Acta Neurol Belg (2013) 113:139–145
DOI 10.1007/s13760-012-0137-7

ORIGINAL ARTICLE

Outcome and frequency of sodium disturbances in neurocritically ill patients

Vera Spatenkova · Ondrej Bradac · Pavel Skrabalek

Received: 22 August 2012 / Accepted: 13 September 2012 / Published online: 2 October 2012

Abstract Sodium disturbances are frequent and serious complications in neurocritically ill patients. Hyponatremia is more common than hypernatremia, which is, however, prognostically worse. The aim of this study was to analyse outcome and frequency of sodium disturbances in relation to measured serum osmolality in neurologic-neurosurgical critically ill patients. A 5-year retrospective collection of patients (pts) and laboratory data were made from the Laboratory Information System database in the Clinical Biochemistry Department. The criteria for patients' inclusion was acute brain disease and serum sodium (SNa^+) <135 mmol/l (hyponatremia) or SNa^+ >150 mmol/l (hypernatremia). Hypoosmolality was defined as measured serum osmolality (SOsm) <275 mmol/kg, hyperosmolality as SOsm >295 mmol/kg. We performed analysis of differences between hyponatremia and hypernatremia and subanalysis of differences between hypoosmolal hyponatremia and hypernatremia. From 1,440 pts with acute brain diseases there were 251 (17 %) pts with hyponatremia (mean SNa^+ 131.78 ± 2.89 mmol/l, SOsm 279.46 ± 11.84 mmol/kg) and 75 (5 %) pts with hypernatremia (mean SNa^+ 154.38 ± 3.76 mmol/l, SOsm 326.07 ± 15.93 mmol/kg). Hypoosmolal hyponatremia occurred in 50 (20 % of hyponatremic patients) pts (mean SNa^+ 129.62 ± 4.15 mmol/l; mean SOsm 267.35 ± 6.28 mmol/kg). Multiple logistic regression analysis showed that hypernatremia is a significant predictor of mortality during neurologic-neurosurgical intensive care unit (NNICU) stay (OR 5.3, $p = 0.002$) but not a predictor of bad outcome upon discharge from NNICU, defined as Glasgow Coma Scale 1–3. These results showed that hypernatremia occurred less frequently than all hyponatremias, but more often than hypoosmolal hyponatremia. Hypernatremia was shown to be a significant predictor of NNICU mortality compared to hyponatremia.

Keywords Hyponatremia · Hypernatremia · Neurointensive care · Outcome

V. Spatenkova (✉)
Neurocenter, Neurologic-Neurosurgical Intensive Care Unit, Regional Hospital, Husova 10, 46063 Liberec, Czech Republic
e-mail: vera.spatenkova@nemlib.cz

O. Bradac
Department of Neurosurgery, Central Military Hospital, Charles University, Prague, Czech Republic

P. Skrabalek
Department of Clinical Biochemistry, Regional Hospital, Liberec, Czech Republic

Introduction

Sodium disturbances are frequent and serious complications in neurointensive care [1–6]. Both hyponatremia and hypernatremia cause brain injury, primary in patients without brain damage and secondary in patients with various primary brain injuries. Hyponatremia occurred more frequently than hypernatremia, which is, however, prognostically worse [7–9].

Sodium as the main extracellular cation affects effective extracellular fluid (ECF) osmolality. The osmotic gradient between ECF and intracellular fluid (ICF) spaces is balanced by a shift in water. The shift in water between ECF and ICF is caused by dysnatremias, which are connected with disturbances of serum osmolality. It is in hypernatremia which is always related to serum hyperosmolality, in contrast to hyponatremia. In some cases, hyponatremia has no relation to low serum osmolality, for

example during osmotherapy by mannitol or hyperglycemia. Hypernatremia causes hypertonicity of ECF, and the following shift leads to dehydration of cells [10]. On the other hand, hypoosmolal hyponatremia gives rise to cell edema [11–13]. For these reasons it is necessary to pay attention to dysnatremias in neurointensive care and actively search for them. Daily monitoring of serum sodium should be part of the daily care of every patient with acute brain disease.

