Research Article **IJOPRR (2020) 3:26**

International Journal of Pediatric Research and Reviews
(ISSN:2637-4978)

The Use of a Rapid Fluid Infusion System in Children

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Introduction

Fluid resuscitation is the cornerstone of treatment for pediatric shock caused by conditions such as sepsis, dehydration, trauma, and anaphylaxis. Children presenting to the Emergency Department (ED) in shock have a high risk of mortality, and each hour of delay in shock reversal doubles the odds of death[1,2]. Pediatric Advanced Life Support (PALS) guidelines emphasize the importance of providing rapid fluid resuscitation to prevent the progression to hypotensive or refractory shock[3]. PALS and other septic shock guidelines recommend that patients receive a 20 mL/kg bolus of crystalloid immediately upon recognition of hypovolemic or distributive shock, with 20 mL/kg to be delivered within 5 minutes and up to 60 mL/kg within the first 15-60 minutes[3-6]. Studies based on these guidelines show that earlier fluid delivery directed at reversal of shock reversal leads to decreased morbidity[7-9], mortality[2,7,9-12], and hospital length of stay (LOS)[9,11-13]. Unfortunately, timely fluid delivery is often not achieved due to the technical challenges of obtaining adequate vascular access and delivering fluid boluses quickly in patients with shock or hypotension[11,14-16].

Funding source: This study was funded by Medical 410. However all design, data collection and analysis, manuscript preparation and decision to submit was conducted independently by the authors.

Conflict of Interest: Judy Fuller, RN is a consultant for Medical 410. No other authors have any conflicts.

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How to cite this article:
Sai Surapa Raju, Judy Fuller; Stacy L. Gaither, Hui-Chien Kuo, Inmaculada Aban, Nancy M. Tofil. The Use of a Rapid Fluid Infusion System in Children. International Journal of Pediatric Research and Reviews, 2020, 3:26

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Website: https://escipub.com/

Current methods of fluid bolus delivery in the pediatric emergency care setting include infusion pumps, gravity drip, pressure bags, rapid infusers, and the push-pull syringe technique[17,18]. Each of these methods are limited by speed, ease of use, or safety concerns. Infusion pumps provide a maximum rate of 999 mL per hour, which for a 25kg child would provide a 60 mL/kg bolus in 90 minutes. In most patients, infusion pumps are therefore too slow to provide adequate fluid resuscitation. Gravity drip rates are unpredictable and inadequate for the treatment of shock and hypotension. For example, up to 50 minutes are required for one liter of fluid to flow through a 22G intravenous (IV) line, and up to 200 minutes via the intraosseous (IO) route[19-22]. A pressure cuff may speed flow modestly, but requires constant re-inflation, makes volume of infusion difficult to track, and carries the risk of inadvertent air embolism[3,20,22-25]. Rapid infusers can deliver fluids very quickly but are expensive, require frequent training, are not readily available in many emergency care settings, and importantly do not provide adequate flow with the small gauge IV or intraosseous (IO) access typical of pediatric resuscitation[19,26].

Due to the limitations of these common fluid delivery methods, pediatric emergency providers commonly use a syringe and 3-way stopcock to repeatedly draw fluid from the container of crystalloid and then deliver to the patient. This technique is referred to as the “push-pull” method and is recommended in the PALS guidelines[3]. An alternate technique involves disconnecting and reconnecting multiple pre-filled 60mL syringes, which often requires two providers[18]. Both methods may be associated with increased risk of nosocomial infection due to the difficulty of maintaining syringe sterility[27-31].

The LifeFlow® infuser (410 Medical, Inc; Durham, NC) is a new manually operated device for rapid fluid bolus delivery that overcomes some of these common barriers. The device is currently FDA-cleared for infusion of crystalloid and colloid fluids, and is in use at our center for emergency resuscitation. Using common IV gauges LifeFlow can deliver fluid 2 to 4 times faster than standard techniques, and allows providers to observe a clinical response immediately by improvements in vital signs, mental status and skin perfusion[29,32-34]. This study describes the use of the LifeFlow device in a busy academic children’s hospital ED with 74,000 patient visits per year.

