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ORIGINAL ARTICLE

Hospital-acquired hyponatremia: Does the type of fluid therapy affect children admitted to intensive care?

Hiponatremia adquirida en el hospital: ¿influye el tipo de fluidoterapia en los niños ingresados a cuidados intensivos?

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Abstract

Introduction: The objective of this study was to evaluate the association between the type of initial fluid therapy used (isotonic or hypotonic solutions) and the development of hyponatremia, the plasma chlorine values and the tolerance of venous access. **Patients and Method:** Retrospective cohort study in a Pediatric Intensive Care Unit (PICU) of a high complexity hospital. There were included children younger than 15 years old hospitalized during the first semester of 2010 and 2013 who received intravenous maintenance fluid therapy, excluding patients undergoing cardiac surgery, kidney transplant and admissions that lasted less than 24 hours. Epidemiological, comorbidity and admission-related data were collected, including type of solution received, sodium and chlorine values in the first 72 hours of hospitalization and the incidence of extravasation of peripheral intravenous lines. **Results:** 111 children were included; 68 children (61.3%) were treated with hypotonic solutions and 43 (38.7%) with isotonic solutions. There were no differences in pathology and severity, and also in the volume of fluid received. Among the patients who received hypotonic solutions, 28 (41.2%) developed hyponatremia, wich was moderate (Na <130 mEq/Kg) in 11 cases, compared with 8 children (18.6%) who received isotonic solutions, with only one case of moderate hyponatremia ($p = 0.027$). No cases of hypernatremia were recorded, and there were no differences in plasma chlorine values. There was also no increased frequency of venous access loss in patients treated with isotonic solutions (4.7% versus 7.4%, $p = 0.704$). **Conclusion:** Treatment with initial isotonic solutions in children hospitalized in PICU is associated with a lower incidence and severity of hyponatremia, without changes in the plasma chlorine values and it is well tolerated by peripheral intravenous lines.

Keywords:
Hyponatremia;
hyperchloraemia;
intravenous fluid therapy;
pediatric intensive care;
tolerance venous access

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Introduction

Hyponatremia, defined as a plasma sodium concentration lower than 135 mEq/L, is the most common electrolytic disorder in hospitalized patients, and it is associated with increased morbidity and mortality, as well as an increase in the average hospital stay[1]. Sodium is the main influencing factor in plasma tonicity; the decreased tone causes water to pass from the extracellular into the intracellular space until the osmolarity is equalized in both compartments, which could cause a cellular edema; if this happens in the brain, it could result in neurological symptomatology[2,3]. Hyponatremia could be due to a gain of water and/or a deficit of sodium in the extracellular fluid. There are two necessary requirements to produce it: a source of water, which will be for hospitalized children the intravenous fluid therapy administered, and the presence of antidiuretic hormone (ADH) which prevents its excretion[2,4-7].

Intravenous maintenance fluids are used in children who cannot be fed enterally, providing necessary water and electrolyte requirements to cover the physiological needs of the individual. Energy consumption is used to calculate these requirements, which relates hydroelectrolytic demands to the basal metabolic activity of the individual[1], following the recommendations of Holliday and Segar designed in 1957[8]. Based on these recommendations for water intake, and the estimated sodium and potassium requirements of 3 mEq and 2 mEq per 100 kcal per day respectively, a hypotonic solution has been recommended as a maintenance fluid[4,9].

However, it is known today that in seriously ill children, energy consumption and therefore, water and electrolyte requirements, varies significantly according to multiple circumstances Thus, these general rules for the administration of maintenance intravenous fluid therapy may lead to harmful effects on these patients[2,3], many of whom present a non-osmotic secretion of ADH, and therefore a limited ability to excrete water[10,11]. Many authors have related the administration of hypotonic fluids in hospitalized patients with an increased incidence of iatrogenic hyponatremia[1,3,4,6,7,11,12] with complications whose severity will depend on both the magnitude of hyponatremia and its onset speed, which could lead to permanent neurological injuries and death of the patient[2,4,6]. Despite the growing number of studies that suggest the use of isotonics, there is no consensus on this and even today some publications advocate the use of hypotonic fluids as maintenance fluid therapy[13,14]. The current trend is the recommendation of isotonic solutions routinely in hospitalized pediatric patients, given the growing evidence on their safety and the results of recent meta-analyses[12-16] reserving hypotonic solutions for specific cases[9,12].