The aim of this study was to analyse outcome and frequency of sodium disturbances in relation to measured serum osmolality in neurologic-neurosurgical critically ill patients.

Methods

Collection of patients

The 5-year retrospective study was carried out in an eight-bed neurologic-neurosurgical intensive care unit (NNICU) in the Neurocenter of Regional Hospital Liberec. During this period there were 1,440 patients with various acute brain diseases, both neurological and neurosurgical, admitted. Collections of patients and laboratory data were made from the database of Laboratory Information System Stapro (LISSTA) Pardubice in the department of clinical biochemistry in Regional Hospital Liberec with the aid of the programme LisBed.

The criteria for patients' inclusion was acute brain disease and serum sodium (SNa^+) <135 mmol/l (hyponatremia) or SNa^+ >150 mmol/l (hypernatremia). We defined hypernatremia according to Aiyagari's study [2], which was conducted in neurologic/neurosurgical intensive care units in the same population as in our NNICU, and Miulli's definition [14]. Hypoosmolality was defined as measured serum osmolality SOsm <275 mmol/kg, and hyperosmolality as SOsm >295 mmol/kg.

Observed clinical parameters

We observed the parameters related to the patient's prognosis: mortality in NNICU, Glasgow Outcome Scale (GOS) upon discharge from NNICU, bad outcome marked as GOS 1–3, incidence of cerebral complications; parameters to the onset of dysnatremia: Glasgow Coma Scale (GCS), operation, relation to hospitalisation, diuretic and antiedematic therapy, fluid balance: fluid intake (ml/day), fluid output (ml/day), fluid balance (ml/day). Polyuria was defined as diuresis above 4,000 ml/day. We calculated all fluids given by mouth, tube and parentally into fluid intake. Fluid output was from diuresis and drainage.

Observed biochemical parameters

The following parameters were measured: serum sodium (SNa^+), serum potassium (SK^+), serum calcium (SCa^{2+}), serum magnesium (SMg^{2+}), serum chloride (SCl^-), serum phosphorus (SP), serum osmolality (SOsm), urine osmolality (UOsm), serum protein (SProt), serum albumin (SAlb), serum glucose (SGlu), serum urea (SUrea), serum creatinine (SCr), blood pH (BpH), daily output of creatinine (dUCr), sodium ($dUNa^+$) and potassium (dUK^+). Sodium, potassium and chloride measurements in serum and urine were carried out on the COBAS Integra 800 system (Roche, Diagnostics, Switzerland) using selective ion electrodes. Creatinine in serum and urine, protein, albumin in serum were also measured on this equipment, but photometrically. Osmolality was gauged on the cryoscopic osmometer Fiske 210 (Advanced Instruments, Inc, Norwood, MA, USA). BpH was measured on the blood gas analyzer ABL 625 (Radiometer, Denmark). Blood samples for biochemical examination were collected using standard protocol in the NNICU, from extremities without application of infusion.

We used these calculated biochemical parameters from the department of clinical biochemistry. Clearance of creatinine was calculated according to general formulae for clearance with correction for the body's surface.

Values of urine volume (V) are in litres and time in seconds. Serum osmolality calculated: $SOsmC = 2 \times Na^+ +$ glucose + urea. Creatinine clearance: $CCr = (UCr \times V)/(\text{time} \times SCr \times \text{surface})$. Osmotically active substances clearance: $COsm = (UOsm \times V)/(\text{time} \times SOsm)$. Electrolyte clearance: $CEl = V \times [2\times (UNa^+ + UK^+) + UGlu]/[2 \times (SNa^+ + SK^+) + SGlu] \times \text{time}$. Sodium clearance: $CNa^+ = (UNa^+ \times V)/(\text{time} \times SNa^+)$. Solute free water clearance: $CH_2O = (V/\text{time}) - COsm$. Electrolyte free water clearance: $EWC = (V/\text{time}) - CEl$ or $(V/\text{time}) - V \times [2\times (UNa^+ + UK^+) + UGlu]/[2 \times (SNa^+ + SK^+) + SGlu] \times \text{time}$. Fractional excretion of osmotically active substances: $FEOsm = (UOsm \times SCr)/(SOsm \times UCr \times 1{,}000)$. Fractional excretion of sodium: $FENa^+ = (UNa^+ \times SCr)/(SNa^+ \times UCr \times 1{,}000)$. Fractional excretion of free water: $FEH_2O = SCr/(UCr \times 1{,}000)$. Biochemical parameters from urine were processed only from urine collected within 24 h.

