 90 years, hyponatremia at presentation. Clinical history was searched for demographics, comorbidities, pharmacological therapies, type of surgery, operating time, transfusions, post-operative symptoms, length of stay (LOS), delayed discharge. A single laboratory performed all blood tests: sodium, potassium, glucose, creatinine, hemoglobin, and hematocrit were evaluated preoperatively and at day 0-I-II from surgery. If hyponatremia was present, further blood tests was performed before discharge.

2.1. Perioperative management

The same equipe performed all surgeries. All patients underwent spinal anesthesia and double nerve block (femoral and sciatic nerves). Tourniquet was used in all TKA. Intra-venous tranexamic acid (1 g before incision, 1 g after wound closure) and no suction drain were used both in THA and TKA. All patients received 1000 mL fluid infusion during pre- and intra-operative time: 500 mL Ringer lactated solution and 500 mL normal saline solution for patients without history of taking thiazide diuretic therapy; 1000 mL of normal saline solution in patients who had chronic therapy with thiazide diuretics. After surgery the infusion rate was based on patient's weight: only saline solution was given. Patients received 10 mg of morphine and acetaminophen (1 g every 8 hours for 3 days).

2.2. Statistical analysis

Statistical analysis was performed with R version 3.4.4 (R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/). Categorical data were expressed as percentage while continuous variables reported as mean and range. Two sample *t* test and Wilcoxon rank-sum tests were used to compare continuous variables when appropriate. Chi squared test was used to compare categorical variables.

A univariable and multivariable logistic regression model was used to identify which variables had a significant effect on the risk of developing hyponatremia postoperatively as compared with patients who did not develop POH. At univariate analysis only preoperative value of natremia was considered as independent variable while other variables were considered at multivariate analysis (Table 1). The level of significance was set at $P < .05$.

Table 1

Demographics information and differences between patients with and without postoperative hyponatremia.

	No POH patients (294)	POH patients (108)	*P* value
Age (yr)	66.25	67.28	.44
BMI (kg/m^2)	27.84	28.12	.33
Procedure length (min)	98.22	102.14	.28
Preoperative Na serum level (mg/dL)	139.59	139.06	.32
Postoperative Na serum level (mg/dL)	138.51	133.38	<.001
Difference between pre and postoperative Na serum level	1.08	5.69	<.001
Preoperative serum creatinine (mg/dL)	0.86	0.89	.58
Preoperative serum hemoglobin (mg/dL)	13.65	13.54	.54
Postoperative serum hemoglobin (mg/dL)	10.73	10.78	.83
Recovery length (d)	4.23	4.84	.77
Sex (M)	124 (42.2)	54 (50)	.16
THA	187 (63.6)	76 (70.4)	.21
TKA	107 (36.4)	32 (29.6)	.21
Thiazides	48 (16.33)	12 (11.1)	.19
Potassium sparing diuretics	3 (1)	3 (2.8)	.2
NSAIDs	270 (91.8)	91 (84.3)	.03
Beta blockers	48 (16.3)	30 (27.8)	.01
Diabetes	27 (9.2)	20 (18.5)	.01
COPD	20 (6.8)	10 (9.3)	.41
Connective disease	18 (6.1)	9 (8.3)	.43
Postoperative symptoms	50 (17)	24 (22.2)	.23
Postoperative transfusions	38 (12.9)	3 (27.8)	<.001

POH = postoperative hyponatremia, THA = total hip arthroplasty, TKA = total knee arthroplasty.

Odds ratios (ORs) were used to quantify the size and direction of the association.

A stepwise process of elimination was used to select the variables for the final model from the pool of variables we considered in our analysis (Table 2).

Receiver operating characteristic curves (ROC) and area under curve (AUC) were used to estimate the prediction performance of logistic regression models. DeLong test was used to compare AUC. All values are reported as mean, range, and a *P*-value of less than .05 was considered statistically significant.

3. Results

Of the 624 hospitalized patients during 2016 to 2017 only 402 patients met our inclusion criteria. Mean age was 66.5 (29–88), 31.6% were over 80 years, 55.7% were females, mean BMI was 27.98 (14.45–44.96) kg/m^2. THA patients were 65.4%, TKA patients were 34.6%, mean duration of surgery was 100.18

Table 2

Stepwise logistic regression analysis results.

	P value	Odds ratio
Intercept	.01	0.03
Type of surgery (TKA)	.13	0.6
Surgery length	.14	1
Thiazides	.03	0.4
NSAIDs	.14	0.5
Beta blockers	.04	1.97
Postoperative hemoglobin	.03	1.22
Diabetes	.01	2.7
Postoperative transfusion	.02	2.5

(35–230) minutes. Only 16.9% of patients had transfusions. Mean preoperative natremia was 139.32 (135.71–146.74) mmol/L, mean postoperative natremia was 135.94 (127.78–146.78) mmol/L, average natremia variation was 3.38 (0–9.57) mmol/L. The most common comorbidities were: hypertension (273 patients), diabetes (47), chronic obstructive pulmonary disease (30), connective-tissue disorders (27). The most common drugs taken preoperatively were: non steroid anti-inflammatory drugs, NSAIDs, (361 patients), beta blockers (78), thiazides (60).

