Heliyon 10 (2024) e32252

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Exploring the correlation and difference between cerebrospinal fluid in the lateral ventricle and lumbar subarachnoid based on infants with intraventricular hemorrhage treated by the ommaya reservoir

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ARTICLE INFO

Keywords:
Ommaya reservoir
Lumbar CSF
Ventricular CSF
Difference,Correlation
Regression equation

ABSTRACT

Objective: To explore the relationship and difference between ventricular and lumbar cerebrospinal fluid(CSF), this study presents equations transforming their measures. By assessing the viability of substituting lumbar puncture, we aim to minimize the associated medical risks and trauma faced by infants with intraventricular hemorrhage(IVH) from anesthesia and lumbar puncture.

Methods: We retrospectively analyzed CSF data from 27 infants diagnosed with IVH treated by Ommaya reservoir and lumbar puncture at our center, comprising 35 paired samples. Paired-sample and regression analyses were employed to determine test correlations, differences, and to derive transformation equations for the measurements.

Results: Comparative analyses between the CSF from the lateral ventricle and the lumbar vertebrae revealed significant differences in the levels of chloride, glucose, protein, erythrocytes, total cells, and Pandy's test. Specifically:

1. Levels of chloride, glucose, protein, and Pandy's test were higher in the lumbar vertebrae.
2. Conversely, erythrocyte and total cell counts were higher in the lateral ventricle.

There were no significant differences observed for lumbar lactate dehydrogenase(LDH), leukocytes, occult blood, clot, clarity, and color. Nevertheless, significant correlations were identified between various measures, including LDH, glucose, chloride, protein, erythrocyte, leukocyte, total cell count, Pandy's test, occult blood, clot, transparency, and color. Interestingly, the correlation strength and equation fit for each component are inversely proportional to its molecular weight.Notably, well-fitting regression equations were found for LDH, glucose, chloride, protein, leukocytes, erythrocytes, and total cells.

Conclusion: In infants with IVH and unobstructed CSF channels, a robust correlation was noted between ventricular CSF sourced via the Ommaya reservoir and lumbar CSF. This correlation tended to be inversely related to molecular weight, with smaller molecular weights showing lesser disparities. Ventricular CSF data could anticipate lumbar CSF trends, and using regression equations with Ommaya-obtained CSF, one can derive approximate values for lumbar CSF.

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https://doi.org/10.1016/j.heliyon.2024.e32252
Received 6 September 2023; Received in revised form 29 May 2024; Accepted 30 May 2024
Available online 31 May 2024

1. Background

The Invented by Pakistani neurosurgeon Ayub Khan Ommaya in 1963, the Ommaya reservoir offers a means for recurrent access to the intrathecal space. [1] Originally designed for antifungal drug delivery to the cerebrospinal fluid (CSF) [2], its applications have expanded to include central nervous system (CNS) chemotherapy, CSF sampling, addressing ventricular hemorrhage, bacterial meningitis, and cranial hypertension.[3–6] In the context of neonates suffering from intraventricular hemorrhage compounded by hydrocephalus, this device is now frequently favored over lumbar puncture due to its ease of use, reduced pain, and enhanced patient compliance. However, during clinical diagnosis and treatment, discrepancies often emerge between lumbar CSF test results and ventricular CSF profiles—a phenomenon corroborated by prior academic investigations [7]. Such variations, significant because clinical guidelines predominantly draw from lumbar CSF data, [8,9] have introduced challenges in diagnostics and therapeutics.From a clinical perspective, it's pivotal to ascertain potential infections following Ommaya reservoir punctures and to judiciously decide on the timing for shunt surgeries based on CSF data. Given the difficulties associated with lumbar punctures in pediatric patients, which include potential anesthesia complications or physical struggles during the procedure, a deeper exploration into CSF differences across sampling sites is both essential and meritorious.