Statistical processing

STATISTICA 10.0 software (StatSoft CR s.r.o) was used for statistical analysis.

The parametric t tests or non-parametric M–W U tests were used for comparison of continuous variables. Comparison of categorical parameters was carried out using Fisher tests. Univariate logistic regression was used for identifying prognostic factors of mortality and poor

outcome during NNICU stay. Factors from univariate analysis with level of significance defined as $p < 0.1$ were used for multivariate regression analysis with forward stepwise method of final model building (p value for model enter was <0.05, p value for remove from model was >0.05). p values of less than 0.05 were considered significant.

Univariate and subsequent multivariate logistic regression analysis was used for identifying significant predictors of mortality during NNICU stay. Studied factors were age as a continuous predictor, hyponatremia or hypernatremia on admission, administration of steroids, antiedematic therapy, initial GCS less than 9, surgical intervention, cerebral complications, and diffuse or focal brain lesion.

The study was carried out with the approval of the Hospital Ethical Committee.

Results

During the 5-year period there were, out of 1,440 pts with acute brain diseases, 251 (17 %) pts with hyponatremia (mean SNa^+ 131.78 ± 2.89 mmol/l) and 75 (5 %) pts with hypernatremia (mean SNa^+ 154.38 ± 3.76 mmol/l). Hypoosmolal hyponatremia occurred in 50 (20 %) pts (mean SNa^+ 129.62 ± 4.15 mmol/l; mean SOsm 267.35 ± 6.28 mmol/kg).

There was no difference between hyponatremic and hypernatremic patients in length of stay in NNICU ($p = 0.825$), length of dysnatremia ($p = 0.699$), operation ($p = 0.163$) and onset of dysnatremia after operation ($p = 0.061$), but upon admission to the NNICU there was a significantly higher presence of hyponatremia ($p = 0.035$) than hypernatremia. Hypernatremic pts more frequently received antiedematic therapy ($p < 0.001$), had lower GCS on onset of hypernatremia ($p < 0.001$), more cerebral complications ($p = 0.001$), higher mortality in NNICU ($p < 0.001$) and worse GOS upon discharge from NNICU ($p = 0.024$) (Table 1). In the hypernatremia group we found higher serum urea ($p < 0.001$). There were no differences either in fluid intake ($p = 0.240$) or infusion ($p = 0.097$). Significantly higher diuresis ($p = 0.008$) and fluid output ($p = 0.007$) with negative fluid balance ($p = 0.001$) were seen in hyponatremic patients. Further biochemical parameters can be seen in Table 2. Multivariate logistic regression analysis showed that hypernatremia compared to hyponatremia is a significant predictor of mortality during NNICU stay (OR 5.3, $p = 0.002$) but not

