ISOTONIC INTRAVENOUS FLUIDS AND BLOOD PRESSURE IN PEDIATRIC PATIENTS

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Abstract

Background: The standard of care for pediatric intravenous (IV) fluids was previously hypotonic IV fluids as maintenance therapy. Following evidence showing hypotonic fluids leading to an increased risk of iatrogenic hyponatremia, isotonic IV fluids have become the current standard of care maintenance fluids. This study examines the safety of administering isotonic IV fluids for constipation by comparing incidences of iatrogenic high blood pressure in pediatric patients with constipation receiving isotonic vs hypotonic fluids.

Methods: This pre-post study examines the records of children aged 1 to 5 years diagnosed with constipation and admitted to Phoenix Children's Hospital during July 1, 2009 to June 30th 2012 and July 1st 2013 to June 30th 2016 who received hypotonic and isotonic fluids, respectively, according to standard of care protocols. The primary outcome was the proportion of patients developing high blood pressure after receiving IV fluids for at least 24 hours. Blood pressures were collected on admission (baseline), 24 hours, 48 hours, 72 hours, 96 hours, and 120 hours after hospitalization.

Results: Incidences of elevated blood pressure were calculated at baseline, 24 hours, 48 hours, 72 hours, 96 hours, and 120 hours after hospitalization for both groups. When compared to baseline, the isotonic group was not more likely to develop high blood pressure than the hypotonic group at all time points (p value > 0.05).

Conclusion: There is no significant increase in rates of high blood pressure in pediatric patients receiving isotonic IV fluids compared to patients receiving hypotonic IV fluids. This supports the current guidelines for using isotonic IV fluids in pediatric patients as maintenance fluids.

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Introduction/Significance

Hypotonic IV fluids in pediatric patients can result in an increased risk of developing iatrogenic hyponatremia.[1,2] It has been shown that administering isotonic fluids can decrease the incidence of iatrogenic hyponatremia.[2,3] Though the majority of US pediatric residents still prescribe hypotonic fluids,[4] there is now a move to administer isotonic fluids as standard maintenance therapy in some pediatric patients to avoid the development of hyponatremia.[5] However, there is a concern that isotonic fluids may result in high blood pressure. The kidneys require a balance of sodium and potassium to pull water from the bloodstream and filter it into the collecting channels of the kidneys. Increasing the salt in the bloodstream will alter this balance by increasing the oncotic pressure in the glomerular capillaries. This change in pressure balance will cause the kidneys to remove less water from the blood that would usually be filtered into Bowman's Space, and more will stay behind in the glomerular capillaries. This increase in volume in the bloodstream can result in a higher blood pressure. The literature regarding side effects of isotonic fluids, including high blood pressure, is not well described.[6]

Our objective is to compare incidence of high blood pressures between patients who received isotonic or hypotonic IV maintenance fluids in a hospitalized pediatric population. We hypothesize that there will be an increased risk in developing iatrogenic high blood pressures in pediatric patients receiving isotonic intravenous fluids compared to hypotonic fluids.

Methods

In this pre-post study we will examine medical records of otherwise healthy pediatric patients aged 1 to 5 years who have been admitted to Phoenix Children's Hospital for management of constipation between July 1st 2009 – June 30th 2012 and July 1st 2013 – June 30th 2016. A total of 94 medical records were included in this study; 24 records from the first time period and 70 from the second time period. Prior to 2012, pediatric patients were given hypotonic fluids for maintenance therapy. After 2012, Phoenix Children's Hospital changed to administering isotonic fluids.

The diagnosis of management for constipation will be used to retrieve charts, and none of the patients will have congenital nephrogenic diabetes insipidus, central diabetes insipidus, sickle cell disease, obstructive uropathy, reflux nephropathy, renal dysplasia, nephrosis, tubulo-interstitial nephritis, or recovery phase of acute tubular necrosis.

Elevated blood pressure will be defined using blood pressure values >95th percentile according to NHLBI criteria. The primary outcome will be the proportion of patients developing high blood pressure after receiving IV fluids for at least 24 hours.