Methods

The Institutional Review Board approved this study and due to the retrospective nature of the study design, informed consent was waived. The LifeFlow infuser received FDA clearance in August 2016 and use in our hospital began in April 2017. Our retrospective chart review included all pediatric patients presenting to the ED from May 2017 through November 2018 who had at least one fluid bolus delivered with the LifeFlow device. The use of LifeFlow was identified by patient charge through the Pyxis™ Medstation system (Beckton, Dickinson and Company, Franklin Lakes, NJ). This list was then reviewed for erroneous or duplicate entries. All unique patient’s medical records were then reviewed by one of the four authors (SR, JF, SG, NT). Prior to any chart reviews, these same four authors developed a data recording Excel (Microsoft, Inc, Redmond, WA) spreadsheet agreeing on the elements of chart review. Data collected included initial resuscitation volume, change in vital signs, patient disposition, and other outcomes including duration of mechanical ventilation, duration of pediatric intensive care unit (PICU) stay and hospital length of stay. Patients were excluded if 1) a LifeFlow was obtained but no fluids were delivered, or 2) their age was greater than 21 years. We chose 21 years old instead of 18 or 19 years old as we see many children with chronic pediatric medical problems between the age of 18-21 years old.

To ensure quality chart reviews, after each reviewer extracted data from five charts and then the team met and reviewed data to ensure inter-rater agreement[35]. The precise rate of fluid administration was often difficult to determine from

chart review. Given the typical delivery times observed with LifeFlow usage, if no time was recorded 5 minutes was noted as the default time, based on several references documenting the delivery of 500-1000ml of crystalloid in less than 5 minutes[36-39]. Vital signs after fluid bolus was defined as the first set of vital signs immediately following the fluid bolus. This field was left blank if no vital signs were obtained within 60 minutes of the fluid bolus. We grouped children in four different age groups, less than 1 year old, 1-5 years old, 5-12 years old and 12-21 years old in an effort to evaluate if any age difference occurred. These ages were agreed upon a prior to data collection and although somewhat arbitrary were agreed upon by the four clinical authors.

Statistics

Counts and percentages are presented for categorical variables by each age group. Mean with standard deviation and/or median with interquartile range [first quartile (Q1), third quartile (Q3)] used for continuous measures such as length of stay (days) in the hospital for descriptive statistics depending on the normalcy of data distribution. Fisher's Exact Test was used to compare the proportion of categorical outcomes interested such as different proportion in type of principal diagnosis within the four age groups. Logistic regression was applied to model the number of boluses within the four age groups. With respect to the length of stay in the hospital, days in the PICU and days of mechanical ventilation, a generalized linear mixed model assuming Poisson distribution was used with standard variance components by four age groups. Analysis of variance was utilized to compare the mean differences of total fluids within the four age groups. We considered a p value of less than 0.05, statistically significant. All analyses were completed using SAS version 9.4 (SAS Institute, Cary NC).

