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Fluid therapy in surgical patients: composition and influences on the internal milieu

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Nefrología 2008; 28 **(1)** 37-42

SUMMARY

Intravenous fluids administration is the usual practice in the postoperative period. Nonetheless, consensus about the more appropriate fluid reposition recipe is still insufficient. Objective: *To study the type of intravenous reposition used in Surgical Units and its impact on the internal milieu.* Patients and methods: Design: *prospective study of 112 patients with scheduled surgery, receiving only intravenous fluids.* Methods: *biochemical study on postoperative fluids management in uncomplicated surgery. Principal variables: 1. Water and electrolytes administrated. 2. Differences in sodium/water balances before surgery* vs *first day after surgery. 3. Symptoms related to hyponatremia.* Results: *Median P[Na] before and after surgery was 139.9 ± 2.9 and 137.7 ± 3.7, respectively (p < 0.01). Fourteen patients (12.5%) had P[Na] < 135, and 12 of them had a reduction of more than 6 mmol/L; accordingly, twenty-six patients (23.2%) had an increased free-water retention (p < 0.05). Relevantly, they did not receive a higher amount of free-water and the proportion of isotonic saline/free water varied from < 1 to > 3. As possible mechanism of free-water accumulation: the postoperative P[Na] was lower in the patients who had a negative free-water clearance ≥ -1 L (136,7 ± 4,1* vs *138,5 ± 3,2 mmol/L, p 0,015).* Conclusion: *The present study provides new information about the intravenous fluids prescribed in postoperative patients, ie, different proportions saline/water are basically equivalent with respect to inducing symptomatic hyponatremia. The mean value of the relation saline/water is 2:1. Hypotonic fluids input is not clearly related to more intense hyponatremia; the latter appears to depend more on a reduced capacity of the kidney to generate sufficient free water output.*

Key words: *Postoperative. Fluids. Hyponatremia. Free water.*

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RESUMEN

La prescripción de sueros en el postoperatorio es una práctica rutinaria, pero sobre la que no existe un consenso basado en la evidencia. *Objetivo:* Examinar sistemáticamente el tipo de reposición hidroelectrolítica empleado por los Servicios Quirúrgicos y sus consecuencias sobre el medio interno. *Pacientes y métodos: Diseño:* estudio prospectivo en 112 pacientes con cirugías programadas. *Método:* estudio bioquímico del manejo hidroelectrolítico en postoperatorios no complicados tratados solo con sueros intravenosos. Variables principales: 1. agua y electrolitos administrados; 2. diferencias de equilibrio hidrosalino entre pre- y post-operatorio; 3. alteraciones clínicas atribuíbles a hiponatremia. *Resultados:* La [Na]P media pre y postoperatoria fue 139,9 ± 2,9 y 137,7 ± 3,7, respectivamente (p < 0,01) Catorce pacientes (12,5%) alcanzaron [Na]P < 135 mmol/L, y 12 presentaron un descenso de [Na]P ≥ 6 mmol/L, vg, 26 sujetos (23,2%) tuvieron un incremento significativo de agua libre (p < 0,05) Estos pacientes no habían recibido mayor cantidad de agua libre que el resto, siendo la proporción sueros isotónicos/agua libre desde < 1 a > 3. Como posible mecanismo de la retención hídrica, la [Na]P postoperatoria en los pacientes con aclaramiento de agua libre negativo ≥ -1 litro/24 h fue más baja (136,7 ± 4,1 *vs* 138,5 ± 3,2 mmol/L, p 0,015). *Conclusiones:* Se aporta información previamente no disponible: a) diversas proporciones de suero isotónico: agua libre resultaron equivalentes frente al desarrollo de hiponatremia sintomática; b) la relación media suero isotónico: agua libre es 2:1, y c) las soluciones de reposición más hipotónicas no aparecen relacionadas con más hiponatremias. Éstas en cambio dependen de la respuesta renal de retención de agua.

Palabras clave: Postoperatorio. Sueros. Hiponatremia. Agua libre.

INTRODUCTION

Prescription of fluids administered after surgery is a routine practice in the Departments of Surgery and Anesthesia, and usually does not generate research issues. In this same context, studies on possible alternatives to fluid therapy are not conducted either. For this reason, a paramount conceptual issue is that ideas and current practices on post-surgery fluid therapy are usually based on non-systematic clinical experience and individual casuistic, with no available large comparison studies.