Demographic and clinical characteristics between the two IV groups were reported as medians and IQR for continuous variables and frequencies and percentages for categorical variables. The Wilcoxon rank sum was used to compare the continuous variables between the two groups. Chai square/fishers exact were used to compare categorical variables. The generalized estimating equation was used to ascertain the likelihood of elevated blood pressures between the IV groups across the time points. Finally, the linear mixed model was used to ascertain the estimated mean difference in SBP between the IV groups across the time points. Both models were adjusted for age, gender, ethnicity, admit weight, height, admit diagnosis, IV fluid volume and rate, PO fluids, baseline sodium and creatinine. All P values were two sided and $P < 0.05$ was considered statistically significant. All data analyses were conducted using STATA version 14 (College Station, Texas).

Results

Average age of our population was 47.5 months and 55.3% were male (Table 1). The average IV fluid rate was 50 ml/hr (52.5 ml/hr in hypotonic group and 50 ml/hr in isotonic group, p value = 0.33) and the average IV fluid total volume was 1757.5 ml. The average amount of PO fluids was 722.58 mls in the hypotonic group and 1158.5 mls in the isotonic group (p value = 0.18). The baseline systolic blood pressure was 102 in the hypotonic group and 103 in the isotonic group. Table 2 lists the frequencies of elevated blood pressure in each group. There were 5 patients (26.3%) in the hypotonic group and 22 patients (31.8%, p value = 0.64) in the isotonic group with a baseline elevated blood pressure.

Figure 1 demonstrates overall systolic blood (SBP) pressure values over the time period specified. The median SBP was 103 at baseline and 92.5 120 hours after admission (table 3). Figure 2 demonstrates mean systolic blood pressure values between the two groups. The overall baseline mean SBP was 104.6, while the SBP at 120 hours was 93 (table 4). The mean SBP at baseline was 100.3 for the hypotonic group and 106.4 for the isotonic group (p value = 0.73). The mean SBP at 120 hours for the hypotonic was 95.7 and 91.8 for the isotonic group (p value = 0.36). At 72 hours, the mean SBP in hypotonic fluids group was greater than isotonic fluids group (104 vs 90.1, p value = 0.025).

Table 5 evaluates the likelihood of elevated blood pressure between the two groups. At 72 hours, the isotonic group was less likely to have elevated blood pressure than the isotonic group when controlling for time only, as seen in Model 1 (OR 0.29, p value = 0.027). When controlling for age, gender, ethnicity, admit weight, height, admit diagnosis, IV fluid volume, PO fluids, baseline sodium, and creatinine levels, at 72 hours the isotonic group was less likely to have elevated blood pressure, shown in Model 2 (OR 0.37, p value = 0.31). Model 2 also demonstrates that at all time points (24 h, 48 h, 72, 96 h, and 120 h), the isotonic group was less likely to have elevated blood pressure than the hypotonic group (p value = 0.76, 0.85, 0.31, 0.54, and 0.27, respectively).

Table 1. Demographics

Variables	Overall N=-94	0.45% NS w/20 mEq KCl/1000m mL N=24	0.9% NS w/20 mEq KCl/1000m mL N=70	P-value
Age, Months (median, IQR)	47.5 (37, 58)	56.5 (40.5, 62)	44 (36, 57)	0.25
Sex (male, %)	52 (55.3)	14 (58.3)	38 (54.3)	0.73
Ethnicity (Caucasian, %)	59 (64.1)	16 (66.7)	43 (63.2)	0.73
Admit Weight, kg (median, IQR)	16.7 (13.7, 18.7)	17.8 (14.1, 20.8)	16.1 (13.6, 18.3))	0.078
Height, cm (median, IQR)	102.8 (92.5)	110.5 (94, 114.5)	101.3 (92.5, 110)	0.072
Admit Diagnosis (fecal impaction, %)	28 (29.8)	0 (0.0)	28 (40.0)	<0.001
IV Fluid Volume, ml (median, IQR)	1757.5 (1250, 2525)	1715 (1450, 3725)	1800 (1176, 2525)	0.13
IV Fluid Rate, ml/Hr, (median, IQR)	50 (45, 60)	52.5 (40, 60)	50 (45, 56)	0.33
PO Fluids (median, IQR)	902.5 (375, 1720)	722.58 (130, 1480)	1158.5 (450, 1720)	0.18
Baseline Systolic BP (median, IQR)	103 (97, 109)	102 (98, 111)	103.5 (95, 109)	0.73
Baseline Sodium (median, IQR)	139 (138, 140.5)	137 (137, 137)	139 (138, 141)	0.042
Baseline Potassium (median, IQR)	3.90 (3.65, 4.2)	3.8 (3.4, 4.5)	3.9 (3.7, 4.2)	0.71
Baseline Creatinine (median, IQR)	0.345, 0.285, 0.395)	0.40 (0.36, 0.51)	0.34 (0.28, 0.39)	0.11

Wilcoxon Rank Sum to compare continuous variables.
Chi2 / Fisher's Exact to compare categorical variables.

