Intravenous Fluid Bolus Prior to Neonatal and Infant Lumbar Puncture
A Sonographic Assessment of the Subarachnoid Space After Intravenous Fluid Administration

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IMPORTANCE Neonatal and infant lumbar puncture is a commonly performed procedure in emergency departments, yet traumatic and unsuccessful lumbar punctures occur 30% to 50% of the time. Dehydration may be a risk factor for unsuccessful lumbar punctures, but to our knowledge, no studies have investigated the use of intravenous (IV) fluid bolus prior to lumbar puncture.

OBJECTIVE To investigate the association of IV fluid bolus administration with the sonographic measure of the neonatal and infant lumbar subarachnoid space. We hypothesized that IV fluids would increase subarachnoid space size.

DESIGN, SETTING, AND PARTICIPANTS Prospective observational study conducted from August 2012 to April 2015. The study took place at the emergency department of the Children's Hospital Los Angeles, an urban pediatric emergency department with an annual census of 76 000 visits. A convenience sample of patients aged 0 to 3 months were enrolled if they had a clinical presentation consistent with pyloric stenosis. This population was used as a proxy because they are similar in age to patients undergoing lumbar puncture for evaluation of neonatal fever and are routinely given IV fluids for dehydration.

EXPOSURES Patients with a sonographic diagnosis of pyloric stenosis underwent additional ultrasonography evaluation to determine the size of the subarachnoid space before and after IV fluids.

MAIN OUTCOMES AND MEASURES Primary outcomes included the difference in the size of the subarachnoid space in millimeters squared before and 1 hour after administration of an IV fluid bolus in the emergency department. Interobserver consistency for the subarachnoid space measurement between attending radiologists was measured using intraclass correlation coefficient. The Wilcoxon signed-rank test was used to examine changes in subarachnoid space measurements (millimeters squared).

RESULTS The study sample consisted of 40 patients with a mean (SD) age of 37 (11.3) days (range, 15-71 days). The mean (SD) size of the subarachnoid space before and 1 hour after IV fluid bolus was 37.8 (11.1) mm² and 36.9 (11.2) mm² respectively (P = .42). The intraclass correlation coefficient ranged from 0.96 to 0.99 (95% CI, 0.90-0.99).

CONCLUSIONS AND RELEVANCE Intravenous fluid boluses were not associated with a significant increase in the sonographic measure of the neonatal and infant subarachnoid space.
Neonatal and infant lumbar puncture (LP) is a commonly performed procedure in emergency departments (EDs). Although they are a routine procedure, traumatic and unsuccessful LPs occur up to 30% to 50% of the time.1,2 While definitions regarding traumatic LPs differ among studies, unsuccessful lumbar punctures are regarded as attempts in which either no fluid is obtained (the dry tap) or in which such a small amount of fluid is obtained that only culture results are available for interpretation.2 Unsuccessful LPs may create increased anxiety for patients and families and can lead to unnecessary hospitalizations and prolonged courses of intravenous (IV) antibiotics.

Multiple studies have investigated different factors that potentially affect LP success.3-4 Dehydration may be a potential risk factor for unsuccessful or dry LPs.

We performed a prospective, observational study to determine whether administration of an IV fluid bolus increases the cerebrospinal fluid (CSF) volume at the neonatal and infant subarachnoid space. Assuming that an IV fluid bolus should increase the intrathecal fluid content (as well as the intravascular volume elsewhere) in a dehydrated patient, we hypothesized that this difference could be assessed through measuring the subarachnoid space in the lower lumbar region, near the site at which an LP would normally be performed. Using ultrasonography measurements, we sought to investigate the effect of this IV fluid bolus on the neonatal and infant subarachnoid space. It was our hypothesis that the IV fluid bolus would significantly increase the size of the neonatal and infant subarachnoid space in a period clinically relevant to performing an LP in the ED.

Methods

Study Design, Setting, and Participants

This was a prospective, observational study that took place at Children's Hospital Los Angeles, an urban pediatric ED with an annual census of 76,000 visits. Our convenience sample consisted of patients aged 0 to 3 months being considered for pyloric ultrasonography, but not necessarily meningitis. The institutional review board of the Children's Hospital Los Angeles approved the study protocol. Emergency department physicians or research assistants obtained written informed consent from the legal guardian of each study patient prior to any diagnostic testing.

Study Protocol

Patients aged 0 to 3 months with a clinical presentation consistent with pyloric stenosis were identified for enrollment. Figure 1 illustrates our study protocol. All patients in whom the treating physician planned to order an ultrasonography for the evaluation of pyloric stenosis were considered eligible for enrollment. All final diagnoses of pyloric stenosis were made by radiology ultrasonography. We excluded all patients who had received IV fluids in the preceding 24-hour period or patients who were deemed clinically unstable in need of immediate fluid resuscitation.