In this framework, in recent years, and with higher emphasis in recent review articles,[1] some authors insist in the relevance of the composition of electrolyte-containing fluids during surgery and the first days after it. In this setting, complete substitution of isotonic solutions has been proposed in all surgeries in which an unusually high loss of free water is not foreseen.[1] The rationale for this proposal is the prevention of cases with severe hyponatremia, which have important and even lethal consequences widely documented, especially among the pediatric population and menstruating women. However, other authors argue that the type of fluids most frequently used, which traditionally include 50% isotonic saline and (0.9 %, [Na^+] 155 mmol/L) free water as 5% dextrose, do not represent a risk factor themselves.[2] This statement should consider the exception of selected patients suffering from other comorbid conditions and that may need a specific fluid composition.

It is important to note that there is no evidence available, since there are no published works on this issue, allowing to know the possible implications of a generalized use of isotonic saline in all the post-surgical population, although some authors have underlined the possible risks of administering excessive fluids and salt during the post-surgical phase.[3,4]

Searching Medline, we have not found, either in Spain or abroad, a single study largely enough and systematically recording the type of water and electrolyte replacement used at Surgery Departments during the immediate post-surgical period and its consequences on the internal milieu. Even more, we have not detected any evidence-based recommendation supported by comparison data with different fluid therapies. In case reports from the United Kingdom, a combination commonly used for parenteral fluid replacement is 0.18% NaCl in 4% dextrose.[5,6] In another study, almost 50% of the patients received 5% dextrose solutions in water during post-surgery.[7]

Based on these premises, we considered necessary and of practical utility to assess this issue in a prospective way among a normal post-surgical population. With this aim, we used a database generated by our group in order to analyze water and electrolytes management in non-complicated post-surgical patients, considering three specific issues: 1) the volume and composition of administered fluids; 2) the possible deficits in hydro-saline between baseline and the first 24 hours post-surgery; and 3) the existence or not of clinical changes potentially attributable to serum sodium variations.

PATIENTS AND METHODS

We prospectively studied 120 patients from elective surgery under general anesthesia and done at a university hospital.

We applied the following exclusion criteria: 1. *pre-surgery:* extremely complicated surgeries, including cardiac surgery with extracorporeal circulation, radical oncologic surgery, extensive bowel surgery, high comorbidity, especially cardiac, respiratory, or renal failure (sCr > 1.3 mg/dL), and insulin-dependent diabetes mellitus; medication with cardiovascular and renal effects with a possible influence on hyponatremia, essentially diuretics. 2. *Intra- and post-surgery:* fever, bleeding, myocardial ischemia, painful conditions, severe vomiting, and need for re-surgery.

In order to obtain descriptive data really reflecting the daily practice we did not introduce any modification in routine practices of surgeons and anesthesiologists. Data collection was performed by clinical researchers not belonging to the surgical departments. The study was approved by the Institution Ethical Committee and in all cases and according to international and internal regulations, we obtained written informed consent from the patients for data collection and blood analysis for water and electrolyte balance.

The patients were fasting, including beverages, from at least 12 hours before the surgery and until the next morning. All the surgeries were carried out in the morning so that we assured that collection of the second blood sample was done with at least 18 hours of exclusively intravenous fluid reposition.

Urine was collected during 12-24 hours of the preoperative day and for 24 hours of the postoperative day. Blood was drawn at 8:00 a.m. of the surgery day (day 0) and at 8:00 a.m. the next morning.

The following data were recorded: particulars, comorbidity, type of surgery, creatinine, plasma and urine BUN, and plasma and urine osmolality and electrolyte composition. This design implies some differences when comparing the data from pre- and post-surgical days. The schedule used was based on the reality of elective surgery at a tertiary hospital and on ethical issues. All this makes difficult to keep the patient fasting for 24 hours before surgery, which would allow for a better comparison. Data on fluids infused during the operative day were collected, including those administered during and after the surgery [Fluids, free H_2O (dextrose 5%), Na (NS 154 mEq, Ringer-Lactate 132 mEq, colloids 155 mEq)]. Free water clearance was calculated according to the conventional formula. Besides, we collected clinical history data of usual control measurements (BP, pulse, temperature) compatible with more or less severe hyponatremia symptoms, including headache, nausea, vomiting, lethargy, seizures, and difficulty breathing. Hyponatremia was considered when plasma Na levels ([pNa]) were ≤ 135 mmol/L. We considered significant water retention all [pNa] decreases ≥ 6 mmol/L or increased from baseline at 24 hours, whether or not hyponatremia figures were present. This concentration was chosen since it closely represents retention of 1 liter of water in an individual of 70 kg.