On the other hand, the tolerance of peripheral intravenous lines to the administration of this type of saline solutions has not been reported, and some authors have commented that it could mean a higher risk of phlebitis and peripheral venous access loss due to the greater osmolarity of the solution, therefore they do not recommend the use of solutions with an osmolarity higher than 500 mOsm/L[16,17]. However, this limit contrasts with other guidelines, which recommend for peripheral infusion of intravenous solutions an osmolarity between 300-900 mOsm/L, although no specific limit has been proven in controlled studies[18-20].

Another discussed aspect in the use of isotonic solutions for fluid therapy is related to the amount of chlorine or to the possibility of developing hyperchloremia[21,22].

The objective of this study is to assess if the change in initial maintenance fluid therapy based on hypotonic to isotonic fluids has reduced the incidence of hyponatremia in patients admitted to the PICU. Secondarily, it is intended to assess if differences in plasma chlorine values and the tolerance of peripheral intravenous lines to saline solution infusion with an osmolarity higher than 550 mOsm/L occur.

Patients and Method

Design and Patients Retrospective cohort study through the review of Clinical Records, which included all patients over one week old and under 15 years old, who were admitted to the PICU of Gregorio Marañón University General Hospital (HGUGM) between January and June in 2010 and 2013, because these years are representative of the period before and after the change in initial maintenance fluid therapy of hypotonic and isotonic fluids, respectively.

The following patients were excluded: a) patients admitted to the PICU and stayed for less than 24 hours or those who received exclusive maintenance intravenous fluid therapy for less than 8 hours; b) patients who did not have any blood analysis or who had only one performed in the first hours of admission, which prevented an assessment of the sodium levels; c) patients from cardiac surgery and post-renal transplantation patients because they received specific fluid therapies and hydrosaline overload associated with extracorporeal circulation; d) unstable patients who were given a high volume of fluids for volume expansion (over 50 ml/kg in 24 hours).

Ethical aspects

The study was approved by the Institutional Review Board of Gregorio Marañón Children's Hospital Medical Center. Patient confidentiality was maintained at all times.

Data analysis

The review of the Clinical Record included the review of laboratory tests, nursing charts, and prescribing documents. The following variables were gathered: age, gender, weight, previous pathology (including history of prematurity and chromosomopathy), the reason for admission, type of admission (emergency versus planned) and postoperative status when applicable.

For data analysis, the reason for admission was grouped into respiratory (bronchiolitis, pneumonia, asthma and other respiratory insufficiencies), neurological (seizures, head trauma, postoperative neurosurgery and other neurological conditions), postoperative of other surgeries (abdominal, orthopedic/traumatological, non-cardiac thoracic, plastic, maxillofacial, otorhinolaryngology), and miscellaneous (non-surgical cardiology, endocrine, sepsis and others). The information was gathered on other factors that increase ADH secretion such as fever, nausea and vomiting, and on factors that alter sodium removal, such as diarrhea and medications (mainly diuretics and corticosteroids). It was also noted whether they had bladder catheterization for the quantification of urine output. Analytical data were also gathered, repeated in successive days, to observe hydro-electrolytic evolution: sodium, potassium, chlorine, bicarbonate, glucose, urea, creatinine, uric acid, pH, hemoglobin, hematocrit and albumin values.

As related data with morbidity, total days of hospital stay and in the PICU, assisted ventilation data, and mortality were recorded. As a severity scale, PRISM III (Probability Risk Infant Score Mortality) was adopted in the first 24 hours of admission[23,24].