Table 1 Characteristics of the hyponatremic and hypernatremic patients

Parameter	Unit	Hyponatremia ($N = 251$)	Hypernatremia ($N = 75$)	p value
Male	pts	160	41	0.156
Age	year	54.0 ± 15.9	56.8 ± 14.8	0.180
GCS	1	13.6 ± 2.2	11.96 ± 3.4	<0.001
Stay in NNICU	day	11.6 ± 9.6	11.8 ± 10.1	0.825
Admission to NNICU	pts	74	13	0.035
Diagnosis				
Stroke	pts	101 (40.2 %)	43 (57.4 %)	0.009
Tumor	pts	80 (31.9 %)	20 (26.7 %)	0.387
Trauma	pts	33 (13.1 %)	7 (9.3 %)	0.364
Epilepsy	pts	12 (4.8 %)	1 (1.3 %)	0.011
Infection	pts	13 (5.2 %)	0 (0 %)	0.008
Hydrocephalus	pts	7 (2.8 %)	4 (5.3 %)	0.309
Other	pts	5 (2.0 %)	0 (0 %)	0.104
Operation	pts	188	62	0.163
After operation	pts	161	57	0.061
Glucocorticoid	pts	53	26	0.017
Antiedematic therapy	pts	101	55	<0.001
Normal saline	pts	224	71	0.184
Diuretic therapy	pts	20	11	0.085
Polyuria	pts	57	21	0.355
Cerebral complications	pts	115	51	0.001
Bad outcome (GOS 1–3)	pts	94	39	0.024
Mortality in NNICU	pts	7	14	<0.001

NNICU neurologic-neurosurgical intensive care unit, *mean* in age and stay in NNICU, *GCS* Glasgow Coma Scale, *GOS* Glasgow Outcome Scale

Table 2 Parameters in hyponatremia and hypernatremia groups of patients

Parameter	Unit	Reference range	Hyponatremia	Hypernatremia	*p* value
SNa^+	mmol/l	135–146	131.78 ± 2.89	154.38 ± 3.76	<0.001
Length	day		2.6 ± 2.8	2.9 ± 3.8	0.699
Shift/24 h	mmol/l		1.93 ± 4.17	−2.49 ± 5.56	<0.001
SOsm	mmol/kg	275–295	279.46 ± 11.84	326.07 ± 15.93	<0.001
SOsmC	mmol/kg	275–300	276.02 ± 8.1	326.18 ± 11.09	<0.001
UOsm	mmol/kg	50–850	552.13 ± 189.64	562.45 ± 196.47	0.571
SK^+	mmol/l	3.8–5.5	4.16 ± 0.63	3.92 ± 0.54	<0.001
SCa^{2+}	mmol/l	2–2.75	2.10 ± 0.17	2.08 ± 0.22	0.413
SMg^{2+}	mmol/l	0.7–1.1	0.88 ± 0.19	1.01 ± 0.22	<0.001
SP	mmol/l	0.7–1.5	1.08 ± 0.29	1.02 ± 0.33	0.048
SCl^-	mmol/l	97–108	98.00 ± 4.43	113.17 ± 6.64	<0.001
SProt	g/l	66–87	64.73 ± 8.15	56.13 ± 7.30	<0.001
SAlb	g/l	32–53	37.35 ± 5.01	33.54 ± 6.35	<0.001
SGlu	mmol/l	3.3–6.1	7.06 ± 2.84	7.53 ± 2.84	0.057
BpH		7.36–7.44	7.437 ± 0.05	7.424 ± 0.05	0.005
SUrea	mmol/l	2.8–7.5	5.67 ± 3.43	9.49 ± 5.18	<0.001
SCr	μmol/l	35–115	79.51 ± 55.56	95.98 ± 36.17	<0.001
CCr	ml/s	1.15–2	1.98 ± 0.68	1.70 ± 0.78	0.001
$dUNa^+$	mmol/day	100–260	442.17 ± 385.17	218.21 ± 195.35	<0.001
dUK^+	mmol/day	40–90	65.74 ± 37.34	76.23 ± 63.62	0.110
COsm	ml/s	0.03–0.05	0.085 ± 0.05	0.066 ± 0.03	0.002
CH_20	ml/s	−0.027 to −0.007	−0.037 ± 0.031	−0.022 ± 0.03	0.001
CNa^+	ml/s	0.008–0.016	0.051 ± 0.04	0.023 ± 0.02	<0.001
CEl	ml/s	0.011–0.023	0.057 ± 0.04	0.031 ± 0.02	<0.001
EWC	ml/s	−0.000 ± 0.006	−0.008 ± 0.03	0.012 ± 0.03	<0.001
$FENa^+$		0.004–0.012	0.026 ± 0.02	0.016 ± 0.01	<0.001
FEOsm		0.01–0.035	0.043 ± 0.02	0.043 ± 0.02	0.828
FEH_20		0.01–0.02	0.025 ± 0.01	0.030 ± 0.02	0.040
Fluid intake	ml/day		4000.91 ± 1504.0	3836.29 ± 980.86	0.240
Infusion	ml/day		2020.32 ± 1334.05	2229.92 ± 984.76	0.097
Fluid output	ml/day		3693.24 ± 1856.30	3210.61 ± 1199.77	0.007
Diuresis	ml/day		3550.86 ± 1849.27	3082.86 ± 1262.16	0.008
Negative fluid balance	pts		118	21	0.001