Statistical analysis: the results are expressed as mean ± SD. The statistical analysis was done, as needed, by using 2 x 2 contingency tables and Chi-square and Student t test. A p value < 0.05 was considered to be statistically significant. The SPSS software for Windows, version 13.0 was used.

RESULTS

Eight patients, out of the total mentioned under «Patients and Methods», were excluded, 5 because of deficient data collection and 3 due to intra- or postsurgical complications. Thus, the final analysis included data from 112 patients (64 women), with ages 59.0 ± 20.4 and 59.5 ± 21.5 years (for men and women, respectively, p = NS) and 69.9 ± 8.7 and 61.3 ± 9.6 kg (for men and women, respectively, $p < 0.01$).

The distribution of surgeries was as follows: digestive -biliary (26.2%), gastric (5.3%), intermediate abdominal (hernias and wall repairs, 22.1%), colon (15.8%), gynecological (17.8%), neck (thyroid gland), breast (10.5%), other (2.3%).

Table I shows the relevant analytical data of the day before surgery and of the first post-surgical day. The composition of fluids administered was categorized as isotonic solutions (normal saline: [Na] = 155 mmol/L) or minimally hypotonic (Ringer solution: [Na] = 130 mmol/L) and free water solutions. Average amounts administered for each solution type are shown in Table 2. In no case 0.45% hypo-saline solution was used. As it may be seen, the average amount of i.v. fluids was slightly over 4.5 liters, with a mean relationship isotonic fluids/free water of 2:1. The quantitative distribution of this ratio and the number of cases of water retention per group of fluid type are shown in Table 3.

The proportion of fluids used determined that mean [Na^+] administered was 92.6 ± 24.6 mmol/L. We did not detect differences between the different surgical teams with regards to this scheme of type of fluid distribution (data not shown).

Mean values of pre-surgical [pNa] and that of the post-surgical day were 139.6 ± 2.8 and 137.8 ± 3.2, respectively ($p < 0.01$). Fourteen patients (12.5%, 10 women) had values of [pNa] < 135 mmol/L (minimum 127 mmol/L). Twelve (8 women) had a decrease in [pNa] > 6 mmol/L, so that, as a whole, it may be considered that 26 study subjects (23.2%) had a significant increase in body free water content ($p < 0.05$). Of interest, 18 of them were women, as compared to only 8 men ($p < 0.01$). When analyzing their individual data, we verified that these patients had not received a higher amount of free water than the whole group, having an average proportion of isotonic fluids to free water of 2.1 ± 1.1 (p = NS as compared to patients without [pNa] decrease). We did not recorded any complication related with water and electrolyte changes. Moreover, we did no detect changes attributable to hyponatremia or [pNa] decrease.

There is also a different distribution in Na and OsmP change, conjugating sex and gender. As shown in Figures 1a and 1b, and according to the results of the bi-variable analysis, [pNa] decrease was significantly higher in those individuals younger than 50 years, and among them, in women.

In view of the mentioned findings, further analyses were carried out in order to identify the conditions under which [pNa] decrease occurs. In the first place, we found that two out of the three cases not reaching a [pNa] < 130 mmol/L the proportion of isotonic fluid:free water was lower than 1:1 (in liters, 2:3.5 and 1.2:2.5, respectively), although it was not so for the third one (2.5:1.4). Following the hypothesis that the administration of a isotonic fluid:free water ratio lower than 2:1 may condition a decrease in [pNa], we pooled the patients considering this proportion as a criterion and using a 1:1 ratio as the cut-off point. On this basis, we found that 17 individuals received solutions with a ratio 1:1 or lower —i.e., with more free water. Moreover, this group included 10 patients in whom the volumen:volumen ratio between saline fluid:free water was lower than 0.75 —i.e., they received more free water than isotonic saline. Surprisingly, only two patients within this group (previously mentioned) developed hyponatremia or [pNa] decrease ≥ 6 mmol/L, which was nor relevant (p = NS). Patient distribution by quintiles according to saline fluid:free water ratio is shown in Table 3. An important data shown in this table is that the highest percentage of free water retention occurred in those individuals with isotonic fluid:free water ratio > 2. Even more, 3 out of 8 patients receiving only normal saline had water retention.

