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Hyponatremia management among patients admitted to tertiary hospital: A retrospective evaluation

Sultan Zurnuq[1], Mahmoud Aljurfi[1], Mohamed Albekery[2], Mohammad S Shawaqfeh[1], Ahmed Elmubark[1], Senthilvel Vasudevan[1], Shmeylan Alharbi[1], Mohammed Alkatheri[3], Abdulkareem M Albekairy[1] and Abdulmalik A Al Katheri[1]

Abstract

Objective: The aim of this study is to compare the adherence to the guidelines in patients presenting with hyponatremia defined as a sodium (Na) level ⩽120 mEq/L, treated with 3% hypertonic saline or normal saline. The comparison included 3% hypertonic saline use, safe serum sodium increases within 24 and 48 h, frequency of hyponatremia-related complications, and length of stay.

Methods: This retrospective observational study enrolled 122 patients with serum sodium ⩽120 mEq/L admitted to the Internal Medicine Department, King Abdulaziz Medical City, National Guard-Health Affairs (NGHA), Riyadh, Saudi Arabia, from January 2016 to December 2017. The patients were treated with either 3% hypertonic saline or normal saline.

Results: Of the 122 patients, 105 (83.3%) received normal saline, and 17 (13.5%) received hypertonic saline. In the normal saline group, the mean serum sodium increase at 24 h was lower (6.60 ± 4.75) compared to the hypertonic saline group (9.24 ± 5.04). The length of stay was longer in the normal saline group (10.35 ± 13.90) compared to the hypertonic saline group (4.35 ± 3.39). A small proportion (8.7%) of the normal saline group had a serum sodium increase >12 mg/dL at 24 h compared to 29.4% for the hypertonic saline group, and the difference was statistically significant (p value = 0.013). Almost one-third of the sample (36%) presented with complications, the majority (77.3%, n = 34) had a serum sodium of ⩽115 mg/dL, and 22.7% (n = 10) with a serum sodium of 116–120 mg/dL (p value = 0.041).

Conclusion: Despite the strong recommendation for 3% hypertonic saline use in severe hyponatremia, many practitioners still use normal saline, even in patients with serum sodium ⩽120 mEq/L. Normal saline showed some efficacy in managing hyponatremia in asymptomatic cases; however, severe cases may have a delayed correction, hyponatremia-related complications, and an extended length of stay.

Keywords

Hyponatremia, hypertonic saline, normal saline, overcorrection, complications

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[1]College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[2]King Fahd Military Medical Complex, Dhahran, Saudi Arabia
[3]King Abdulaziz Medical City, Riyadh, Saudi Arabia

*Mohammad S Shawaqfeh, Ahmed Elmubark and Senthilvel Vasudevan is also affiliated to King Abdullah International Medical and Research Center, Riyadh, Saudi Arabia; Shmeylan Alharbi, Abdulkareem M Albekairy and Abdulmalik A Al Katheri is also affiliated to King Abdullah International Medical and Research Center, Riyadh, Saudi Arabia and King Abdulaziz Medical City, Riyadh, Saudi Arabia

Corresponding author:
Mohammad S Shawaqfeh, College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, Riyadh 11481, Saudi Arabia.
Email: shawaqfehms@gmail.com

