Fluid Prescribing Patterns in the Intensive Care Unit

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Student Researcher: Omar Gutierrez, MS4

Faculty Mentor: Julian Seifter, MD

Introduction

Intravenous fluids are routine orders—seldom thought about more than a check box. In most healthy individuals, this is a simplicity we can afford. Our kidneys are well suited to deal with fluids differing in osmolality and adjusting appropriately. In a hospital setting, though, many patients have abnormal physiology and sub-optimal renal capacity. If administered fluids prove too difficult to adjust, they may be at risk of developing an adverse outcome. Given the frequency at which fluids are prescribed for maintaining homeostasis, a more focused investigation is warranted. This retrospective chart review characterizes the prescribing patterns of intravenous fluids in the ICU.

Background

In the discussion of maintenance fluid, a debated issue is whether to start intravenous fluids. While some argue that all patients should receive fluids to maintain homeostasis when not able to intake by mouth, others contend that most patients should not—the less, the better. The literature supporting either view is vast but the community has yet to reach a consensus. Clinically, it would be useful to have an approach to determine whether maintenance fluid is needed, whether the fluid solution or rate may have an undesired effect, and indications to guide further fluid administration.

Misconceptions about fluid was inevitable. For decades physicians have relied on the recommendations of Holiday and Segar whose work established the benchmark for prescribing fluids [1]. Yet, the limitations of their research have drastic implications. Estimations of electrolytes replacement were not sufficient given their understanding of physiology at the time and they did not account for physiological variation in disease states [2-5]. Both aspects are essential because the composition and amount of fluid may result in undesired consequences if: 1. it is not isotonic to plasma and 2. auto-regulatory mechanisms are altered such that they lead to an abnormal response to fluid-loading.

This concern arose largely from findings in children who developed hyponatremia, cerebral edema, or death secondary to fluid-loading [6-10]. The focus in children led to a critical analysis of the etiology and a re-evaluation of prescribing patterns [7, 11, 12]. In adults this information has not translated adequately, though there are similar case reports detailing a negative response to normal saline [13-18]. On the other hand,

there is recognition throughout the medical community about the need to clarify this topic and various groups have made recommendations [19-22].

The hesitation toward viewing fluid-loading as a potential harm is largely based on a disagreement about the effect of fluids on physiology and a proper distinction between maintenance and resuscitation fluid [22-24]. While the focus in the discourse is entirely surrounding fluid type, one potential contributor that is not considered routinely may lie in the abnormal physiology of hospitalized patients in the setting of disease and medications [25-27]. As aforementioned, the tonicity of a fluid is crucial to predict the response, however, the setting in which that fluid is sensed and regulated is equally important.

In summary, we hypothesize that the discrepancy in the literature regarding adverse outcomes following fluid administration may simply reflect differences in individual physiological contexts. Within this framework, fluid type and amount are likely to impact outcomes in patients who are susceptible and thus are unable to tolerate the fluid-loading.

Methods

Patient population

Charts of hospitalized patients over the course of 3 months in 2016 was reviewed. Study groups were selected from the medical intensive care unit and surgical intensive care unit. For clinical significance, fluid associated complications are defined as pulmonary edema, peripheral edema, hyperchloremic acidosis, hypo- and hypernatremia, and acute kidney injury following administration of fluids for maintenance. Notes were evaluated for further evidence suggesting the indications for prescribing fluids.

Data collection

The following data was recorded from patients who received maintenance fluids: reason of admission, vital signs, fluid type/rate/indications for starting fluids, biochemical parameters, fluid balances, and documented history of kidney disease, cardio-vascular disease /related risk factors, and select medications. Fluids were defined as normal saline (NS), 5% dextrose in water (D5W), lactated ringer's (LR). Data were retrieved from data management system (EPIC Systems Corporation, Virona, WI, USA) and reviewed manually. A review of charts and discharge notes was also performed.

Statistical analysis

Data were analyzed using SPSS (version 24.0, Chicago, IL, USA). A sub-analysis was performed leaving out all AKI patients and their matched controls, because a posi-

tive fluid balance could have been a therapeutic objective in these patients to prevent further damage. For all analysis, a P-value of ≤ 0.05 was considered significant. Power and effect size: there are few and highly variable reports on incidences in the literature regarding fluid-related complications with a range between roughly 10%-60%.