Given the lack of a significant relationship between the free water volume administered and the occurrence of hyponatremia, we examined the potential relationship of the latter with water renal retention. Figure 2 shows how the group of women younger than 50 years had CH2O2 significantly more negative than male patients of the same age. With older ages, the values did not show statistical significance although a similar trend was observed.

This analysis was completed with the comparison of all individuals presenting negative free water clearance respectively higher or equal to (n = 67) or lower than (n = 45) -1

Table I. Mean pre-surgical (day 0) and post-surgical (day 1) values

	Day 0	Day 1
pNa (mEq/L)	139.6 ± 2.8	137.8 ± 3.2**
PK (mEq/L)	4.0 ± 0.4	3.8 ± 0.4
Chloride (mEq/L)	106.4 ± 3.8	107.2 ± 4.5
Creatinine (mg/dL)	0.9 ± 0.2	0.86 ± 0.2
BUN (mg/dL)	16.5 ± 8.7	11.2 ± 5.2
pOsm (mOsm/L)	296.6 ± 6.8	292.8 ± 6.6*
uOsm (mOsm/L)	467.1 ± 250.6	404.7 ± 167.8

*p < 0.05 **p < 0.01

Table II. Mean amounts of fluids (liters) and electrolytes (total mmol) administered during the first pre-surgical day

Isotonic fluids (L)	3.1 ± 1.3
Free water (L)	1.6 ± 0.56
Isotonic fluid/water ratio	2.0 ± 1.4
Total Na^+ administered (mmol)	457.6 ± 200
Mean [Na^+] administered (mmol/L)	96.1 ± 20.3
Total K^+ administered (mmol)	37.4 ± 33.9

Table III. Relationship isotonic fluid/free water, calculated from the ratio of the volumes administered. All groups but the first one received more saline than free water. The cases only receiving saline are presented without a ratio (divided by zero)

Ratio Isotonic fluid/water free	Num. patients (%)	Num. of cases with water retention > 1 liter or hyponatremia
0.5-1	17	2
1-2	38	3
2-3	36	14
3-4	13	4
Solo salino	8	3

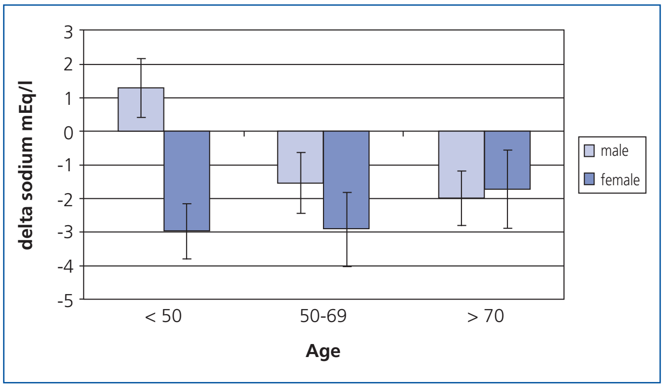

Figure 1a. Variation in plasma Na (mEq/L) in the first post-surgical day. Comparison by genders. *p < 0.01 between genders.

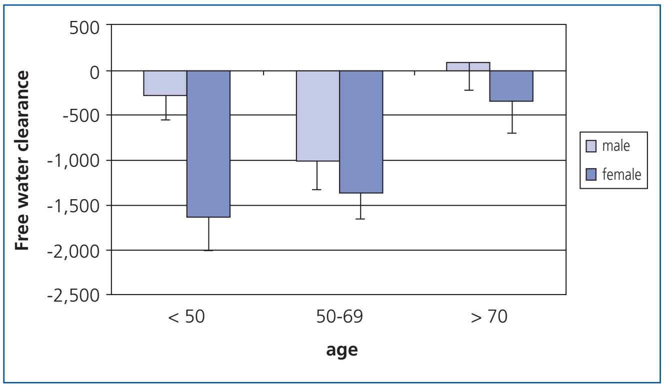

Figure 2. Free water clearance in the first post-surgical day. Comparison by genders. *p < 0.01 between genders.