Table 2. Frequencies of high blood pressure between groups

High blood pressure	Overall	0.45% NS w/20 mEq KCl/1000m mL	0.9% NS w/20 mEq KCl/1000m mL	P-value
	(N %)	(N %)	(N %)	
Baseline N=88	27 (30.68)	5 (26.3)	22 (31.8)	0.64
24 hours N=85	24 (28.2)	7 (36.8)	17 (25.8)	0.34
48 hours N=17	17 (26.9)	1 (7.14)	16 (32.7)	0.088
72 hours N=36	4 (11.1)	2 (16.7)	2 (8.53)	0.58
96 hours N=17	4 (23.5)	1 (25.0)	3 (23.1)	>0.99
120 hours N=10	1 (10.0)	0 (0.0)	1 (14.3)	>0.99

Chi2 / Fisher's Exact to compare categorical variables.

Figure 1. Overall SBP

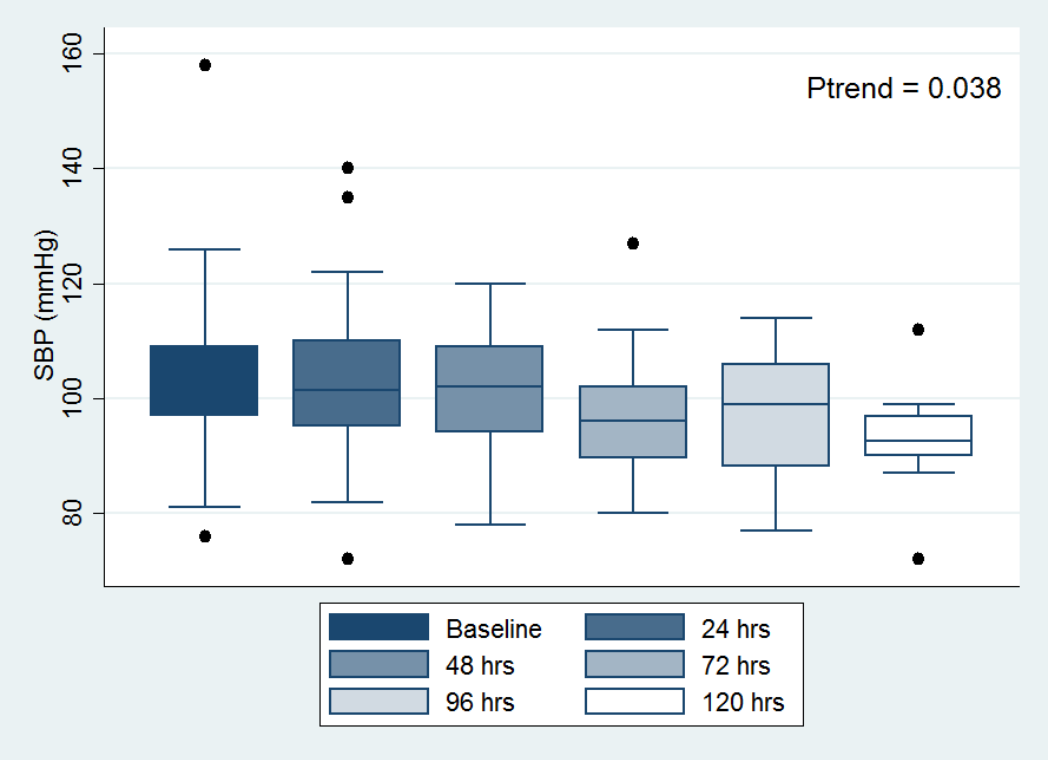

Table 3. Overall SBP

High blood pressure	Overall
	Median (IQR)
Baseline N=88	103 (97, 109)
24 hours N=85	101.5 (95, 110)
48 hours N=17	102.0 (94, 109)
72 hours N=36	96.0 (89.5, 102)
96 hours N=17	99 (88, 106)
120 hours N=10	92.5 (90, 97)