The patient did not have pyloric stenosis, the study protocol continued for the enrolled patient: each patient underwent initial subarachnoid space ultrasonography. The patient then returned to the ED where vital signs, a naked weight, and a study physical examination were performed, followed by administration of a normal saline IV fluid bolus. The amount of IV fluids given was left to the discretion of the treating physician. All physician assessments were completed by board-certified pediatric ED attendings or fellows and are recorded in the eTable in the Supplement. Approximately 1 hour after the fluid bolus was complete, the patient returned to the radiology suite, where the second subarachnoid space ultrasonography was conducted. The patient then returned to the ED, where a second set of repeated vital signs, naked weight, and study physical examination were recorded. Our original protocol included a third ultrasonography procedure to be completed 12 hours to 24 hours after IV fluid administration, but because this third measure was completed in less than 50% of patients secondary to early next-day surgery (before radiology ultrasonography hours), we did not include these data in our analysis. If ultrasonography was not performed 1 hour post-IV fluid bolus owing to availability of ultrasonography technicians, the ultrasonography obtained 12 hours to 24 hours after initial IV fluid administration was used in the data analysis. These patients (n = 3) were considered euvolemic because all admitted patients receive 1.5 times maintenance fluids prior to surgery.

Main Outcomes and Measures

Ultrasonography was conducted by licensed ultrasonography technicians using a General Electric E9 Logiq ultrasound machine and a 15-MHz linear probe. The subarachnoid space was estimated by measuring the spinal canal (at the level of the conus medullaris) with the ultrasonography probe in a transverse orientation with respect to the vertebral bodies. Using the elliptical region of interest measuring tool on the picture archiving and communication system, the spinal canal at the level of the conus and the conus medullaris were measured in millimeters squared. An example of ultrasonographic images obtained both prebolus and postbolus are depicted in Figure 2. The conus medullaris measurement in millimeters squared was then subtracted from the spinal canal measurement in millimeters squared to give the estimated subarachnoid space in millimeters squared.

Key Points

Question: Does intravenous fluid administration increase the size of the neonatal and infant subarachnoid space?

Findings: In this study of 40 neonates and infants, intravenous fluid bolus was not associated with a significant change in the size of the neonatal and infant subarachnoid space as measured by ultrasonography.

Meaning: Intravenous fluid bolus prior to neonatal and infant lumbar puncture may not increase the success of lumbar puncture.
Because there is some subjectivity in determining the borders of the spinal canal and conus medullaris, the recorded images were reviewed by 2 pediatric radiology attending physicians to improve the validity of their interpretations. The radiologists were not blinded to fluid administration status with respect to each ultrasonography because it was not possible to remove the timestamp from the recorded image.

Primary outcomes included the differences in the size of the subarachnoid space in millimeters squared before and 1 hour after (or 12-24 hours after) administration of an IV fluid bolus in the ED.

**Data Analysis**

Sample size calculation yielded 40 patients necessary to detect a 10% increase in the subarachnoid space (effect size $d = 0.4$) for a Wilcoxon signed-rank test (with 80% power and 1-tailed $\alpha = .05$). A 10% increase was chosen as the minimum clinically significant change in the subarachnoid space.
A mixed-model (average measures) intraclass correlation coefficient (maximum value, 1.00) was chosen to ascertain interobserver consistency between the radiologists’ interpretations for subarachnoid space size.

The Wilcoxon signed-rank test was used to examine changes in subarachnoid space measurements (millimeters squared). All analyses were conducted using IBM SPSS, version 19 (IBM Corporation).

Data analysis was performed with the 12-hour to 24-hour substitute measure (in 3 cases) and without the 12-hour to 24-hour measure (using raw data). The results were not significant with each analysis (Table 2).

### Results

The study period was approximately 32 months, from August 2012 to April 2015. Forty-four patients diagnosed as having pyloric stenosis were enrolled in our study, with data from 40 patients available for final analysis: 6 girls and 34 boys, with a mean (SD) age of 37 (11.3) days (range, 15–71 days). Data from 40 patients were available for analysis because 2 patients did not receive the initial pre-IV fluid ultrasonography, 1 patient had a nondiagnostic pre-IV fluid ultrasonography, and 1 patient did not receive an IV fluid bolus between ultrasonography procedures (Figure 1). Patient characteristics are shown in Table I. The mean (SD) percentage dehydration based on initial weight and presurgical weight was 2.0% (2.0%) (available for 20 patients). Based on presenting physical examination, 20% of patients (n = 8) were classified as having normal to mild dehydration, while 80% (n = 32) were moderately dehydrated. The mean (SD) amount of fluids given between the first and second ultrasonographic procedures was 22.0 (7.5) mL/kg (range, 20–60 mL/kg). The mean (SD) time between the initial fluid bolus and the second ultrasonography was 59.9 (36.2) minutes.