Patients were divided in 2 groups: group A, patients with normal postoperative natremia (294 patients); group B, patients who developed POH (108, 26.9%). In group A the mean preoperative natremia was 139.59 (135.71–146.74) mmol/L, mean postoperative natremia was 138.51 (135.6–146.78) mmol/L, average natremia variation was 1.08 (0–5.32) mmol/L. In group B the mean preoperative natremia was 139.06 (135.72–144.73) mmol/L, mean postoperative natremia was 133.38 (127.78–134.85) mmol/L; in this group the greatest natremia variation was observed: 5.69 (0.87–9.57) mmol/L. Of the patients who developed hyponatremia, 72 (66.7%) developed it within 24 hours postoperatively.

Among group B 106 patients had mild hyponatremia (98.2%), only 2 patients (1.8%) developed moderate hyponatremia, no severe hyponatremia was documented. Both these patients had diabetes, underwent TKA and received transfusions. No significant difference between groups in terms of age ($P=.44$), sex ($P=.16$) and BMI ($P=.33$). Patients with diabetes in group A were 27 (9.1%) and 20 in group B (18.5%) ($P=.01$). Patients treated with NSAIDs in group A were 270 (91.8%) and 91 in group B (84.2%) ($P=.02$). Type of surgery (TKA vs THA), operation time, number of transfusions, LOS and presence of postoperative symptoms did not show statistically significant differences within groups.

At univariate logistic analysis no association was found between preoperative values of natremia and POH (OR = 0.92; $P=.07$; Table 3). The associated ROC curve showed an AUC of 0.54 (CI: 0.5–0.61) (Fig. 1.tif).

At multivariate analysis the chronic use of thiazides was the only variable associated to a decreased risk of developing POH (OR = 0.39; $P=.03$). Chronic use of beta blockers was associated to an increased risk of developing POH (OR = 1.97; $P=.04$), along with postoperative hemoglobin values (OR = 1.22; $P=.03$), the need of postoperative transfusion (OR = 2.50; $P=.02$) and history of diabetes (OR = 2.70; $P=.01$). Type of surgery (TKA or THA), duration of surgery and pre or postoperative administration of NSAIDs were not significantly associated with postoperative developing of hyponatremia (Table 1). ROC of multivariate analysis showed an AUC of 0.71 (CI = 0.64–0.77) (Fig. 1.tif).

There was a statistically significant difference between ROC curves drawn for assessing the performance of the univariate and multivariate logistic models ($P<.001$).

Table 3

Univariate logistic regression model results. Preoperative plasmatic Na does not show a statistically significant association (OR = 0.92, $P=.07$) with postoperative hyponatremia.

	P value	Odds ratio
Intercept	.09	56442.15
Preoperative plasmatic Na	.07	0.92

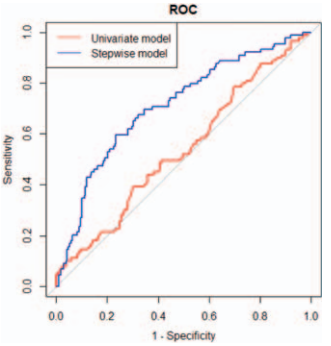

Figure 1. univariate and multivariate analysis performance (receiver operating characteristic curves analysis).

4. Discussion

Physiopathology of POH is still a question among clinicians. Several mechanisms have been proposed; among them, 2 are the most accepted. During surgery, stress-induced increase in antidiuretic hormone secretion is recognized as a possible mechanism of this electrolyte disorder.[9] Another stress induced response is the increased cellular membrane permeability that could be considered in the redistribution of solutes during surgery.[10]

Considering orthopedic surgery, most of interventions, especially joint replacements, are performed under spinal anesthesia. It is precisely here that patients need fluids infusion, because of the spinal induced sympathetic block.[11] The choice of the fluid infusion aims in maintaining the electrolyte balance.

The onset of acute POH after orthopedic surgery is feared by clinicians because of the possible complications, especially neurological ones.[12] Hyponatremia symptoms are often mistaken for usual post-operative conditions, so the knowledge of this electrolyte disorder is crucial in order to recognize and treat it early.