As for the initial fluid therapy used, the type of main saline solution (classified as isotonic or hypotonic) and the volume of saline solution administered in the first 72 hours were recorded, as well as the hours of drip and absolute diet. The volume of saline solutions with medication, fluids for volume expansion, and blood products infused during this period were also registered. The isotonic solution contains 0.9% NaCl (sodium 154 mmol/L) with 5% of glucose, with or without ClK (20-40 mmol/L) added; the hypotonic one contains glucosaline solution 1/3 (sodium 51 mmol/L and glucose 3.3%) or glucosaline 1/2 (sodium 77 mmol/L and glucose 5%), with or without ClK (20-40 mmol/L) added. The volume of this main fluid therapy was normalized by the size of the patient and the theoretical calories consumed based on the Holliday formula[8], in addition to the treatment hours. It was finally expressed in ml/100 K calories/h.

Plasma sodium values between 135-145 mEq/L were considered normal. Plasma sodium values between 120 and 135 mEq/L were considered clinically significant hyponatremia, and within these values, the ones less than 130 mEq/L were considered moderate hyponatremia and those less than 120 mEq/L were considered severe[2,6]. According to the plasma sodium evolution, patients were classified into: a) patients with previous sodium (basal Na) ≥ 135 mEq/L, who did not develop hyponatremia during the assessed admission period; b) patients with basal Na < 135 who traced the hyponatremia; c) patients with basal Na ≥ 135 who did develop it; and d) patients with basal Na < 135 who did not correct the hyponatremia in the assessed admission period.

Finally, for the evaluation of the tolerance of peripheral vascular access for isotonic solutions with an osmolarity higher than 550 mOsm/L is concerned, information on other added elements that may increase such osmolarity was collected, such as potassium chloride, calcium gluconate or sodium bicarbonate. Moreover, we collected information about extravasations or changes in the peripheral vascular accesses.

Statistical analysis

Data were processed with SPSS 18.0 software. The normal distribution of quantitative variables was checked with the Kolmogorov-Smirnov test. Variable data without normal distribution are presented as median (P_{25}-P_{75}) and those with a normal distribution as mean ± standard deviation. Qualitative variables are presented as frequency and percentage. Comparisons of qualitative variables were made with Chi-square test and Fisher's exact test if necessary. Comparisons of quantitative variables between groups were made with the Mann-Whitney U test (if they did not have normal distribution) or with Student T-test for independent samples (for those with normal distribution) and intra-group comparisons with the Wilcoxon Test. Values of $p < 0.050$ were considered significant.

Results

During the study period, 396 patients were admitted (213 in the first half of 2010 and 183 in the first semester of 2013), and the following ones were excluded: 177 patients from cardiac surgery and post-renal transplantation; 59 patients due to a lack of sufficient analytical data throughout the study period; 46 patients due to a duration of treatment with exclusive intravenous fluid therapy of less than 8 hours; and 3 patients due to having been administered a volume of fluids for volume expansion higher than 50 ml/kg; remaining 111 patients for the study (62 in the semester of 2010 and 49 in 2013). Out of the 62 children in 2010, 58 of them received hypotonic fluids, compared to 10 in 2013, making a total of 68 patients (61.3%) who were given this type of fluid therapy. Regarding

isotonic fluids, 4 patients received them in 2010 and 39 in 2013, with a total of 43 patients (38.7%) (figure 1). Table 1 shows different demographic and pathology characteristics as well as data related to clinical evolution of patients in the PICU. There were statistically significant differences in age and weight values, both being smaller in the group of patients who received hypotonic solutions, without differences in the rest of variables. There were no significant differences in assisted ventilation or patient severity between groups. In addition, it is possible to observe that the type of saline solution administered did not condition an extension of the average stay in the PICU or hospital admission in its entirety.

The infusion rate of fluid therapy administered was similar in both groups. There were no statistically significant differences in extravasation and changes of peripheral intravenous lines between different types of fluid therapy, although a higher rate of this complication was observed in the hypotonic fluid group (7.4% versus 4.7%). For this assessment, the similar co-administration of potassium chloride, 10% calcium gluconate and sodium bicarbonate in both patient groups was also considered (table 2).