Introduction

Hyponatremia is an abnormal decrease of the sodium (Na) level in the blood (<135 mEq/L). Hyponatremia is considered a complication that is associated with other diseases such as heart failure, liver failure, renal failure, or pneumonia. Symptoms of hyponatremia0 vary, with mild symptoms such as nausea and malaise, and more severe symptoms like seizures and coma.[1–3] The classification of hyponatremia is based on the volume status and plasma osmolality. These include (1) hypovolemic hyponatremia which is characterized by deficit in the fluid volume. (2) euvolemic hyponatremia, where the fluid volume is normal. (3) Hypervolemic hypernatremia, where the fluid volume is in excess.[1,3] The European Renal Best Practice Guideline recommends that hypovolemic hyponatremia patient with severe symptoms should receive 3% hypertonic saline (HS) intravenously (IV), 150 mL infusion over 20 min. Multiple repeated doses should be infused over 20 min until achieving a 5 mmol/L increase. Should the symptoms persist, it is recommended that 3% HS IV infusion be continued until achieving a 1 mmol/L increase in the sodium concentration.[4] If the symptoms improved, the guideline recommends that the sodium level should not be increased more than 10 mmol/L during the 24 h, and no more than 8 mmol/L increase in any subsequent day until a serum sodium concentration of 130 mmol/L is achieved.[5] If there is an acute decrease in the sodium level (more than 10 mmol/L) without severe symptoms, the guideline suggests treating the cause and infusing a single IV infusion of 150 mL 3% HS over 20 min. In the case of moderate or profound chronic hyponatremia without severe symptoms, treating the cause is recommended and avoiding an increase above 10 mmol/L in the first 24 h and no more than 8 mmol/L in the second 24 h.[4,5] In patients diagnosed with the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) or expanded extracellular fluid, the guideline recommends fluid restriction as the first line of therapy.[4,5]

Hyponatremia is a common laboratory issue that can occur in many clinical situations. These include heart failure, liver cirrhosis, and nephrotic syndrome in addition to diuretic use.

Limited literature is available related to a comparison of the different treatment modalities, especially HS and normal saline. An observational study of 58 patients receiving 3% HS infusion at a rate of 100 mL/4 h, reported a 9 mEq/L increase in the sodium level in the first 24 h of treatment.[6] Sood et al. conducted a study in which desmopressin was combined with 3% HS in patients with a sodium concentration of <120 mEq/L to prevent overcorrection. The authors reported an increase in the sodium level after the first 24 h of 5.8 ± 2.3 without any overcorrection (defined as a serum sodium increase >12 mEq/L in 24 h).[7] A prospective observational study comparing the use of 3% HS and tolvaptan, indicated that the 3% HS was more efficient in increasing the sodium concentration (8.03 ± 0.65 after 24 h) compared to the tolvaptan (5.11 ± 0.66 after 24 h).[8] Another study investigated the use of desmopressin acetate if the rate of sodium correction is excessive and indicated that desmopressin acetate decreased the sodium at a rate of 0.81 mmol/L per hour.[9] Although there are studies comparing 3% HS with various medications, there are many aspects in the management of hyponatremia that requires additional research, such as comparing HS with normal saline. A second question is the decision to initiate HS when the serum sodium is below 120 mEq/L compared to the current practice of delaying the HS until the sodium concentration is less than 115 or 110 mEq/L. In addition, comparing the complications between initiating correction at ⩽120 mmol/L and delayed correction at ⩽115 mmol/L.[1]

Hyponatremia is both common and important clinical feature that may be encountered in about 15%–20% of emergency admissions. The management is usually complicated and managed differently by different clinicians. The guidelines are not so agreed upon and lack the evidence-based approach. Clinicians using previous guidance may have noted several problems.[10]

This study aimed to compare the adherence to the hyponatremia guidelines in patients presenting with hypovolemic hyponatremia (a sodium level ⩽ 120 mEq/L) and treated with 3% HS or normal saline. The comparison included the 3% HS use, safe serum sodium increases in 24 and 48 h, the frequency of hyponatremia complications and length of stay (LOS). Hyponatremia complications are diverse and can range from neurologic symptoms due to cerebral edema to impaired mental status or coma and even death.[11]

Materials and methods

This was a retrospective observational study at the Internal Medicine Department, King Abdulaziz Medical City, National Guard-Health Affairs (NGHA), Riyadh, Saudi Arabia, from January 2016 to December 2017. Ethical approval for this study was obtained from King Abdullah International Medical Research Center (KAIMRC) (SP17/159/R). As the study is a retrospective chart review to evaluate practice, institutional review board (IRB) waived the requirement for written informed consent.

Selection of the patients

The sample size in this study was conveniently selected from all patients who met the inclusion criteria. In total, 322 patients were evaluated. The inclusion criteria were adults aged ⩾18 years who had hypovolemic hyponatremia with serum sodium ⩽120 mEq/L, confirmed by a laboratory test at the Emergency Department. Patients were excluded if they had edema or any edematous disorder such as heart failure or chronic kidney disease on dialysis, the SIADH, a history of neurological disease, neurological symptoms not caused by hyponatremia, or cancer patients (Figure 1). Finally, 122 patients were included according to the inclusion and exclusion criteria.