Table 1. Demographics

	AGE GROUP				
Variable	<1 year old (n=10)	1-5 year old (n=41)	5-12 year old (n=57)	12-21 years old (n=83)	p value
Admission Unit					0.1089
PICU	3 (30%)	24 (59%)	24 (42%)	40 (48%)	
Step-down ICU	7 (70%)	7 (17%)	15 (26%)	20 (24%)	
Floor	0 (0%)	8 (20%)	10 (18%)	17 (20%)	
Data missing/other	0 (0%)	2 (5%)	8 (14%)	6 (7%)	
Chronic Disease - Yes/Total (percent)	1/10 (10%)	21/41 (51%)	33/57 (58%)	61/83 (73%)	0.0004
Principal Diagnosis					0.0254
Sepsis	3 (30%)	10 (24%)	24 (42%)	32 (39%)	
Respiratory Failure	5 (50%)	10 (24%)	7 (12%)	18 (22%)	
Trauma	1 (10%)	12 (29%)	12 (21%)	5 (6%)	
Dehydration/Vomiting	0 (0%)	2 (5%)	5 (9%)	5 (6%)	
Status Epilepticus	1 (10%)	3 (7%)	3 (5%)	2 (2%)	
Ingestion	0 (0%)	2 (5%)	0 (0%)	3 (4%)	
Other	0 (0%)	2 (5%)[a]	6 (11%)[b]	18 (22%)[c]	
Median LOS (days) (Q1, Q3)	3 (2, 4)	5 (3, 13)	4 (2, 8)	7 (3, 13)	< 0.0001
Mean LOS (days) ± STD	3.1 ± 2.2	10.7 ± 13.8	11.9 ± 23.9	12.4 ± 19.1	
Median PICU LOS (days) (Q1, Q3)	n=3 2 (1, 3)	n=24 3 (1, 6)	n=24 2 (1, 6)	n=41 2 (1, 5)	0.2765
Mean PICU LOS (days) ± STD	2.0 ± 1.0	4.2 ± 4.4	7.0 ± 10.7	6.6 ± 12.0	

a. anaphylaxis (2)
b. post-operative (2), full arrest (2)
c. gastrointestinal bleed (4)diabetic ketoacidosis (3), cerebrovascular event (1), anemia (1), intracranial hemorrhage (1), uterine bleed (1), heat stroke (1), hypotension not otherwise specified (1), pleural effusion (1), pelvic inflammatory disease (1)

Table 2. Patient Interventions

Variable	AGE GROUP <1 year old (n=10)	1-5 year old (n=41)	5-12 year old (n=57)	12-21 years old (n=83)	p value
Mean Total Fluid (cc/kg) ± STD	40 ± 18	34 ± 16	33 ± 16	36 ± 17	0.5010
Number who Got:					0.0052
1 Fluid bolus	3 (30%)	15 (37%)	28 (49%)	21 (25%)	
2 boluses	4 (40%)	17 (41%)	15 (26%)	24 (29%)	
3 boluses	2 (20%)	7 (17%)	11 (19%)	34 (41%)	
Data missing	1 (10%)	2 (5%)	3 (5%)	4 (5%)	
Median Days on Mechanical Ventilation (Q1, Q3)	n=2 2 (0, 3)	n=20 3 (1, 9)	n=16 2 (1, 12)	n=29 3 (2, 6)	0.0532
Mean Days on Mechanical Ventilation ± STD	1.5 ± 2.1	4.3 ± 4.1	16.9 ± 34.5	9.5 ± 18.3	
Number who got Vasopressors	0 (0%)	5 (12%)	10 (18%)	17 (20%)	0.3875
Data missing	2 (20%)	7 (17%)	5 (9%)	10 (12%)	
First Vasopressor (n=32)	n = 0	n = 5	n = 10	n = 17	0.2265
Epinephrine	0	5	6	10	
Norepinephrine	0	0	3	1	
Dopamine	0	0	1	4	
Phenylephrine	0	0	0	2	
Number (%) Intubated	2 (20%)	11 (27%)	12 (22%)	27 (33%)	0.4786