The mean (SD) size of the subarachnoid space before and 1 hour after IV fluid bolus was 37.8 (11.1) mm² and 36.9 (11.2) mm², respectively (P = .42). The intraclass correlation coefficient ranged from 0.96 to 0.99 (95% CI, 0.90–0.99).

### Discussion

Administration of an IV fluid bolus did not demonstrate statistically significant increases in the size of the neonatal and infant subarachnoid space measured 1 hour after IV fluid bolus. Our prospective, observational study of patients aged 0 to 3 months presenting to the ED with the diagnosis of pyloric stenosis was used as a proxy population because these patients are invariably dehydrated, receive IV fluids, and require ultrasonography for evaluation.

The dynamics of CSF production, absorption, and circulation remain controversial. The “traditional hypothesis” describes most (65%) CSF as produced by the choroid plexus at a rate of 0.3 to 0.6 mL/min in both children and adults for a daily volume of approximately 500 mL. The total volume of CSF is replaced approximately 4 times per day in an adult. The fluid flows in one direction through the ventricles into the subarachnoid space before being absorbed by the arachnoid granulations. The “microvessel hypothesis” instead describes a constant exchange of fluid between the subarachnoid and extracellular spaces without mention of net unidirectional flow.

Maintenance of normal CSF volume is essential to brain health and is largely based on 3 factors: changes in brain compliance, CSF hemodynamic/hydrodynamic factors, and vascular parameters. Cerebrospinal fluid hemodynamics in both the brain and spinal cord are regulated intracranially. In terms of hemodynamics, the inverse relationship between cerebral blood volume and CSF volume is defined by the Monro-Kellie doctrine. Simply stated, the total intracranial volume is fixed and bound by a rigid skull and therefore constantly maintained by reciprocal changes in brain, blood, and CSF volumes. This principle is less absolute in the context of an open neonatal fontanelle but provides a loose cognitive framework while considering changes in CSF volumes. The brain will compensate in the event of an acute expansion of arterial cerebral volume by displacing CSF from the cranial to the lumbar space in a matter of seconds to minutes. Martins et al described the elastic nature of the spinal dural sac and documented its change in size via myelography in healthy volunteers in response to several centrally acting maneuvers, including hyperventilation and inhalation of 10% carbon dioxide. These changes in subarachnoid space size were seen within seconds of each maneuver, supporting the notion of a fixed but displaceable volume that is governed intracranially. Minute to minute and even hour to hour, the CSF volume is relatively fixed but can be displaced based on acute intracranial changes. Cerebrospinal fluid volume does not acutely change owing to the well-developed ability of the brain to autoregulate. Cerebral autoregulation allows for cerebral blood flow to be maintained over a wide range (60-160 mm Hg) of mean arterial pressures. A constant cerebral blood flow translates into a constant CSF rate of production and volume. Understanding this, a small, peripheral

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<th>Amount of fluid administered, mL/kg</th>
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Abbreviation: IV, intravenous.
Intravenous Fluid Bolus and Neonatal/Infant Lumbar Puncture

Hanson et al3 retrospectively studied 134 LPs to see whether family presence had no statistical effect on LP success. Although some physicians believe that volume status can affect LP success, to our knowledge, there is no mention in the neurosurgical or neurological literature of mild, acute dehydration causing significant changes in CSF volume. Similarly, the clinical examination finding of sunken fontanelle in pediatric dehydration literature has rarely performed well as a clinical predictor of dehydration.12-14

It is possible that although CSF volume did not change in our patients, CSF pressure was altered by IV fluid bolus. The literature does not support this explanation because CSF pressure is highly variable among individuals and is even normal in patients with clinical and radiological evidence of CSF hypovolemia.11 Although a loose association exists because hydration status has been proposed as a potential risk factor for symptoms secondary to CSF hypovolemia (ie, post-LP headache), acute changes in intravascular hydration status have not been directly linked to acute changes in CSF volume status. Although CSF hypovolemia has been clinically and radiographically described, it remains unknown whether and how rapidly IV fluid administration affects CSF volume.

Many studies have investigated potential factors for LP success. Baxter et al1 concluded through prospective observation of 428 LPs that patient age (>12 weeks), use of local anesthetic, and early stylet removal were associated with increased success. Through retrospective medical record review of 1474 LPs, Nigrovic et al2 determined less physician experience, lack of local anesthetic use, advancement of the spinal needle with the stylet in place, increased patient movement, and age of younger than 3 months were all associated with traumatic or unsuccessful LP. In a follow-up study,4 it was noted that family presence had no statistical effect on LP success. Hanson et al3 retrospectively studied 134 LPs to see whether the sitting flexed or lateral flexed positions had any effect on LP success and found no difference in success rates between the 2 positions but did find a higher first-time success rate with the sitting flexed position (odds ratio, 2.74).