SNa^+ serum sodium, *length* length of dysnatremia, *SOsm* serum osmolality, *SOsmC* serum osmolality calculated, *UOsm* urine osmolality, *SK^+* serum potassium, *SCa^{2+}* serum calcium, *SMg^{2+}* serum magnesium *SP* serum phosphorus, *SCl^-* serum chloride, *SProt* serum protein, *SAlb* serum albumin, *SGlu* serum glucose, *BpH* blood pH, *SUrea* serum urea, *SCr* serum creatinine, *CCr* creatinine clearance, *$dUNa^+$* daily output of sodium, *dUK^+* daily output of potassium, *COsm* osmotically active substances clearance, *CH_2O* solute free water clearance, *CNa^+* sodium clearance, *CEl* electrolyte clearance, *EWC* electrolyte free water clearance, *$FENa^+$* fractional excretion of sodium, *FEOsm* fractional excretion of osmotically active substances, *FEH_2O* fractional excretion of free water

a predictor of bad outcome upon discharge from NNICU, defined as GOS 1–3. Results of multivariate regression analysis are summarised in Table 3.

Subanalysis between hypernatremic patients and hypoosmolal hyponatremic patients showed more antiedematic therapy ($p < 0.001$) and lower GCS on onset of dysnatremia ($p = 0.026$) in hypernatremic patients, but no significant differences in cerebral complications ($p = 0.846$), mortality in NNICU, ($p = 0.061$) and worse GOS upon discharge from NNICU ($p = 0.100$), (Table 4).

Discussion

Dysnatremia is a frequent dysbalance of effective osmolality in acute brain diseases [1–6] which was also shown in our study. Dysnatremia occurred in 23 % of patients with acute brain diseases hospitalised in our neurologic-neurosurgical care unit. Hyponatremia was found more often (17 %) than hypernatremia (5 %), but hyponatremia connected with low serum osmolality was less frequent (3 %), only in 20 % of all hyponatremias. This means that this

Table 3 Results of multivariate logistic regression analysis in hyponatremia and hypernatremia

Mortality predictive factor	Odds Ratio	Lower CL 95 %	Upper CL 95 %	*p* value
GCS <9	11.0	3.8	31.8	<0.001
Cerebral complication	6.4	1.4	30.0	0.019
Hypernatremia	5.3	1.9	15.0	0.002
Poor outcome predictive factor	**Odds Ratio**	**Lower CL 95 %**	**Upper CL 95 %**	***p* value**
GCS <9	21.2	4.7	95.1	<0.001
Cerebral complication	2.9	1.8	4.8	<0.001
Surgical intervention	1.8	1.0	3.1	0.042
Steroids administration	0.4	0.2	0.8	0.005
Antidiuretic therapy	0.2	0.1	0.9	0.028

CL confidence limit

Table 4 Parameters in hypoosmolal hyponatremia and hypernatremia groups of patients