Table 3. Vital Sign Changes

	AGE GROUP <1 year old (n=10)	1-5 year old (n=41)	5-12 year old (n=57)	12-21 years old (n=83)
Median (Q1, Q3) Initial HR	195 (164, 200)	160 (143, 175)	146 (124, 160)	138 (124, 159)
Median (Q1, Q3) HR after 1st Bolus	176 (172, 179)	136 (123, 152)	130 (108, 153)	125 (113, 144)
Median (Q1, Q3) HR after 2nd Bolus	171 (171, 172)	147 (118, 169)	148 (119, 155)	130 (110, 144)
Median (Q1, Q3) HR after 3rd Bolus	173 (165, 181)	146 (113, 158)	141 (110, 157)	128 (115, 137)
Median (IQR) Percent Change in HR after: *1 Fluid Bolus* *n*	-2.7 (-15, 18.2) n = 6	-9.9 (-18.5, 4.4) n = 30	-7.7 (-16.6, 1.4) n = 50	-10.3 (-14.5, -2.8) n = 71
2 Fluid Boluses *n*	-13.4 (-18.0, -11.9) n = 6	-9.8 (-23.3, 8.9) n = 22	-9.1 (-13.2, 8.5) n = 23	-11.4 (-21.7, -3.8) n = 51
3 Fluid Boluses *n*	-17.0 (-17.5, -16.6) n = 2	0.0 (-15.0, 12.0) n = 7	-9.8 (-16.6, 6.7) n = 11	-15.9 (-28.7, 0.8) n = 31
Median (Q1, Q3) Initial RR	60 (50, 62)	32 (28, 48)	30 (24, 36)	24 (20, 36)
Median (Q1, Q3) RR after 1st Bolus	44 (38, 68)	31 (22, 34)	30 (24, 42)	26 (20, 36)
Median (Q1, Q3) RR after 2nd Bolus	51 (48, 54)	32 (28, 39)	31 (25, 37)	24 (20, 29)
Median (Q1, Q3) RR after 3rd Bolus	72 (72, 72)	34 (28, 38)	25 (21, 28)	25 (20, 30)
Median (Q1, Q3) Percent Change in RR after: *1 Fluid Bolus* *n*	0.4 (-31.5, 105.7) n = 4	3.0 (-21.4, 16.7) n = 29	0.0 (-6.7, 25.0) n = 41	0.0 (-11.1, 17.6) n = 62
2 Fluid Boluses *n*	-17.8 (-20.0, -2.9) n = 6	-3.0 (-20.0, 7.7) n = 21	3.2 (-10.5, 23.3) n = 21	-9.1 (-33.3, 11.1) n = 47
3 Fluid Boluses *n*	2.9 (2.9, 2.9) n = 1	-10.0 (-22.7, 16.7) n = 7	-3.3 (-16.7, 10.0) n = 10	-4.5 (-22.2, 14.1) n = 28

Legend: (Q1, Q3) – interquartile Q1: first quartile; Q3: third quartile; HR – heart rate; RR – respiratory rate

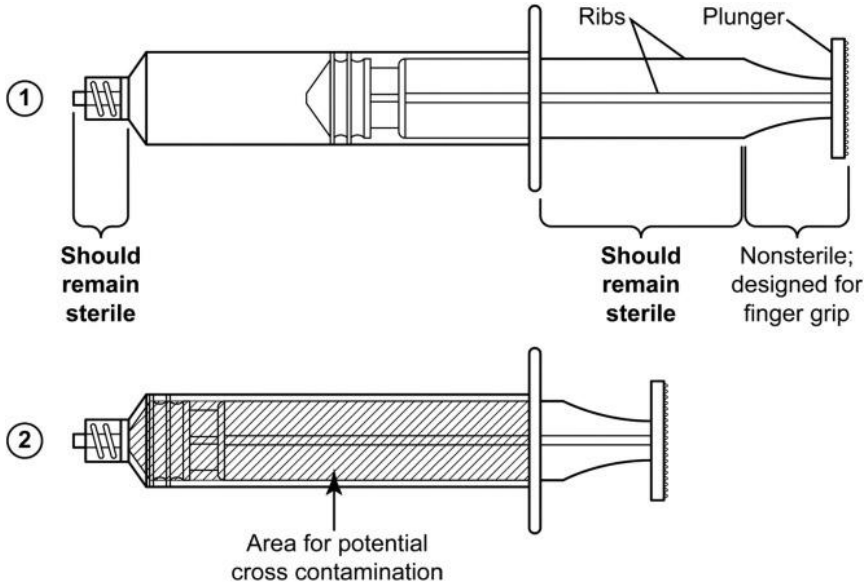

Figure 1. Illustration of intended design of syringe to maintain sterility of fluid. Illustration 1 shows different areas of standard syringe. Illustration 2 shows area of potential contamination.