Several studies have examined the association between hyponatremia and patients undergoing orthopedic surgery.[13–18]

Our aim was to evaluate sodium imbalance in joint replacement surgery and its clinical effect. In hip fractured patients, different authors report different incidence of post-operative hyponatremia after surgery, ranging from 2.8% to 29.5%.[14–16]

In their series Hennrikus et al documented 30% of patients who developed POH. While the incidence is similar to our study, they included also 7% of patients presenting preoperative hyponatremia and, moreover, they included patients undergoing different type of orthopedic surgery, not only TKA and THA. In their experience authors claim an association of POH and length of hospitalization.[13] Sah, studying TKA and THA patients, reported 39.5% of POH: 32.4% mild, 5.6% moderate, and 1.5% severe hyponatremia. POH was present mostly in TKA patients and the combination TKA and POH resulted in a prolonged LOS, data not observed in our series. Mean age in the population examined by Sah was 70.4 years, slightly older than ours (66.5 years). In addition, the percentages of the type of surgery are inverted compared to our work (THA: 35.5% vs 65.4%; TKA: 64.5% vs 34.6%). However, they included patients with preoperative hyponatremia (8.4%). Preoperative imbalance could mask the real role of this type surgery in the onset of the disorder.

Preoperative hyponatremia in TKA has been already related to prolonged LOS and re-operation rate.[19] However, it is unclear if hyponatremia is a causative predictor of such consequences or is a surrogate marker of underlining fragility. Unlike previous studies, we excluded from our analysis patients with hyponatremia at presentation. This choice is crucial to point out the role of joint replacement surgery in the development of POH. Thus, no significant difference in operating time was found between patients with or without POH. The balanced use in perioperative period of Ringer lactate solution and normal saline solution in our opinion could explain the lack of association of operating time and POH.

In our series POH had an incidence of 26.9%, although mostly mild and often of a transitory nature. In fact, 66.7% of patients with POH developed the disorder within 24 hours postoperatively. Blood loss and surgical stress could be the main culprits of the immediate onset of POH. We hypothesized, on the other side, that the recovery of POH in a few hours is linked to the use of saline solution during postoperative period. POH incidence between THA and TKA patients was similar. There was no difference in terms of postoperative symptoms and LOS in patients who developed POH or not. Therefore, POH in patients who underwent total joint arthroplasty with normal electrolyte formula is a mild or moderate and transient laboratory condition that has no clinical impact if there is a cautious use of perioperative IV fluid management. In case of preoperative hyponatremia instead, it must be corrected before intervention: it can lead a mild hyponatremia into a severe POH, bringing complications seen in previous studies.

Use of hypotonic fluids like dextrose or dextrose containing fluids is a predisposing factor for POH.[20–23] In their series Tambe et al reported all cases of POH in patients who had infusion of hypotonic fluids.[7]

Considering clinical history, the use of thiazide has been considered as predisposing factors of POH.[24,25] For this reason patients who chronically took thiazide diuretics performed a different perioperative infusion protocol than other patients, 1000 mL normal saline solution instead 500 mL Ringer lactated solution and 500 mL normal saline solution. Thiazides were inversely related to POH: this result could be explained by the different infusion protocol given to patients taking thiazides.

Chronic use of beta blockers and history of diabetes resulted in an increased risk of developing POH. Therefore, particular attention must be taken to these patients to adapt infusion therapy and try to avoid the onset of POH and its consequences.

Perioperative transfusions were associated with POH, probably due to their use to counteract the blood loss and the relative decline of sodium serum levels and other electrolytes occurred during surgery. Tailoring perioperative fluid infusion, focusing on the predisposing factors mentioned above and on blood loss could be helpful to avoid POH.

Average natremia variation was 3.38 ± 2.95 mmol/L: this data is very important for management of pre- and postoperative electrolyte balance. Patients with borderline levels of serum sodium are at risk of developing POH, in this way an adaptation of the perioperative infusion protocol and a possible preoperative integration are fundamental.

4.1. Study limitations

This study presents some limitations: the number of the patients examined is still low considering a retrospective study; data have been recorded by different physicians and it may lead to poor standardization; the different perioperative infusion protocol chosen based on the clinical history of patients; fluid balance and the blood loss during hospitalization have not been calculated.

5. Conclusions

Orthopedic fast track surgery is possible only with an optimization of preoperative clinical conditions. Our study demonstrates an incidence of 26.9% of POH in normonatriemic patients at admission. Diabetes and transfusion are factors most often associated to POH. The onset of this disorder had no implication on postoperative symptoms and on LOS when an adequate perioperative fluid administration, using same average of normal saline solution and Ringer lactated solution, is given. Perioperative fluid management is of absolute importance balancing the loss of serum sodium due to surgery. Whenever symptomatic POH is present, it is consequence of a general state of fragility. Therefore, in case of preoperative hyponatremia, this must be corrected before intervention: it can lead a mild hyponatremia into a severe POH.

Author contributions

All authors have made substantial contributions to draw this study, specifically: E. Sinno and D. De Meo made conception and wrote the paper, C. Villani and P. Persiani made design and critic revision giving the final approval of submitted version. D. Ferraro, L. Petriello and G. Fornara made data collection. A. U. Cavallo made conception and statistical analysis.

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