Parameter	Unit	Reference range	Hypoosmolal Hyponatremia ($N = 50$)	Hypernatremia ($N = 75$)	*p* value
Age	year		48.5 ± 18.9	56.8 ± 14.8	0.007
Stay in NNICU	day		18.7 ± 12.7	11.8 ± 10.1	<0.001
GCS	1		13.2 ± 2.2	11.96 ± 3.4	0.026
Operation	pts		43	62	0.804
After operation	pts		36	57	0.678
Cerebral complications	pts		35	51	0.846
Bad outcome	pts		18	39	0.100
Mortality	pts		3	14	0.061
Glucocorticoid	pts		8	26	0.025
Antiedematic therapy	pts		15	55	<0.001
Diuretic therapy	pts		0	11	0.006
Polyuria	pts		29	21	0.001
SNa^+	mmol/l	135–146	129.62 ± 4.15	154.38 ± 3.76	<0.001
Shift/24 h	mmol/l		1.33 ± 4.62	−2.49 ± 5.56	<0.001
SOsm	mmol/kg	275–295	267.35 ± 6.28	326.07 ± 15.93	<0.001
SOsmC	mmol/kg	275–300	269. 20 ± 9.18	326.18 ± 11.09	<0.001
UOsm	mmol/kg	50–850	624.93 ± 114.12	562.45 ± 196.47	0.006
SK^+	mmol/l	3.8–5.5	4.08 ± 0.49	3.92 ± 0.54	0.019
SCa^{2+}	mmol/l	2–2.75	2.11 ± 0.20	2.08 ± 0.22	0.451
SMg^{2+}	mmol/l	0.7–1.1	0.81 ± 0.16	1.01 ± 0.22	<0.001
SP	mmol/l	0.7–1.5	0.10 ± 0.24	1.02 ± 0.33	0.504
SCl^-	mmol/l	97–108	96.60 ± 5.46	113.17 ± 6.64	<0.001
SProt	g/l	66–87	65.17 ± 7.60	56.13 ± 7.30	<0.001
SAlb	g/l	32–53	37.30 ± 4.75	33.54 ± 6.35	0.012
SGlu	mmol/l	3.3–6.1	6.18 ± 1.28	7.53 ± 2.84	<0.001
BpH		7.36–7.44	7.44 ± 0.05	7.424 ± 0.05	0.080
SUrea	mmol/l	2.8–7.5	4.05 ± 1.70	9.49 ± 5.18	<0.001
SCr	μmol/l	35–115	68.35 ± 13.94	95.98 ± 36.17	<0.001
CCr	ml/s	1.15–2	2.07 ± 0.57	1.70 ± 0.78	0.008
$dUNa^+$	mmol/day	100–260	567.66 ± 391.01	218.21 ± 195.35	<0.001
dUK^+	mmol/day	40–90	70.23 ± 40.35	76.23 ± 63.62	0.533
COsm	ml/s	0.03–0.05	0.09 ± 0.04	0.066 ± 0.03	<0.001

Table 4 continued

Parameter	Unit	Reference range	Hypoosmolal Hyponatremia ($N = 50$)	Hypernatremia ($N = 75$)	p value
CH_20	ml/s	−0.027 to −0.007	−0.05 ± 0.02	−0.022 ± 0.03	<0.001
CNa^+	ml/s	0.008–0.016	0.06 ± 0.04	0.023 ± 0.02	<0.001
CEl	ml/s	0.011–0.023	0.07 ± 0.04	0.031 ± 0.02	<0.001
EWC	ml/s	−0.000 ± 0.006	−0.023 ± 0.02	0.012 ± 0.03	<0.001
$FENa^+$		0.004–0.012	0.030 ± 0.02	0.016 ± 0.01	<0.001
FEOsm		0.01–0.035	0.048 ± 0.02	0.043 ± 0.02	0.160
FEH_20		0.01–0.02	0.021 ± 0.01	0.030 ± 0.02	0.037
Fluid intake	ml/day		4059.61 ± 1267.96	3836.29 ± 980.86	0.142
Infusion	ml/day		2032.42 ± 1049.23	2229.92 ± 984.76	0.156
Fluid output	ml/day		3768.16 ± 1812.12	3210.61 ± 1199.77	0.008
Diuresis	ml/day		3606.07 ± 1807.03	3082.86 ± 1262.16	0.014
Negative fluid balance	pts		28	21	0.008