IRB Considerations:

The study protocol was reviewed and approved by the Institutional Review Board of the Brigham and Women's Hospital as well as Harvard Medical School through the Harvard School of Public Health.

Limitations

Chart Review

The population sample at Brigham and Women's Hospital may not be representative of other hospitals, may include more patients with complex medical problems, and may be more likely to have complications. Because we did examine patients, surveillance and diagnostic bias will be likely given patients' pre-existing risk factors. Moreover, we relied on what people wrote in the chart so information may have been omitted or not adequately captured. Likewise, because incidence is not listed consistently in the literature, we may not have the power to detect any differences.

Results

The charts of 130 patients, 65 from the MICU and 65 from the SICU, were reviewed. The following admissions data is shown in Table 1. The average age was nearly 10 years older in the SICU than in the MICU. There were more individuals admitted for respiratory failure, and requiring vasopressors in the MICU than the SICU. There were nearly double the individuals at baseline with a Cr > 2.5 mg/dL in the SICU than the MICU (14 vs 8). The strong ion surrogate (Na^+ - Cl^-), which is 95% sensitive and 93% for a strong ion acidosis if less than 32.5 mEq/L, was used as indicated by the Youden's index [28]. Both groups had an average pH lower than normal at admission.

After four days, the following select labs were recorded in Table 2. The sodium in the SICU group was lower than the MICU despite starting out higher at admission. The Chloride also was higher in the SICU group compared to the MICU group. The Cr in both groups worsened at Day 4. The pH improved in both groups by Day 4. There was a presence of strong ion acidosis in both groups, although the SICU had an average strong ion surrogate that fits criteria for a strong ion acidosis.

Table 1: Patient admission characteristics, outcomes, and laboratory data averages.

	MICU (n=65)	SICU (n=65)
Age	47.38 (29 - 77)	58.8 (45 - 69)
Female sex, n (%)	41 (63%)	37 (57%)
Vasopressors n (%)	34 (52.3%)	31 (47.6%)
ROA		
--resp failure n (%)	57 (87.6%)	13 (20%)
--septic shock n (%)	24 (37.5%)	26 (41%)
Na, mEq/L	140.36 (129-152)	142.11 (134-149)
K	4.34 (3.3-6.1)	3.93 (3.2-4.5)
Cl	101.0 (93-111)	103.0 (95-114)
Ca	8.36 (7.3-9.93)	7.79 (7.3-8.6)
Mg	1.91 (1.3-2.7)	1.97 (1.6-2.2)
Albumin	3.00 (2.2-3.6)	1.98 (1.4-2.5)
Cr	0.86 (0.31-4.74)	0.99 (0.49-3.73)
Cr >2.5 mg/dL n (%)	8 (12.5%)	14 (21%)
Lactate	2.29 (0.8-6.4)	2.73 (1.1-5.0)
pH	7.32 (7.11-7.46)	7.30 (7.04-7.40)
Strong Ion Surrogate	39.36 (37.29 – 41.20)	36.91 (33.43 – 39.10)

Table 2: Patient laboratory data at Day 4.

	MICU (n=65)	SICU (n=65)
Na, mEq/L	139 (134-151)	136 (131-145)
K	4.38 (3.3-5.5)	4.00 (3.4-5.0)
Cl	102.1 (95-115)	108.2 (97-117)
Ca	8.91 (7.6-11.1)	7.77 (6.6-8.4)
Mg	2.24 (1.7-2.6)	1.92 (1.7-2.1)
Albumin	2.56 (1.8-3.1)	1.90 (1.9-1.9)
Cr	1.29 (0.22-2.96)	1.42 (0.40-3.87)
Cr >2.5 mg/dL n (%)	8 (12.5%)	14 (21%)
pH	7.36 (7.29-7.45)	7.34 (7.25-7.43)
Strong Ion Surrogate	34.99 (31.60 - 36.86)	29.20 (24.23 – 37.42)

The average amount of fluids per hour is described in Table 3. There is a larger average rate and variation on Day 1 compared to Day 4 though it was not significant (P = 0.023). The SICU group had an overall larger rate overall throughout the 4 days compared to the MICU although the difference was not significant (P = 0.064). Likewise, the total amount of fluid on average was higher on Day 1 vs Day 4 (Table 4). The SICU group had a larger daily amount compared to the MICU (P = 0.018).

Table 3. Average intravenous fluids (mL/hr). All patients included in the respective day and with their ICU group.