Figure 2. Mean SBP over time between groups

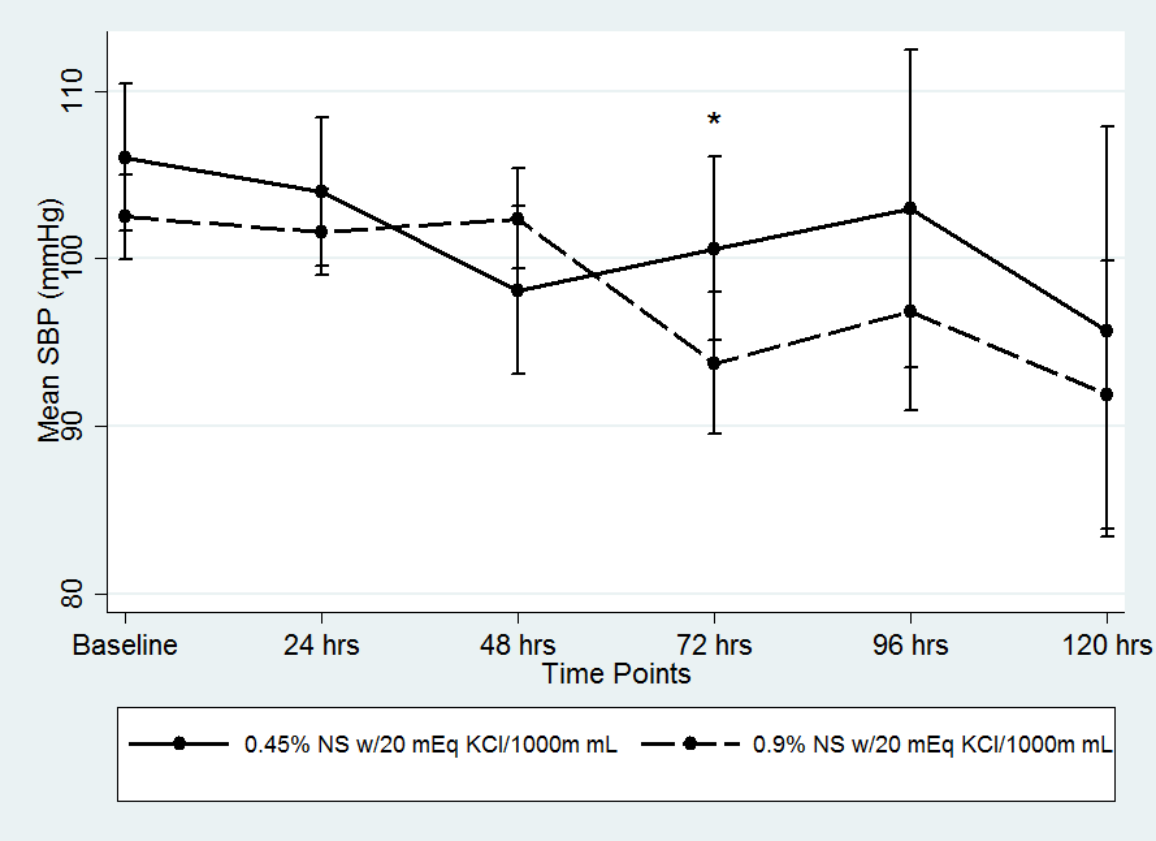

Table 4. Mean SBP over time between groups

High blood pressure	Overall	0.45% NS w/20 mEq KCl/1000m mL	0.9% NS w/20 mEq KCl/1000m mL	P-value
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	
Baseline N=88	104.6 (98.8, 110.4)	100.3 (76.2, 124.5)	106.4 (99.5, 113.3)	0.73
24 hours N=85	98.8 (91.2, 106.3)	104.3 (57.8, 150.8)	96.4 (91.5, 101.3)	0.46
48 hours N=17	99.6 (91.8, 107.4)	99.0 (72.7, 125.2)	99.8 (88.9, 110.8)	0.14
72 hours N=36	94.3 (83.6, 105.0)	104.0 (51.9, 156.0)	90.1 (79.8, 100.4)	0.025
96 hours N=17	100.4 (94.3, 106.5)	100.7 (71.0, 130.3)	100.3 (92.9, 107.6)	0.19
120 hours N=10	93.0 (85.8, 100.2)	95.7 (85.3, 106.0)	91.8 (80.8, 102.9)	0.36

Wilcoxon Rank Sum to compare between groups.