The aforementioned studies investigated many different factors that could affect LP success. To our knowledge, this is the only study investigating how IV fluids affect the subarachnoid space and potentially LP success. To our knowledge, there are no randomized clinical trials investigating how IV fluid administration changes LP success rates. Through this investigation, we aimed to answer the initial question of how this CSF-containing space changes in response to IV fluid administration. It is reasonable to assume that CSF volume and subarachnoid space size are likely a factor in LP success. The extrapolation of our results to the clinical situation suggests that administration of IV fluid bolus prior to LP may not increase the success of LP. However, this is an assumption because our study does not prove that the size of the subarachnoid space correlates with LP success. The question of hydration status and LP success would be more directly investigated through a randomized controlled trial of neonatal and infant lumbar puncture with vs without IV fluid bolus.

Several limitations should be considered when interpreting the results of our study. Although we obtained an adequate sample size to obtain 80% power, this is a relatively small number of patients and as such, the results may not be generalizable.

In terms of patient characteristics, our patients were only mildly dehydrated at approximately 2% based on triage, pre-surgical weights, and physical examination, although our clinical measures of dehydration suggested more significant dehydration. This level of dehydration may not be great enough to cause changes in CSF volume. Our study does not answer how CSF volume may change in response to a fluid bolus in a patient with severe dehydration. Therefore, these study results are only generalizable to patients with euvolemia and mild dehydration. Even so, this mild level of dehydration in patients presenting with vomiting and a diagnosis of pyloric stenosis is likely greater than patients with neonatal fever in whom fluid deficits are most commonly related to insensible losses from fever and tachypnea. Additionally, the mean age of our patient population (37 days) is slightly older and therefore different than the population of maximum interest in the evaluation of neonatal fever (neonates <28 days old).

As mentioned previously, we were unable to blind the attending radiologist to the IV fluid administration status of each ultrasonography because this could be discerned by the timestamp recorded on each image. This lack of blinding could have influenced image interpretation through unintentional transfer of their attitudes for or against our intervention. Similarly, the attending radiologists were interpreting the same images and were not blinded to their colleagues’ interpretation of the size of the subarachnoid space. It is possible that the variability between the 2 radiologists would be much greater had the images been separately obtained by different, blinded sonographers. This was not possible at our institution because only 1 ultrasonography technician was available at any given time.

The actual measurement of the subarachnoid space is not a commonly reported measure in radiology. Also, there is some subjectivity in determining the borders of the spinal canal and the conus medullaris because these are irregular and traced manually. However, because our results demonstrated excellent interobserver reliability, we believe these measures to be both reproducible and accurate. We chose to measure the subarachnoid space at the level of the conus medullaris because this provided an easily identifiable structure where each

### Table 2. Subarachnoid Space Measurements Pre- and Post-IV Fluid

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<th>Variable</th>
<th>Subarachnoid Space Measurements, Mean (SD), mm²</th>
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<td>Pre-IV Fluid</td>
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<td>Using raw datab</td>
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Abbreviation: IV, intravenous.

a We used 12 to 24 hour measurements to replace missing 1-hour measurements in 3 patients.
b Missing 1 hour measurements not replaced.
patient could be measured, as opposed to a more time-consuming approach of counting specific vertebral levels to designate the location of image acquisition. This seemed acceptable because it would be even less likely for the dural sac to be more distended at a level distal to our site of measurement. As such, our images were obtained near but not exactly at the most common anatomical sites for LP. We chose to measure the subarachnoid space in millimeters squared as a proxy for a reflection in the change of volume in the subarachnoid space. Although a 3-dimensional measure would have been more accurate, this is similar in design to previous studies that have used subarachnoid space width to reflect changes in CSF volume. The mean time of the post-IV fluid bolus ultrasonography was approximately 60 minutes after fluid administration and might not reflect the actual time of neonatal LP in practice because most centers target expeditious completion of testing and antibiotic administration.

Last, we investigated the effect of IV fluid administration on the size of the subarachnoid space. While we do provide baseline data toward answering the question of hydration status and ability to obtain CSF, we did not prove a correlation between subarachnoid space size and LP success.

Conclusions

We performed a prospective, observational study of patients aged 0 to 3 months to determine whether administration of an IV fluid bolus increases the size of the subarachnoid space as measured by ultrasonography. Intravenous fluid boluses were not associated with significant increases in the size of the neonatal and infant subarachnoid space. The application of our results to the clinical situation may suggest that IV fluid bolus prior to LP does not increase the success of LP. Our study did not directly correlate IV fluid administration and LP success rates and is therefore a surrogate to a more invasive, randomized clinical trial of neonatal and infant LP with vs without IV fluid bolus.