	N	Mean	St. Dev	Min	Max
Day					
1	130	293.69	90.60	11.50	563.00
2	130	80.13	51.78	22.90	183.03
3	130	105.72	104.76	18.86	395.50
4	130	81.52	63.90	10.00	200.00
ICU type					
SICU	65	155.00	145.94	11.50	563.00
MICU	65	116.69	93.63	10.00	455.28

Table 4. Total intravenous fluids per day (mL). All patients included in the respective day and with their ICU group.

	N	Mean	St. Dev	Min	Max
Day					
1	130	2080.22	1891.50	34.5	6329.3
2	130	2649.42	2351.62	45.8	7594.2
3	130	2418.08	1725.47	575.0	5726.9
4	130	1990.52	1801.55	0.0	6254.6
ICU type					
MICU	65	1562.44	1292.34	34.5	6254.6
SICU	65	3439.96	2205.70	0.0	7594.2

Table 5. Net fluid balance (mL). All patients included in the respective day and with their ICU group.

	N	Mean	St. Dev	Min	Max
Day					
1	130	612.92	1938.38	-2445	4527
2	130	1148.54	2278.76	-1194	5883
3	130	1026.69	2585.50	-2851	5534
4	130	805.46	2310.97	-1895	5520
ICU type					
MICU	65	330.03	1962.72	-2851	5534
SICU	65	1807.80	2379.81	-2426	5883
Net on Day 4					
Negative	52	-1057.60	838.92	-2851	-41
Positive	78	2120.91	1935.98	120	5883

Table 5 describes the variation of fluid balance accounting for all the inputs and the outputs for the day. The MICU shows a mean closer to net even than the SICU (P = 0.018), although both groups have a large variation for fluid balance. Most patients (78/130) were net positive overall throughout the 4 days. Of the fluid composition, all patients received NS and D5W throughout their admission either in the form of fluids for volume replacement or accompanied with medications. 47% received LR in addition NS and D5W, mostly in the form of boluses. 31% received some other fluid in addition to NS and D5W. 22% received NS, D5W, LR and another fluid. SICU gives more of each fluid overall. The different types of fluids in the other category are listed in Table 7.

Table 6. Total fluid average per fluid type over 4 days. NS = normal saline; D5W = 5% dextrose in water; LR = lactated ringer's.

	NS	D5W	LR	Other
MICU	1710.43	760.12	437.50	348.93
SICU	2748.75	1268.90	3031.43	1498.9

Table 7. Composition of other fluids given and frequency within MICU and SICU groups.

Other Fluids	MICU (11)	SICU (18)
whole blood	3	6
D5-1/2 NS infusion	8	3
D10W infusion		2
albumin 5%		3
plasma		1
RBC's		3

There was an average urine output per hour that decreased each day (Table 8) that corresponded with a total urine output per day (Table 9) although the difference was not significant between Day 1 and Day 4 (P = 0.305). Lastly, 60/130 patients received a fluid bolus at any time during the 4 days. It was exclusively in the form of NS or LR and ranged from 100 mL to 1000 mL. No notes documented the use of fluids as "maintenance fluid" although all patients had some sort of intravenous fluid running at any instantaneous moment in time. Fluid boluses or continuous fluids intended for resuscitation were only documented 43% of the time in notes.

1. **Table 8.** Average urine output (mL/hr).

	N	Mean	St. Dev	Min	Max
Day					
1	130	285.96	478.79	35.72	1837.50
2	130	134.30	111.06	5.50	325.00
3	122	147.32	93.63	20.00	282.14
4	115	170.59	102.51	7.50	312.50
MICU/SICU					
MICU	65	228.03	324.50	5.50	1837.50
SICU	65	119.30	72.41	26.06	260.00

Table 9. Total urine output (mL).

	N	Mean	St. Dev	Min	Max
Day					
1	130	1438.31	1018.53	85	3675
2	130	1349.08	843.68	22	2990
3	122	1400.17	1181.09	20	4570
4	115	1867.27	973.08	15	3210
MICU/SICU					
MICU	65	1356.23	916.20	15	3675
SICU	65	1731.11	1099.88	417	4570

Discussion

Fluid prescribing patterns vary on the clinician which is exemplified through practices in the medical and surgical intensive care units. Monitoring of these patients in the intensive care unit over four days highlights some important findings.