Regarding to sodium values (table 3), there were no differences in pretreatment ones. However, in the first and second days, there were statistically significant differences in the mean sodium values between one group and another ($p = 0.001$ and $p = 0.039$, respectively), being higher in the population that received isotonic fluids. From day three and on, modifications were made in the intake of ions and intravenous fluid therapy (especially because they had initiated oral intake or enteral nutrition) in some patients. In some other patients the fluid therapy was removed. These changes could contribute to the fact that no differences were found in the values of days three and four.

Table 4 shows that among the patients who received fluid therapy based on hypotonic fluids, 28 (41.2%) presented hyponatremia at some point during the study period of admission, with < 130 mEq/L in 11 of them (16.2%). In the contrary, among those who received isotonic fluids, only 8 (18.6%) had sodium values of < 135 mEq/L, and only one of them (2.3%) had < 130, being this difference statistical significant ($p = 0.027$).

Regarding the previous sodium value and the development, persistence or correction of hyponatremia in relation to the type of saline solution received (**table 4**), out of the 40 patients who did not have hyponatremia in the group treated with hypotonic fluids, 32 (47.1%) of them started from a baseline situation of sodium equal to or higher than 135 mEq/L, and the remaining eight (11.8%) had a basal hyponatremia that was corrected 24 hours after; out of the 28 that did present hyponatremia, 14 (20.6%) of them did not have basal hyponatremia and developed it throughout the studied admission period, while another 14 (20.6%) already had it and did not correct it during the assessed period. In the group treated with isotonic fluids, out of the 35 patients that did not develop hyponatremia, 29 (67.4%) of them had basal sodium equal to or higher than 135, and the remaining six (14.0%) had a basal hyponatremia corrected 24 hours after; out of the eight that did present hyponatremia, five (11.6%) of them did not have basal hyponatremia and developed it, while the other three (7.0%) already had it and did not correct it during the assessed time period.

Therefore, it is possible to observe that in the group of patients treated with hypotonic fluids, 14/22 (63.6%) children with basal sodium of < 135 mEq/L continued with the same values the day after, while in the group of those treated with isotonic fluids, only 3/9 (33.3%) had the same sodium values, with statistically significant differences ($p = 0.011$). Only one patient of the group treated with hypotonic fluids developed mild hypernatremia (Na > 145 mEq/L) with a Na value of 146 mEq/L.

There were no significant differences in chlorine (table 3) or urea, creatinine, uric acid or potassium values.