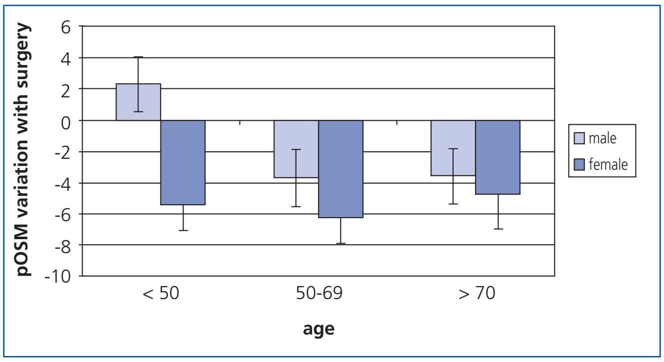

Figure 1b. Variation in plasma Osm (mOsm/L) in the first post-surgical day. Comparison by genders. *p < 0.01 between genders.

liter/24 hours. The [pNa] value for the post-surgical measurement in patients with free water clearance < -1 liter/24 hours was significantly lower (136.7 ± 4.1 *vs* 138.5 ± 3.2 mmol/L, p = 0.015). By using the chi-square test, we verified that the frequency of [pNa] values falling within the hyponatremic range was also higher in this group (p < 0.01).

DISCUSSION

The results from the present study provide information not previously available, describing the amount and type of solutions used in intra- and post-surgical management of patients submitted to different surgeries, and particularly it brings systematic and prospective evidence regarding the effects of these fluids on the internal milieu. As it has been mentioned at the introduction, this is a relevant topic with a certain degree of controversy. [1]

A methodological procedure is important when assessing the results. Thus, our focus of observation was not exclusively limited to the cases developing hyponatremia, but we included those having water retention in general, even if they had not reached hyponatremic values. This approach allows us examining and quantifying the true physiologic fact, which is water retention, and constitutes an original proposal to broaden the analysis tools applied to this topic to date. Limiting the analysis only to hyponatremia episodes gives an insufficient view of water management. In this sense, had this way of data distribution introduced a bias (by increasing the N towards hyponatremia episodes) it would have been in favor of the fact that reposition schedules containing hypotonic fluids would be more inducers of sodium decrease. However, this has not been the case. So, from the data obtained it follows that the incidence of moderate water retention, represented by hyponatremia plus marked decrease in [pNa], affects almost one fourth of operated patients. In this setting, the most relevant finding is that using a fluid regimen with varied isotónic:free water ratio with an average ratio of approximately 2:1, the incidence of hyponatremia is only 12.5%, all cases being asymptomatic. This percentage of hyponatremia episodes is coherent with the observations made by Coulthard et al.[8], who found that post-surgical administration of saline 1:3, i.e., a very hypotonic regimen and with clearly more free water than those used in our study, induced hyponatremia in 37% of the patients. The hyponatremia incidence in the present series is higher than that reported by others,[9] although we may consider that a relatively high cut-off point has been used (135 mmol/L) and since we do not have data on the type of fluids used in other series we cannot analyze the causes with sufficient certainty.

Of critical importance as well is the fact that hyponatremia and water retention episodes found were quantitatively mild, which adds to their asymptomatic nature. In the same line of thought, the average data for the whole population indicate a significant biochemical serum sodium decrease, although clinically irrelevant —lower than 2 mmol/L. These data are in agreement with the findings by Wijdicks and Larson[2] on more than 200,000 patients from the Mayo Clinic. These authors defend that severe post-surgical hyponatremia syndrome, as it has been described in other works, may have considerable consequences, although it is extremely infrequent quantitatively speaking. This feature renders difficult the extrapolation of big solutions to the whole surgical population, which is enormous.

The hydro-electrolytic behavior found suggests that the schedule of fluids used (with different combinations of isotonic saline and free water, with an average ratio of 2/3 isotonic

+ 1/3 of free water, does not affect [pNa] in most of the surgical patients, considering elective and non-complicated surgery without significant associated comorbidity. Even more, this low incidence of [pNa] impairments comprises a wide range of isotonic saline:free water ratios, including values under the one unit value, i.e., a definitely hypotonic solution. In this sense, we must insist on the fact that the use of hypotonic fluids may induce hyponatremia as well, as has been reported by Steele et al.[11] and Guy et al.[12] These authors found hyponatremia during the first 24 hours after surgery in 135 patients only receiving isotonic fluids. The explanation for this apparently paradoxical finding is based on the already mentioned desalinating phenomenon, which allows for free water retention from a fluid by eliminating the salt. This explanation is compatible with the findings of the present work regarding free water clearance (table III).