Most patients were admitted with pH values conclusive of an acidotic process. Overall, this acidosis improves in both the SICU and MICU. This suggests that, no matter the fluid regimen, their clinical status improves—presumably from the treatment of their underlying condition. However, there is an increase in chloride loads for the patient in the SICU, which is consistent with the strong ion surrogate results on Day 4 [16]. Given these findings, there may be an acidosis component that is due to the strong ion difference alone on top of the contribution from the underlying condition

[16, 29]. Perhaps any residual acidosis present at Day 4 could be attributed to this contribution from excessive chloride loading or may have delayed improvement which would otherwise be more rapid. Although there was a range of patients in the MICU who also meet the criteria for a strong ion acidosis, the chloride levels did not increase to the same degree as those in the SICU and the overall average was above the threshold for strong ion acidosis criteria.

We also recognize that the fluid prescribing regimens of the MICU vs SICU are different with regards to the type of fluids, average rate of fluid, and total fluid administered over the course of their admission. The MICU exclusively uses NS but nearly all the medications used in this group are given with D5W. The theoretical response to fluid loading with NS and D5W suggests that there should be more of a decrease in serum osmolarity of sodium and an increase in diuresis [3]. Both in the MICU group were modest. Likewise, the chloride load in the MICU group would be expected to have a greater impact on the serum chloride, particularly in comparison to the SICU, but this too was only modestly increased.

On the other hand, the SICU group, which had preference to LR, had both a larger decrease in serum sodium and increase in serum chloride in comparison to the MICU. This relationship could be attributed to the overall prescribing patterns in the SICU. Although they preferred LR, they were also liberal in their approach with boluses, which were sometimes were given with NS. Also, many of their medications were given with NS and the total amount of fluid of each was greater in the SICU group than the MICU group (Table 6). This is consistent with the total fluid average in the SICU group and net positive balance at Day 4 (Table 5) which was greater than the MICU group. This suggests that the total amount of fluid had more of an impact than the fluid composition which is consistent with other studies regarding positive fluid balances [29, 30].

Lastly, the reporting of fluid prescribing is disjointed and lacking. Maintenance fluids were not mentioned in the notes documenting clinical care yet often have continuous fluids written in the medications section or in the medication administration report. They were implied when documenting goals of fluid balance as net even or net negative. However, this was usually with the focus of increased urine output with diuretics or limiting fluid intake. There is only documentation of resuscitation fluids 43% of the time they are given and often in the setting of a clinical exam reported to be “euvolemic”. There appears to be less of a diligent effort to think about fluids with the same degree of detail that is afforded to medications.

Recommendations

Most individuals do not have difficulty maintaining a steady state and will be able to tolerate intravenous fluids without issue despite the type and amount. Therefore, maintenance fluids should only be considered if the patient needs assistance to maintain a steady state of gains to losses. This would include identifying the amount

and content of fluid needed to maintain this steady state, measuring and estimating all ins and outs with reference to water and electrolyte content, and recalculating at regular intervals. If they are unable to maintain that input, boluses and medications with fluid in addition to what the patient can tolerate enterally should be the first approach.

If a patient requires resuscitation, keeping in mind the various etiologies of shock, the underlying goal should be to return to euvolemia. Therefore, volume expansion should be monitored and titrated to a clinical endpoint. For example, a beneficial response to fluid administration can be defined as increased BP, decreased HR, or increased pulse pressure. Another reasonable approach titrates fluids to obtain a urinary output of 30–50 mL/hr [31]. Absence of either beneficial or negative endpoints indicates that challenges were inadequate. An initial fluid challenge of 1000 mL or 20-30 mL/kg over 10 minutes and monitoring for a response is a reasonable strategy, keeping in mind that a conservative strategy is associated with better outcomes [29]. Reaching even to negative fluid balances and eventually a cumulative fluid balance of zero during the admission should be the goal. Likewise, fluid therapy should be discontinued when information no longer guides therapy and some advocate for the early consideration of vasopressors instead [22, 29, 32].

Regarding the composition of the fluids, balanced crystalloids (LR, Plasma-lyte, and Hartmann's) are preferred over NS and colloids for both maintenance and resuscitation[22, 33]. Because of its modest effect on physiology, D5W is a reasonable choice for minimum caloric intake and should preferentially be used for dilution of medications [29]. In summary, in the intensive care unit, where patients are more likely to have abnormal physiology, a more prudent approach to fluid and electrolyte balance is warranted.

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