Other types of hyponatremia regardless of the etiology were excluded as we included only the hypovolemic

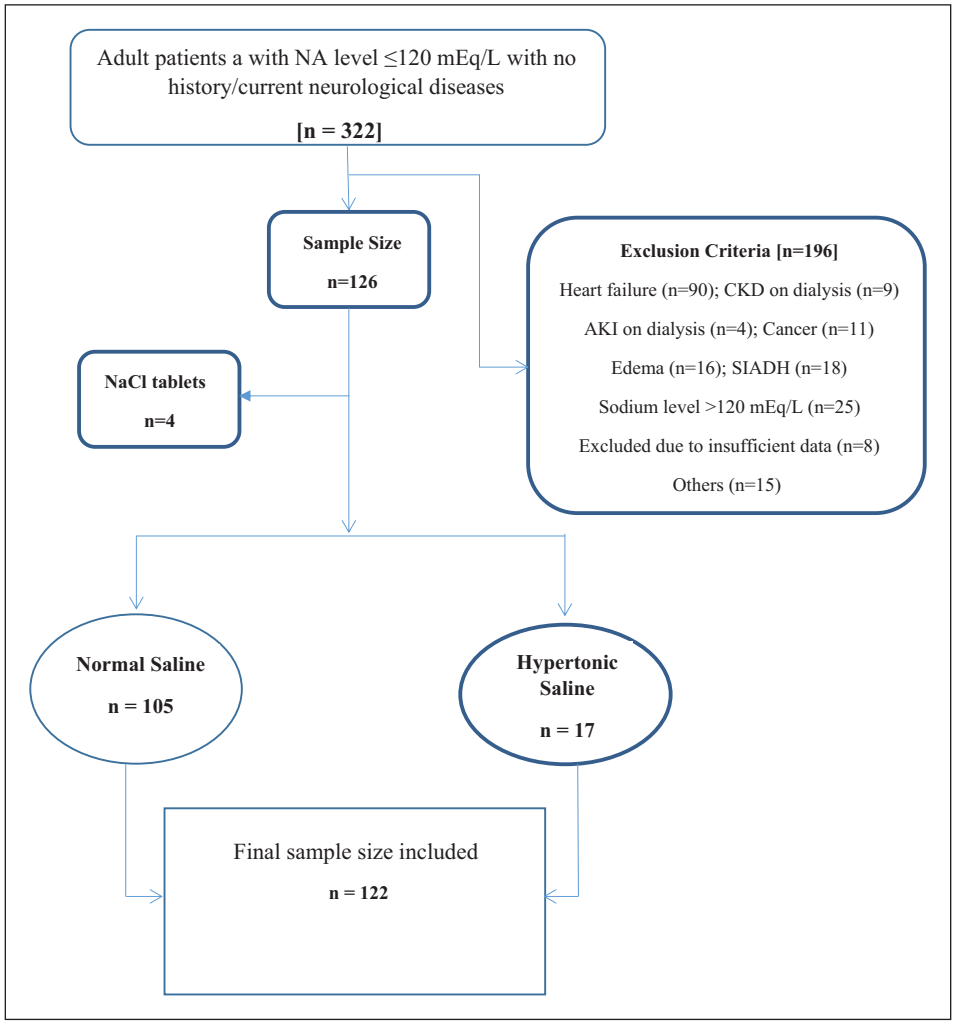

Figure 1. Sample size.

hyponatremia where the HS is indicated as the treatment of choice. The other hyponatremia not associated with hypovolemia are managed differently with fluid restrictions, diuretics, and vaptans. These were excluded from this study as HS is not indicated.[12]

Method of intervention

The sample was divided into two groups. The normal saline group who received normal saline (0.9%) and the HS group who received 3% HS. The data extracted from the electronic medical records included the admission date, gender, age, diagnosis at admission, complications, and laboratory values of sodium level and LOS. Subsequently, we identified all patients who developed hyponatremia complications. We collected the baseline serum sodium level before hyponatremia management, after 24 and 48 h. We extracted the patients' data by scrutinizing the medical records, and the data were entered in an Excel sheet.