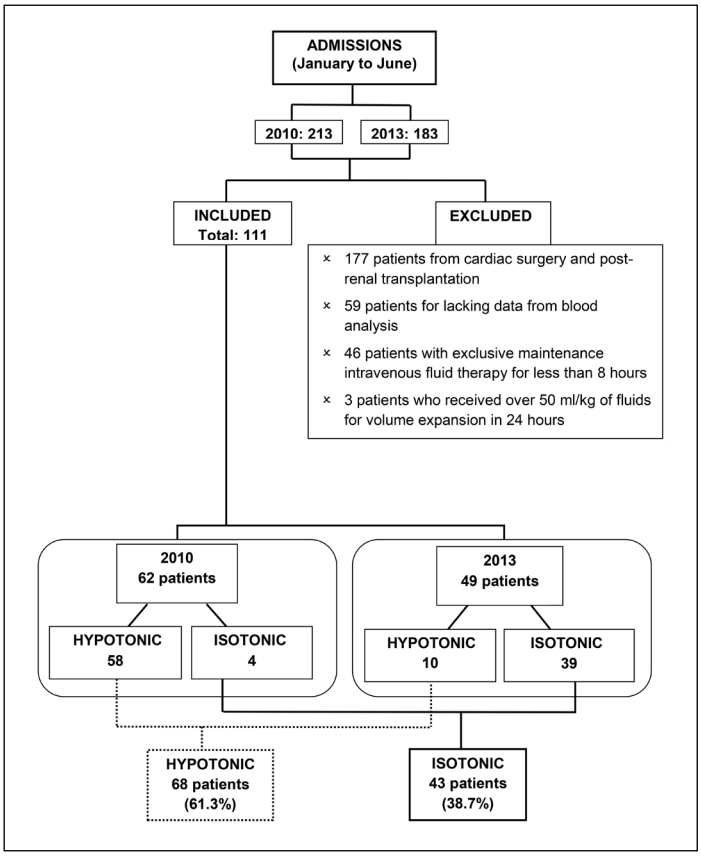

Figure 1. Children admitted to the study.

Table 1. Baseline characteristics and clinical evolutionary data of the children admitted to the PICU in relation to the type of maintenance intravenous fluid therapy

	All	Hypotonic	Isotonic	P value
Number of patients	111 (100.0%)	68 (61.3%)	43 (38.7%)	
Age (months)	33 (11-103)	25 (7-95)	39 (23-108)	0.031
Sex				0.134
- Female	42 (37.8%)	22 (32.4%)	20 (46.5%)	
- Male	69 (62.2%)	46 (67.6%)	23 (53.5%)	
Weight (kg)	12.0 (8.3-28.0)	11.2 (7.0-26.0)	14.0 (9.7-28.0)	0.049
Baseline Sodium (mEq/L)	136 (134-139)	136 (134-138)	137 (135- 139)	0.328
Urgent admission	88 (79.3%)	51 (75.0%)	37 (86.0%)	0.162
Fever	29 (26.1%)	17 (25.0%)	12 (27.9%)	0.734
Diarrhea	3 (2.7%)	2 (2.9%)	1 (2.3%)	1.000
Vomiting	21 (19.0%)	15 (22.1%)	6 (14.0%)	0.288
Postoperative status	33 (29.7%)	24 (35.3%)	9 (20.9%)	0.107
Previous treatment diuretics	12 (10.8%)	9 (13.2%)	3 (7.0%)	0.363
Admission pathology				0.879
- Respiratory	41 (36.9%)	23 (33.8%)	18 (41.9%)	
- Neurological or Neurosurgical	20 (18.0%)	12 (17.6%)	8 (18.6%)	
- Postsurgery*	23 (20.7%)	20 (29.4%)	3 (7.0%)	
- Miscellaneous	27 (24.3%)	13 (19.1%)	14 (32.6%)	
PRISM III	3.0 (1.0-7.0)	3.5 (1.0-7.0)	3.0 (0.0-9.0)	0.744
Assisted ventilation	70 (62.2%)	41 (58.8%)	29 (67.4%)	0.424
- CMV	44 (38.7%)	29 (41.2%)	15 (34.9%)	0.553
- Non-invansive ventilation	26 (23.4%)	12 (17.6%)	14 (32.6%)	0.106
Bladder catheterization	31 (27.9%)	20 (29.4%)	11 (25.6%)	0.661
Lenght of stay at PICU (days)	4 (1-9)	4 (2-9)	3 (1- 9)	0.176
Length of Hospital Admission (days)	16.0 (7.0-30.0)	16.0 (8.0-31.5)	17.0 (7.0-26.0)	0.460
Duration of CMV (hours)	48 (24-192)	72 (27-192)	24 (8-168)	0.091
Death	2 (1.8%)	2 (2.9%)	0 (0.0%)	0.521

Quantitative variables are presented as median and quartiles (P25-P75) and are compared with the Mann-Withney U test; Qualitative variables are presented as frequencies and percentages and compared with the Chi-square test. *Patients in no neurosurgical postsurgery situation. CMV = Conventional Mechanical Ventilation. PICU = Pediatric Intensive Care Unit. PRISM = Probability Risk Infant Score Mortality.