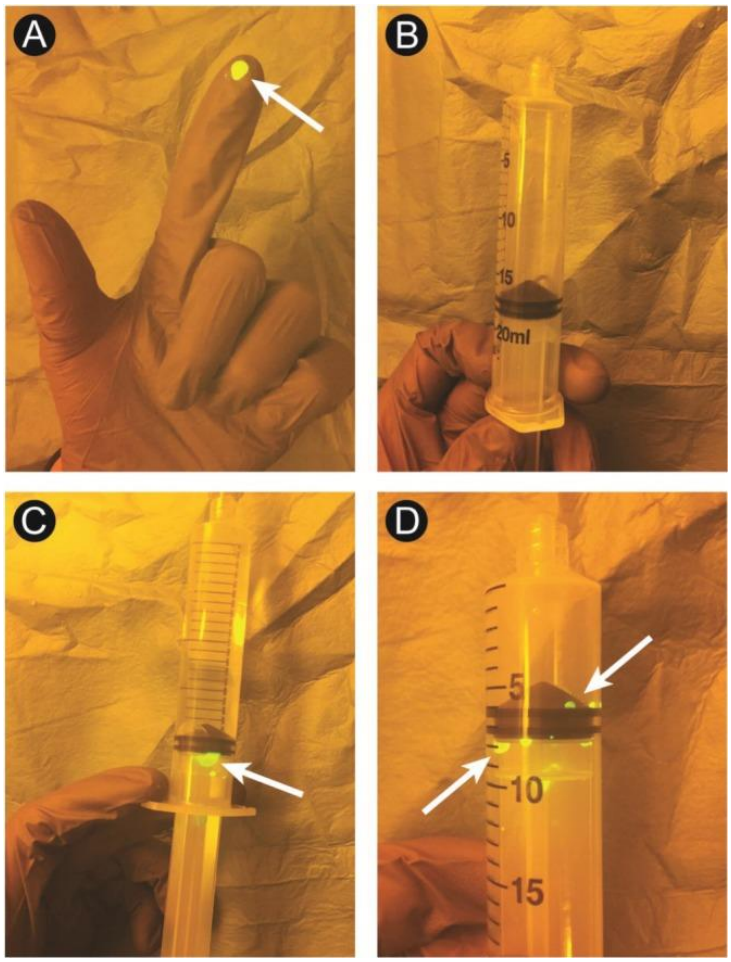

Figure 2. Illustration of contamination sequence of a syringe after repeated use. Photographs were taken under UV light during various stages of the 500-mL bolus. All images were taken through a UV filter to visualize only the fluorescence and not the UV light: A) Initial placement of simulated contamination on glove. B) Syringe shown before use. C) Contamination from contact with plunger during initial stroke. D) Contamination observed on both sides of plunger after simulated 500-mL infusion. Abbreviation: UV, ultraviolet. Courtesy of 410 Medical, Durham, NC.

Results

218 patients were reviewed with 27 charts excluded due to pre-determined exclusion criteria (6 patients were excluded due to being over the age of 21 years old and 21 patients were excluded due to not receiving any fluids), resulting in 191 (88%) charts for statistical analysis. Demographic data are found in Table 1. The median age of the patients was 10 years old with an inter-quartile range of 11 years old. The most common admitting diagnoses were fever/sepsis (36%), hypoxia/respiratory failure (21%) and trauma at (16%). Forty-eight percent were admitted to the PICU, 26% were admitted to the Step-down ICU and 18% were admitted to a general pediatric floor. One child died in the ED and two were discharged home from the ED. The overall mortality was 7%. Most patients received the fluid resuscitation via a peripheral intravenous line 89%, while 13% received the bolus via a central venous access with a power port and 4% through IO access. No complications were noted in any patient with LifeFlow when using the IV or IO route.

The average length of stay (LOS) for all subjects was 11.4 ± 19.2 days and for those who were admitted to the PICU the average PICU LOS was 6.0 ± 10.0 days. 67/191 (35%) received invasive mechanical ventilation for an average of 9.5 ± 21 days. Table 2 shows interventions patients received. The average amount of fluids given to the patient was 35 ± 17 mL/kg. 32/191 (17%) were started on vasopressors with the most common being epinephrine (21/32 (66%)).