Statistical analysis

Descriptive statistical analyses were performed. Continuous variables were described as mean ± standard deviation (SD) and the categorical variables as frequency and proportions. Student t-test was used to compare the 24- and 48-h correction and the LOS at the hospital. Further analysis compared the proportions using the chi-square test. The proportions of the sample were based on the guidelines (e.g. 24-h change from baseline serum sodium not exceeding 10–12 mg/dL; 48-h change from baseline serum sodium not exceeding 18 mg/dL) was evaluated with a chi-square test. Similarly, the comparison of the proportions of complications per group with delayed correction of hyponatremia (⩽115 mg/dL at admission) and corrected patients (116–120 mg/dL) was done with a chi-square test. The statistical significance level was set as p value < 0.05. The collected data were entered in Microsoft Excel 2010 (Microsoft office 360, Microsoft Ltd., USA) and all statistical analyses were performed using SPSS 21.0 version (SPSS IBM, USA).

Table 1. Distribution of basic characteristics and clinical data (N = 122).

Variables	No. of patients	Percentage
Gender		
Male	50	41
Female	72	59
Age (in years)		
Age (mean ± SD)	73.75 ± 13.4 (range: 27–101) years	
Age groups (in years)		
⩽50	6	4.9
>50	116	95.1
Groups		
Normal saline	105	86
3% Hypertonic saline	17	14
Presence of complications due to delayed correction of hyponatremia		
Symptoms/complications	46	38
No symptoms/complications	76	62
Coma	4	9
Confusion	39	85
Delirium	1	2
Seizure	2	4
Baseline serum sodium (N = 122)		
⩽115 mg/dL	80	65.6
116–120 mg/dL	42	34.4

SD: standard deviation.

Results

The sample size of included patients was 122. The majority (59%, n = 72) were female. The majority (86%, n = 105) received normal saline, 14% (n = 17) received 3% HS. More than half (62%, n = 76) had no symptoms or complications and 38% (n = 46) with symptoms or complications. As for complications, the majority of the patients 39 (85%) were confused, 4 (9%) were comatose, 2 (4%) had seizures, and 1 (2%) was delirious. On admission, 65.6% of the sample had a serum sodium ⩽ 115 mg/dL, and 34.4% a serum sodium of 116–120 mg/dL (Table 1).

For the normal saline group, the mean serum sodium increase at 24 h was lower (6.60 ± 4.75) compared to the 3% HS group (9.24 ± 5.04). The test was statistically significant (t-test value −2.108, p value = 0.037). At 48 h, the mean for the normal saline group was also lower (10.65 ± 6.17) compared to the 3% HS group (13.18 ± 4.85), which was not statistically significant (t-test value −1.610, p value = 0.110). In terms of LOS, the mean for the normal saline group was higher (10.35 ± 13.90) days compared with the 3% HS group (4.35 ± 3.39) days which was also not significant (t-test value 1.764, p value = 0.080; Table 2). In assessing the adherence to the guidelines for serum sodium increase after initiating hyponatremia correction (at 24 and 48 h, the serum sodium should not exceed 12 and 18 mg/dL respectively),

At 24 h, the majority (91.3%) of the normal saline group increased ⩽12 mg/dL compared to 70.6% in 3% HS group (This was statistically significant; chi-square test value 6.154, p value = 0.013). A small proportion (8.7%) of the normal saline group increased >12 mg/dL compared to 29.4% in 3% HS group (This was statistically significant; chi-square test value 6.154, p value = 0.013).

At 48 h, for the majority (90.5%) of the normal saline group, the increase was ⩽18 mg/dL compared to 88.2% in the 3% HS group, and an increase >18 mg/dL was observed in the normal saline group (9.5%) compared with the HS group (11.8%). The difference was not significant (p value = 0.674; Table 3).

The association between complications and serum sodium level before treatment was investigated. Of the sample receiving IV sodium (n = 122), just more than a third (38%) presented with complications (Table 1). Of this group, the majority (78%, n = 36) had a serum sodium level ⩽115 mg/dL, and 22% (n = 10) a level of 116–120 mg/dL (this was statistically significant; chi-square test value 0.041, p value = 0.041; Table 4).