Table 2. Data related to the fluid therapy administered

	All	Hypotonic	Isotonic	P value
Infusion rate day 1	3.5 (2.3-4.1)	3.5 (3.0-4.3)	3.6 (3.0-3.9)	0.712
Potassium chloride 2M	92 (82.9%)	57 (83.8%)	35 (81.4%)	0.741
10% calcium gluconate	80 (72.1%)	52 (76.5%)	28 (65.1%)	0.194
Sodium bicarbonate	10 (9.0%)	5 (7.4%)	5 (11.6%)	0.506
Changes of peripheral vascular access (intravenous line)	7 (6.3%)	5 (7.4%)	2 (4.7%)	0.704

Quantitative variables are presented as median and quartiles (P25-P75) and are compared with the Mann-Withney U test; Qualitative variables are presented as frequencies and percentages and compared with the Chi-square test. Infusion rate day 1: ml/100 Kcalories /h in the first 24 hours.

Table 3. Evolution of the pretreatment values of sodium, chlorine, potassium, creatinine, urea and uric acid during the first days of admission

Values of sodium and chlorine (mEq/l)	Hypotonic	Isotonic	P value
Na pretreatment	136.0 (134.0-138.0)	137.0 (135.0-139.0)	0.328
Na day 1	135.9 ± 4.1	138.9 ± 4.6	0.001
Na day 2	136.2 ± 4.4	138.8 ± 4.0*	0.039
Na day 3	135.7 ± 4.7	137.3 ± 3.2	0.255
Na day 4	135.7 ± 4.7	137.3 ± 4.0	0.307
Cl pretreatment	103.6 ± 6.8	103.9 ± 6.2	0.839
Cl day 1	104.7 ± 6.1	106.7 ± 4.9	0.105
Cl day 2	103.5 ± 5.7	104.4 ± 5.7	0.559
Cl day 3	101.4 ± 5.5	102.5 ± 6.9	0.580
Cl day 4	101.1 ± 4.9	102.7 ± 6.6	0.426
K pretreatment	4.38 ± 0.99	4.12 ± 0.65	0.143
K day 1	4.17 ± 0.87	3.99 ± 0.67	0.245
K day 2	3.94 ± 0.67	3.86 ± 0.44	0.600
Creatinine pretreatment	0.34 (0.25 - 0.45)	0.37 (0.24 - 0.48)	0.628
Creatinine day 1	0.32 (0.20 - 0.42)	0.28 (0.20 - 0.56)	0.818
Creatinine day 2	0.24 (0.20 - 0.41)*	0.29 (0.20 - 0.39)	0.935
Urea pretreatment	27 (17 - 34)	25 (16 - 34)	0.899
Urea day 1	19 (15 - 26)*	17 (12 - 31)*	0.807
Urea day 2	19 (8 - 25)*	22 (11 - 28)	0.284
Uric acid pretreatment	4.7 ± 2.1	4.8 ± 2.9	0.833
Uric acid day 1	3.7 ± 1.9	3.5 ± 2.0	0.793
Uric acid day 2	2.6 ± 1.3*	3.4 ± 1.5	0.106

Valus of pretreatment Na, creatinine and urea are presented as median and quartiles (P25-P75) and are compared with the Mann-Withney U test; the rest of the values are presented as mean + standard deviation and are compared with the Student T-test for independent samples. *P < 0.050 in relation to the pretreatment value (comparisons intragroup with the Wilcoxon test).

Discussion

In the medical literature of the last decade, we found several publications that evaluate the possible increase in the incidence of hospital hyponatremia, as a consequence of the use of hypotonic fluid therapy[1,4,6,7,7,25,26], demonstrated in two recent meta-analyses[15,27]. Already in 2006, a systematic review of six previous studies[4] highlighted the significant increase in the risk of developing hyponatremia, and its impact on patients morbidity, after the administration of maintenance hypotonic fluids; it also pointed out the protective role of isotonic solutions, despite the lack of rigorous clinical trials comparing both regimens, which coincides with the findings of recent randomized studies[10-12].