NNICU neurologic-neurosurgical intensive care unit, *mean* in age, *GCS* Glasgow Coma Scale, *bad outcome* Glasgow Outcome Scale 1–3, SNa^+ serum sodium, *length* length of dysnatremia, *SOsm* serum osmolality, *SOsmC* serum osmolality calculated, *UOsm* urine osmolality, SK^+ serum potassium, SCa^{2+} serum calcium, SMg^{2+} serum magnesium, *SP* serum phosphorus, SCl^- serum chloride, *SProt* serum protein, *SAlb* serum albumin, *SGlu* serum glucose, *BpH* blood pH, *SUrea* serum urea, *SCr* serum creatinine, *CCr* creatinine clearance, $dUNa^+$ daily output of sodium, dUK^+ daily output of potassium, *COsm* osmotically active substances clearance, CH_2O solute free water clearance, CNa^+ sodium clearance, *CEl* electrolyte clearance, *EWC* electrolyte free water clearance, $FENa^+$ fractional excretion of sodium, *FEOsm* fractional excretion of osmotically active substances, FEH_2O fractional excretion of free water

serious type of hyponatremia which influences the shift of water between ICF and ECF and causes cell edema was not a frequent type of sodium disturbance in our neurologic-neurosurgical critically ill patients, and even less common than hypernatremia (5 %). For this reason it is important while managing hyponatremia to find out the value of measured serum osmolality [15] as the first step. Hyponatremia had a significantly higher presence upon admission to the intensive care ($p = 0.035$) than hypernatremia, which was also seen in Funk's study [16]. Hypernatremia arises more often during stay in intensive care [17]. In literature, it is known that antiedematic therapy is a risk factor that causes hypernatremia [2]. In our study hypernatremic patients received more antiedematic therapy. Another cause of onset of hyponatremia or hypernatremia is fluid therapy, but we did not find differences either in fluid intake ($p = 0.240$ in hyponatremia; $p = 0.142$ in hypoosmolal hyponatremia) or infusion ($p = 0.097$ and $p = 0.156$). Significantly higher diuresis ($p = 0.008$ and $p = 0.014$) and then fluid output ($p = 0.007$ and $p = 0.008$) were seen in hyponatremic or hypoosmolal hyponatremic patients. Another reason for occurrences of dysnatremia is diuretic therapy. In our study, we found significant differences in diuretic therapy only in comparison of hypernatremic with hypoosmolal hyponatremic patients ($p = 0.006$). The occurrence of dysnatremia has an influence on the type of diuresis. Water diuresis leads to hypernatremia and salt diuresis to hyponatremia, which was seen in these results. Renal function parameters [18, 19] of water diuresis EWC and FEH_2O were significantly higher in hypernatremia, on the other hand in hyponatremia and hypoosmolal hyponatremia there was a higher daily output of sodium ($dUNa^+$, $p < 0.001$, $p < 0.001$, respectively), COsm ($p = 0.002$ and $p < 0.001$), CEl ($p < 0.001$, and $p < 0.001$), CNa^+ ($p < 0.001$ and $p < 0.001$) and $FENa^+$ ($p < 0.001$ and $p < 0.001$).

From observed parameters influencing sodium homeostasis, in hypernatremic patients we found significantly higher serum urea concentration, which is another factor that can cause hypernatremia [20]. On the other hand we found significant differences in serum glucose concentration ($p < 0.001$) only between the hypoosmolal hyponatremia and hypernatremia groups.

Hypernatremia is a prognostically serious complication in critically ill patients [21, 22] which was also evident in our study. Multivariate logistic regression analysis showed that hypernatremia in comparison with hyponatremia is a significant predictor of mortality during NNICU stay (OR 5.3, $p = 0.002$), Further predictors are presence of cerebral complication (OR 6.4, $p = 0.019$) and GCS less than 9 (OR 11.0, $p < 0.001$). Different results were found when bad outcome upon discharge from NNICU (defined as GOS 1–3) was studied. In this analysis risk factors such as cerebral complication (OR 2.9, $p < 0.001$) and GCS less than 9 (OR 21.0, $p < 0.001$) remained. New predictors of bad outcome were surgical intervention (OR 1.8, $p = 0.042$), steroid administration (OR 0.4, $p = 0.005$) and antidiuretic therapy (OR 0.2, $p = 0.028$). These results

have the limitations of a retrospective study and further prospective cohort studies are needed to confirm these findings.