Discussion

Several hyponatremia guidelines recommend initiating 3% HS in severe cases, especially when the serum sodium levels are lower than 120 mg/dL. However, currently, many practitioners still prefer to start with minimal risk or a lenient intervention such as normal saline or sodium chloride (NaCl) tablets due to lower adverse events and for additional safety concerns. However, these interventions may lead to delayed hyponatremia correction and consequently,

Table 2. Comparison of mean serum sodium increase at 24 and 48 h and length of stay (n = 122).

	Groups	Total (n)	Mean	SD	p value
Serum sodium increase 24 h from baseline	Normal saline	105	6.60	4.75	0.037*
	Hypertonic saline	17	9.24	5.04	
Serum sodium increase at 48 h post baseline	Normal saline	105	10.65	6.17	0.110#
	Hypertonic saline	17	13.18	4.85	
Length of stay	Normal saline	105	10.35	13.90	0.080#
	Hypertonic saline	17	4.35	3.39	

*p value < 0.05 statistically significant.
#p value > 0.05 statistically not significant.

Table 3. Comparison of serum sodium increase at 24 and 48 h in normal saline group versus hypertonic saline group (n = 122).

	Serum sodium	n (%)	Groups		p value
			Normal saline, n (%)	Hypertonic saline, n (%)	
Serum sodium increase at 24 h	⩽12 mg/dL	107 (88)	95 (91.3)	12 (70.6)	0.013*
	>12 mg/dL	15 (12)	10 (8.7)	5 (29.4)	
Serum sodium increase at 48 h	⩽18 mg/dL	110 (90.2)	95 (90.5)	15 (88.2)	0.674#,^
	>18 mg/dL	12 (9.8)	10 (9.5)	2 (11.8)	

*p value < 0.05 statistically significant.
#p value > 0.05 statistically not significant.
^Fisher's exact test value.

Table 4. Association between complications at baseline and serum sodium (n = 122).

	Serum sodium level	Total, n (%)	Complications present, n (%)	Complications absent, n (%)	p value
Complication present before treatment	⩽115 mg/dL delayed	80 (66)	36 (78)	44 (58)	0.041*
	116–120 mg/dL	42 (34)	10 (22)	32 (42)	

*p value < 0.05 statistically significant.

hyponatremia-related complications. This study was designed to assess whether hyponatremia correction adheres to the recommended guidelines for prescribing 3% HS to patients admitted with hypovolemic hyponatremia (a serum sodium ⩽ 120 mg/dL), safe serum sodium increases in the first 24 h (10–12 mEq/L), and 48 h (18 mEq/L) and further investigating the presence of complications due to the delayed correction.[11]

The results of this study indicate that the management of hyponatremia does not adhere to the guidelines. The study provides a comparison between the outcomes of patients treated with either 3% HS or normal saline. Of 122 patients admitted with a hypovolemic hyponatremia (serum sodium ⩽ 120 mg/dL), only 14% received 3% HS, even though the majority 66% (n = 80) had a serum sodium ⩽ 115 mg/dL and 38% (n = 46) had serious hyponatremia-related complications on admission. Comparing the mean serum sodium increase at 24 and 48 h, indicated better correction of hyponatremia in the 3% HS group when compared to the normal saline group. The guideline-based hyponatremia correction rate is indirectly reflected in the LOS. The LOS was two times in the normal saline group when compared to the 3% HS group. A second finding is that approximately 30% (n = 5) of the 3% HS group was overcorrection, as defined by a serum sodium increase >12 mg/dL at 24 h, without reporting any adverse effect, compared to 9% (n = 10) overcorrected in the normal saline group.