Table 4. Development or no of hyponatremia during the admission, in relation to the pretreatment values of sodium and the type of maintenance intravenous fluid administered

Hyponatremia	Hypotonic	Isotonic	All
No hyponatremia	40 (58.9%)	35 (81.4%)	75 (67.6%)
- Basal Na ≥ 135	32 (47.1%)	29 (67.4%)	61 (55.0%)
- Basal Na < 135	8 (11.8%)	6 (14.0%)	14 (12.6%)
Yes hyponatremia	28 (41.2%)	8 (18.6%)	36 (32.4%)
- Basal Na ≥ 135	14 (20.6%)	5 (11.6%)	19 (17.1%)
- Basal Na < 135	14 (20.6%)	3 (7.0%)	17 (15.3%)
All patients	68	43	111

The values are expressed in frequencies (%). Na basal is expressed in mEq/L. P = 0.011.

In our Unit, the initial maintenance fluid therapy was changed between the years 2011-2012, thus, we have analyzed a previous period in which hypotonic fluids constituted the initial maintenance fluid therapy of routine (2010), and a subsequent one with isotonic fluids (2013). Treatment groups were similar, except for age and weight. Also, the percentage of postoperative patients was higher in 2010 due to the care of some of these patients in another Unit since 2012. The severity of the studied patients, assessed by the PRISM III Score, was similar between both treatment groups, as well as was the required ventilation support, and length of admission to PICU. It was also found that the amount of fluids administered was not related to the development of hyponatremia, being similar in both groups.

No patient had diabetes insipidus, and the lack of urinary biochemical studies (such as sodium or osmolarity) and the retrospective nature of our study did not allow to discriminate if any of these patients could have inadequate ADH secretion (SIADH). Likewise, the possible difference in edema development could not be evaluated among the groups, given the retrospective nature of our study.

Children who received a high volume of fluids for volume expansion were excluded because these fluids use to be isotonic and may constitute a bias for our assessment. In addition, we exclude patients with a period of admission of less than 24 hours in the PICU because the fluid therapy policy in the different Services changes.

Children treated with hypotonic fluids at admission had a more severe hyponatremia, although no clinical impact was observed associated with it. We can highlight with our results that no cases of hypernatremia were found in children who were treated at admission with isotonic fluids, a potential complication argued by some authors[13,14]. Likewise, no differences in chlorine values were found among children treated with hypo or isotonic solutions, another potential complication[21,22]. In addition, an increased frequency of extravasation and peripheral intravenous line changes was not observed with the use of isotonic fluid therapy, despite of their higher osmolarity that could condition potential phlebitis[16-20].

One of the limitations of this study is its retrospective nature, which conditioned the lack of quantification of fluid losses in a large number of patients by urinary or digestive route, as well as all useful clinical data related to the development of hyponatremia. Also, an identical sequential collection could not be made for all patients at the time of the information. Another limitation was the fact that the study was carried out in only one center, which implies a possible bias due to the variability of clinical practice among the different centers and the pathology treated according to the characteristics of the population.

Therefore, it is possible to say that the incidence of hyponatremia has been significantly reduced with the use of isotonic fluids as initial maintenance fluid therapy. Moreover, a higher percentage of patients corrected their basal hyponatremia using isotonic fluids. Furthermore, there has been no significant increase in blood chlorine values with the use of isotonic fluids and these have been well tolerated by peripheral intravenous lines of children.

In conclusion, this study has shown a reduction in the incidence of hyponatremia with the initial use of isotonic fluids as maintenance fluid therapy in patients admitted to the PICU, as well as a lower condition severity in those cases that did present it. In addition, a larger number of patients in this treatment group corrected their basal hyponatremia, and a smaller percentage of children also developed it or did not correct it, compared to those who received hypotonic fluids at admission. On the other hand, no differences in chlorine blood values were found after the administration of isotonic fluids. An adequate tolerance of peripheral veins in infants and children to intravenous administration of this fluid therapy has also been confirmed. Therefore, we can conclude that the use of isotonic fluids as maintenance fluid therapy at admission in critical patients reduced the incidence of early hyponatremia and was well tolerated.

Ethical responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Acknowledment

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