Discussion

The results of this study found no statistically significant increase in likelihood of elevated blood pressure between the isotonic and hypotonic IV fluid groups. It was found that the hypotonic group had a higher mean SBP at 72 hours than the isotonic group, but when comparing incidences of elevated blood pressure when controlling for a variety of variables, no significant differences between high blood pressure rates were found.

Previous literature has not evaluated the rates of high blood pressure in the pediatric population since switching to the administration of isotonic fluids from hypotonic fluids. This study supports the current practice of continuing to administer isotonic fluids to pediatric populations without an increased risk of developing iatrogenic high blood pressure. It should be noted that the sample size of our population was a total of 94 patients. The small power of the study may be a reason we did not find a significant difference. Furthermore, this study evaluates children ages 1-5, but further studies may need to be done to increase the applicability of the findings.

Table 5. Association between groups and high blood pressure

	Model 1[1] OR (95% CI)	P-value	Model 2[2] OR (95% CI)	P-value
Group				
0.45% NS w/20 mEq KCl/1000m mL	REF		REF	
0.9% NS w/20 mEq KCl/1000m mL	1.15 (0.53, 2.48)	0.71	0.03 (0.0007, 1.20)	0.063
Time Points				
Baseline	REF		REF	
24 hours	0.82 (0.46, 1.44)	0.49	0.82 (0.25, 2.75)	0.76
48 hours	0.79 (0.39, 1.58)	0.51	0.88 (0.24, 3.24)	0.85
72 hours	0.29 (0.09, 0.86)	0.027	0.37 (0.05, 2.56)	0.31
96 hours	0.64 (0.19, 2.10)	0.46	0.53 (0.07, 4.03)	0.54
120 hours	0.20 (0.02, 1.81)	0.15	0.24 (0.02, 3.01)	0.27

	Model 3 Beta (95% CI)	P-value	Model 4 Beta (95% CI)	P-value
Group				
0.45% NS w/20 mEq KCl/1000m mL	REF		REF	
0.9% NS w/20 mEq KCl/1000m mL	0.027 (-0.12, 0.18)	0.71	-0.18 (-0.56, 0.19)	0.34
Time Points				
Baseline	REF		REF	
24 hours	-0.028 (-0.14, 0.085)	0.62	0.001 (-0.16, 0.17)	0.98
48 hours	-0.035 (-0.16, 0.088)	0.57	0.011 (-0.17, 0.19)	0.90
72 hours	-0.18 (-0.33, -0.026)	0.027	-0.10 (-0.33, 0.13)	0.38
96 hours	-0.041 (-0.24, 0.16)	0.69	-0.050 (-0.33, 0.23)	0.72
120 hours	-0.22 (-0..48, 0.036)	0.092	-0.18 (-0.52, 0.14)	0.26

[1]Model 1. Generalized Estimating Equation to ascertain the likelihood of high blood pressure between IV groups controlling for time.
[2]Model 2. Generalized Estimating Equation to ascertain the likelihood of high blood pressure between IV groups controlling for time with further adjustments of age, gender, ethnicity, Admit Weight, height, Admit Diagnosis. IV fluid volume, PO fluids, baseline sodium and creatinine levels.
[3]Model 3. Linear mixed model to ascertain the mean difference in SBP between IV groups controlling for time.
[4]Model 4. Linear mixed model to ascertain the mean difference in SBP between IV groups controlling for time with further adjustments of age, gender, ethnicity, Admit Weight, height, Admit Diagnosis. IV fluid volume, PO fluids, baseline sodium and creatinine levels.

Future Directions

Based on our findings, it is reasonable to continue use isotonic fluids as maintenance fluids in the pediatric population. However, it should be noted that this study may not have had a large enough sample size to find a true difference. Future studies should be pursued that involve a much larger sample size.

Conclusion

There is no increased risk of developing high blood pressure in the pediatric population when administering isotonic fluids compared to hypotonic fluids. Future larger studies should be done to evaluate for possible lack of power in this study.

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