In conclusion, this study showed that hypernatremia occurred less frequent than all hyponatremias, but more often than hypoosmolal hyponatremia. Hypernatremia in comparison with hyponatremia is a significant predictor of NNICU mortality.

Conflict of interest None.

References

1. Tisdall M, Crocker M, Watkiss J et al (2006) Disturbances of sodium in critically ill adult neurologic patients: a clinical review. J Neurosurg Anesthesiol 18:57–63
2. Aiyagari V, Deibert E, Diringer M (2006) Hypernatremia in the neurologic intensive care unit: how high is too high? J Crit Care 21:163–172
3. Diringer MN, Zazulia AR (2006) Hyponatremia in neurologic patients: consequences and approaches to treatment. Neurologist 12:117–126
4. Fisher LA, Ko N, Miss J et al (2006) Hypernatremia predicts adverse cardiovascular and neurological outcomes after SAH. Neurocrit Care 5:180–185
5. Fraser JF, Stieg PE (2006) Hyponatremia in the neurosurgical patient: epidemiology, pathophysiology, diagnosis, and management. Neurosurgery 59:222–229
6. Rabinstein AA, Wijdicks EF (2003) Hyponatremia in critically ill neurological patients. Neurologist 9:290–300
7. Qureshi AI, Suri MF, Sung GY et al (2002) Prognostic significance of hypernatremia and hyponatremia among patients with aneurysmal subarachnoid hemorrhage. Neurosurgery 50:749–756
8. Takaku A, Shindo K, Tanaka S et al (1979) Fluid and electrolyte disturbances in patients with intracranial aneurysms. Surg Neurol 11:349–356
9. Disney L, Weir B, Grace M et al (1989) Trends in blood pressure, osmolality and electrolytes after subarachnoid hemorrhage from aneurysms. Can J Neurol Sci 16:299–304
10. Diringer MN (1992) Management of sodium abnormalities in patients with CNS disease. Clin Neuropharmacol 15:427–447
11. Nathan BR (2007) Cerebral correlates of hyponatremia. Neurocrit Care 6:72–78
12. Dvir D, Beigel R, Hoffmann C et al (2009) Hyponatremic brain edema: correlation with serial computed tomography scans. Isr Med Assoc J 11:442–443
13. Schrier RW, Bansal S (2008) Diagnosis and management of hyponatremia in acute illness. Curr Opin Crit Care 14:627–634
14. Miulli D (2008) Fluid management. In: Siddiqi J (ed) Neurosurgical intensive care. Thieme, New York, pp 290–312
15. Vaidya C, Ho W, Freda BJ (2010) Management of hyponatremia: providing treatment and avoiding harm. Cleve Clin J Med 77:715–726
16. Funk GC, Lindner G, Druml W et al (2010) Incidence and prognosis of dysnatremias present on ICU admission. Intensive Care Med 36:304–311
17. Polderman KH, Schreuder WO, Strack van Schijndel RJ et al (1999) Hypernatremia in the intensive care unit: an indicator of quality of care? Crit Care Med 27:1105–1108
18. Shoker AS (1994) Application of the clearance concept to hyponatremic and hypernatremic disorders: a phenomenological analysis. Clin Chem 40:1220–1227
19. Lolin Y, Jackowski A (1992) Hyponatraemia in neurosurgical patients: diagnosis using derived parameters of sodium and water homeostasis. Br J Neurosurg 6:457–466
20. Sam R, Feizi I (2012) Understanding hypernatremia. Am J Nephrol 36:97–104
21. Hoorn EJ, Betjes MG, Weigel J et al (2008) Hypernatraemia in critically ill patients: too little water and too much salt. Nephrol Dial Transpl 23:1562–1568
22. Lindner G, Funk GC, Schwarz C et al (2007) Hypernatremia in the critically ill is an independent risk factor for mortality. Am J Kidney Dis 50:952–957