We may generally state, but with the following exceptions, that our results indicate that the regimens used were sufficiently safe. These are consistent data based on more than one hundred subjects. Indeed, a similar viewpoint was already defended by Talbot et al.[3] who concluded that the range of compositions for safe fluid therapy is wide; besides, these authors did not favor the use of 0.9% NaCl, based on the impression that it would not provide enough free water, with resulting potential fluid overloads.[3]

Considering the mechanisms, the results obtained point, once again, the importance of renal water retention, although the identification of the causes for [pNa] decrease was not the main focus of this paper. This finding, already made by others[11,12] lessen the importance of the role of fluid composition, underscoring however that of intrinsic mechanisms of water retention. It is so that in the present series we observe how at least three out of eight patients only receiving isotonic saline (see table III) had water retention. This supports what has been described by Guy et al.[12] and by Steele et al.[11], who detected the occurrence of post-surgical hyponatremia in women exclusively treated with isotonic or minimally hypotonic fluids, such as the Ringer solution. This hyponatremia was due to free water and electrolytes renal reabsorption. In the presence of enough levels of vasopressin, the free water generated will be retained, inducing [pNa] decrease, a result that is in agreement with the findings of the present work (see table I). Of interest, Aronson et al. have described a similar behavior in patients with [pNa] decrease after cardiac catheterization; in these patients, they also observed that [pNa] decrease is asymptomatic in all of them.[13] Our recent data from a series of patients managed with fluid therapy for prevention of radio-contrast media toxicity indicate that in those individuals with normal or slightly decreased renal function, the administration of 0.45% saline did not produce differences in [pNa] as compared with 0.9% saline, which may be expected due to the compensating capability of the kidney.[14]

These findings underscore the critical role of the kidney in producing hyponatremia by generating water free from electrolytes. In the presence of enough levels of vasopressin, this free water is retained inducing [pNa] decrease. This phenomenon lessens the role of the type of fluid. It is interesting that not out work, nor those by Steele et al.[11] and Guy et al.[12], and certainly no other study with an exclusively observational design, allow elucidating whether free water amount would have been greater provided that higher amounts of isotonic fluids had been administered to patients predisposed to hyponatremia. The performance of prospective interventional studies on this obviously interesting topic would require a multicenter study with a large number of patients, likely more than one hundred per study arm. Practically speaking, our work emphasizes the importance of considering fluid composition adjustment by urinary sodium and water clearances; we are convinced that with this minimal control most of the potential changes in the composition of the internal milieu caused by fluid therapy might be prevented. The introduction of urine ions measurements in the management of post-surgical patients, and of other patients with potential impairments of the internal milieu, is simple innovation with huge potential practical implications.

As a complementary finding, the observation of the preponderance of water retention in women is highly interesting. Our data indicate that the frequency of hyponatremia is higher in women younger than 50 years, as compared to male patients. These data differ from those reported by Ayús et al., who did not find significant differences between male and female patients in the incidence of post-surgical hyponatremia; however, when reanalyzing their data by adding up all patients with hyponatremia, both symptomatic and asymptomatic, higher incidence occurs among women.[9]

The specific issue of the relationship between water retention and the secretory profile of arginine-vasopressin, partly supported by the present database, will be sent for another publication. A summary of these outcomes may be looked up as a free communication to the SEN meeting.[15] Basically, this work points out the absence of linear relationship between the level of arginine-vasopressin increase and water retention. Stimulation of vasopressin secretion during the post-surgical period is a classical finding, although with individual variations.[15-17]

As we already stated, there is not sufficient consensus on this topic; reviews focusing on what type of fluid is more convenient, and why, are even scant (see the example from reference 18).

Up to here, it is necessary to consider the limitations of the present study. We will point out those that we have considered more important. In the first place, carrying out the study at a single center interferes with the possibility of generalizing the type of fluid regimens really administered to surgical patients. However, this limitation does not affect the findings on the change of the internal milieu due to the use of these fluids. A second limitation is that the study is limited to the use of fluids during the first 24 hours after surgery, so that we could not analyze the occurrence of late hyponatremia episodes.[1] Thirdly, the comparison between days 0 and 1 has the limitations already mentioned in Patients and Methods. In the last place, we underline that the findings cannot be extrapolated to pediatric patients, in whom the risks and conditions for hyponatremia occurrence might be different, since we have only studied an adult population.[19]

Acknowledgments: The authors thank the Jiménez Díaz-Capio Foundation and the Alvarez de Toledo Renal Foundation for their help supporting this study.

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