Table 3 shows vital sign changes over time. The heart rate decreased an average of 10% with each subsequent fluid bolus. There was no significant difference in the percent change between any of the four age groups ($p = 0.755$). In general the respiratory rate was stable over time in all age groups.

Discussion

We describe a retrospective observational study comprising of the largest series of pediatric patients who were resuscitated with LifeFlow rapid infusion system in an emergency department. Our study demonstrated that the rapid flow infusion system can be safely used to deliver fluid boluses in pediatric patients with signs of shock as young as 2 months of age. This study demonstrates the feasibility of using this rapid infusion system in patients with shock states due to a wide variety etiologies and pre-existing conditions. We also noted that LifeFlow appears to effectively deliver fluid via the IO route as evidenced by its use in 8 critically ill patients.

We found that most patients were admitted either to our PICU or step down ICU. Thirty-five percent of the study population required invasive mechanical ventilation and 17% required vasopressors. Overall mortality rate in the study population was 7%. Mortality from pediatric severe sepsis and septic shock ranges from 11.4% to 30%, and while we did not specify criteria for shock in our systematic chart review, the majority of patients presumably had signs of shock that prompted clinicians to administer one or more fluid boluses[2,40-43]. Also, a majority (61%) of our patients had a chronic disease, a risk factor for increased mortality from septic shock[44]. This frequency of chronic illness aligns with other reports finding rates of 40-70% of patients admitted to the PICU having a chronic illness[45,46].

Even after recognition of shock states, lack of knowledge of fluid resuscitation guidelines and technical limitation of fluid delivery often delay adequate resuscitation[1,2,11,15]. The LifeFlow device serves as technique that appears to offer speed, efficiency and control of volume infused and as a resource to overcome the barrier of fluid delivery in shock states. LifeFlow has two potential advantages over the traditional push-pull method or the use of multiple syringes for fluid resuscitation. First, it facilitates fluid bolus delivery by a single provider, in contrast to the use of multiple 60 mL syringes which is an effective method of rapid fluid administration but requires two to three healthcare providers. Second, in contrast to the push-pull method, the closed LifeFlow system allows a single syringe

to be reused without environmental contamination of the plunger. It is important to note that standard disposable syringes are indicated for single use only due to the risk of contamination through user contact with the exposed syringe plunger. Figure 1 shows the design of a syringe and areas of potential contamination. Figure 2 shows a simulation demonstrating syringe contamination during push-pull technique. Practically, however, many times larger syringes such as 60 mL syringes are reused leading to the possibility of contaminated resuscitation fluids[4].

The LifeFlow provides a closed system which prevents contact between the provider's hands and the syringe plunger, potentially limiting the risk of Central Line Associated Blood Stream Infections (CLABSI). According to the Centers for Disease Control and Prevention, there are approximately 250,000 CLABSIs each year in the United States. The cost of admission for a patient requiring CLABSI treatment is $70,000 and the increase in the risk of a patient's mortality is twice the normal risk. In comparison, the cost of a LifeFlow device for the hospital is approximately $240. Although LifeFlow costs more than a single 60cc syringe, if each syringe was used once as indicated, to administer 1000 mL of fluid would take 17 syringes and the cost at this point is nearly identical.

Limitations

There are limitations to our study. This was a single center study which evaluated only patients initially presenting to the ED. Our chart reviews had some missing data especially related to vital signs after fluid administration. Some age groups had small numbers limiting our ability to make strong conclusions. Although eight children received fluids via an IO, this small number limits our ability to draw other conclusions. Our observational study should be considered as an illustrative example of the use of this novel device and not as evidence that it is superior to other fluid administration methods.

In conclusion, we present the largest series of pediatric patients who received fluid administration using the LifeFlow fluid system. Our next steps are to design a prospective observational study to document vital signs real or near real time to have more accurate data describing change in vital signs and patient outcomes after fluid administration.

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