The common adverse effects of HS are related to route of administration and these include infections at the IV site, thrombophlebitis, fever, hypervolemia, and extravasation.[12] This may explain why healthcare practitioners refrain from utilizing it. Clinicians should consider the benefit of using 3% HS that will lead to a convenient and safe correction in contrast to using other safer modalities like normal saline that will lead to delayed correction and consequently hyponatremia-related complications and longer LOS. Another result indicated that 78% of the sample admitted with hyponatremia complications had serum sodium of ⩽115 mg/dL, which necessitated immediate and rapid correction to avoid serious complications. A retrospective cohort study enrolled 56 patients with serum sodium ⩽ 125 mEq/L with initial median level of 115 mEq/L (quartile, 111–119 mEq/L) reported that 94.6% of the participants had symptoms, with about 5.4% considered severe. Only 30% received 3% HS, 19.6% was

overcorrected, 16% at 24 h, 10.7% in 48 h and 7.1% in both 24 and 48 h. However, the study did not mention the overcorrection of patients treated with 3% HS versus patients receiving other treatment modalities. They concluded that low initial serum sodium is associated with a higher risk of overcorrection.[13] A delayed initiation of 3% HS will cause hyponatremia-related complications as well as increase the risk of overcorrection. Geoghegan et al. conducted a retrospective study with 412 patients with serum sodium < 120 mEq/L. This study was designed to determine the association between under correction in the first 24 h (serum sodium increase by ⩽5 mmol/L at 24 h) and morbidity and mortality. The main finding was that prolonged hyponatremia correction was associated with an increased LOS, 27.9% (n = 114) of the patients met overcorrection criteria and 42.2% were critically ill.[14] The results from the preceding studies are consistent with this study and support the hypothesis that prolonged or delayed correction, especially in a case with lower initial serum sodium, increase hyponatremia-related complications, the risk of overcorrection, and LOS. Sterns et al.[2] reported that patients who presented with serum sodium < 105 mEq/L, developed permanent neurological damage and death. Sood et al.[7] reported that 36% of the patients presented with severe hyponatremia, consistent with our findings. A retrospective study enrolling 62 hyponatremia patients treated with 3% HS, reported that the serum sodium increased by 7.1 ± 0.6 mEq/L in the first 24 h, and 11.3 ± 0.7 mEq/L at 48 h. A small proportion (11.3%) was overcorrected at 24 h and 9.7% at 48 h.[15] The findings of the study are consistent with those of Aratani et al.[13] during the first 48 h. It is noteworthy that many patients in the normal saline group were corrected without complications or overcorrection, even though their serum sodium level was ⩽120 mEq/L. Additional prospective controlled studies should be conducted to determine criteria for normal saline use in asymptomatic or mild to moderate symptoms patients with hypovolemic hyponatremia. Although overcorrection of hyponatremia can be potentially risky and may lead to permanent neurological disability (osmotic demyelination syndrome, under correction may impose another risk of development of cerebral manifestations).[16] One of the limitations of the study is the retrospective observational nature, another limitation was with the small sample size in the 3% HS group. It is important to clarify that the LOS was a secondary outcome, and no additional adjustments were performed to determine other patients' factors which may affect the LOS interpretation. Another limitation was that the study sampling technique was conveniently performed to include all eligible patients to preset criteria which did not allow the calculation of power. Finally, no specific matching technique has been conducted between the normal saline group and the 3% HS group and the results must be interpreted considering these limitations. Future randomized controlled studies are required to compare safety and efficacy between the management of hyponatremia modalities especially normal saline, saline tablets, and 3% HS. Furthermore, pharmacoeconomic consideration should be weighted between the different treatment options.

Conclusion

Although there is a clear recommendation for 3% HS use in patients with severe hypovolemic hyponatremia, many practitioners still use normal saline in patients with serum sodium ⩽120 mEq/L. Normal saline showed some efficacy in correcting hyponatremia in asymptomatic cases; however, severe cases may develop delayed correction and consequently hyponatremia-related complications and an increased LOS. The use of HS in eligible patients will assure appropriate time to correction and prevent further complications.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from King Abdullah International Medical Research Center (KAIMRC) (SP17/159/R).

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Informed consent

Informed consent was not sought for this study because the study is a retrospective chart review to evaluate practice, IRB waived the requirement for written informed consent.

ORCID iDs

Mohammad S Shawaqfeh https://orcid.org/0000-0003-0469-2764

Ahmed Elmubark https://orcid.org/0000-0003-1979-4886

Senthilvel Vasudevan https://orcid.org/0000-0001-7175-3534

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