Situated as a leading neonatal critical care center in China, we routinely admit neonates with ventricular hemorrhage, and for patients experiencing ventricular enlargement (i.e., GMH Papile grades III and IV), we perform Ommaya reservoir implantation. In the course of their treatment, cerebrospinal fluid (CSF) is extracted daily from the ventricles using the Ommaya reservoir. This procedure aims to remove intraventricular blood, alleviate intracranial hypertension, and facilitate laboratory tests.Lumbar puncture is occasionally performed for several reasons:(1)Determining potential underlying infections, as CSF bacterial cultures have limited sensitivity and metagenomic next-generation sequencing (mNGS) remains costly.(2)Manometry is used to assess the adequacy of cerebrospinal fluid pumping because intracranial hypertension has persisted for a longer period of time when imaging reveals ventricular widening, and manometry is a more rapid assessment of intracranial pressure.(3)Deciding on the appropriateness and timing of shunt implantation, as well as setting the initial pressure for the procedure. Given the need for sedation during lumbar punctures, we typically perform both the lumbar puncture and the ventricular CSF extraction during the same sedation session. This approach allows us to obtain simultaneous lumbar and intraventricular CSF samples from the same patient. The data derived from this approach are markedly more real-time and precise than those previously obtained via extraventricular drains.[10,11] This consistent and accurate method of CSF sampling provides a robust foundation for our ongoing study, aiming to elucidate the correlation and difference between CSF from the lateral ventricles and lumbar spine.

2. Materials and methods

2.1. Study design and patient selection

We conducted a retrospective analysis of cerebrospinal fluid samples from infant patients diagnosed with intraventricular hemorrhage(Papile grades III and IV). These patients underwent Ommaya reservoir implantation and lumbar puncture at our center between June 2022 and July 2023. For paired analysis, we excluded data where.

a Lumbar spine and ventricular samples weren't obtained in the same sedation.
b There was a suspected cerebrospinal fluid channel obstruction (e.g., pre-existing hydrocephalus before cerebral hemorrhage or an obstruction in the cerebrospinal fluid channels resulting from hematoma-induced compression of the brain parenchyma.).
c The sample was contaminated with fresh blood during puncture.
d The sample was taken within three days post-Ommaya reservoir implantation.

After applying these criteria, we amassed 35 pairs of matched lumbar and ventricular cerebrospinal fluid sample data from 27 patients, resulting in 70 cerebrospinal fluid samples in total.

2.2. Statistical analysis

Statistical analyses were performed as follows.

1 . **Paired Analyses**:
   a ***t*-test**: CSF lactate dehydrogenase (LDH), glucose (Glu), chloride ions (Cl-) and protein (Pro).
   b **Wilcoxon test**: CSF white blood cell (WBC), red blood cell (RBC), total blood cell, color, and Pandy's test data.
   c **McNemar test**: CSF occult blood (OB), clot, and transparency.
2. **Correlation Analyses**:
   a **Pearson linear correlation**: CSF lactate dehydrogenase (LDH), protein (Pro), glucose (Glu) and chloride (Cl-).
   b **Spearman rank correlation**: CSF white blood cell (WBC), red blood cell (RBC), total blood cell (TBC), CSF color, and Pandy's test.
   c **Rank correlation**: CSF occult blood, clot, and transparency.
3. **Regression Analyses**:

a Variables: CSF lactate dehydrogenase (LDH), glucose (Glu), chloride (Cl-), protein (Pro), white blood cells (WBC), red blood cells (RBC), and total blood cell (TBC).
b The regression equation with the highest R^2 value was selected.

All statistical analyses were executed using IBM SPSS Statistics 26,while graphs were generated with OriginPro 2022b. All tests were two-sided, with p-values <0.05 deemed statistically significant.

3. Results

3.1. Demographics & clinical variables

a Presented in Table 1 and Fig. 1. Fig. 1A shows the gestational age of the child at birth; Fig. 1B shows the sampling time after surgery.
b Population：Percentage of females, % 28.6(10/35) Gestational age at birth, weeks 30.96 ± 4.95

3.2. Sampling time after surgery, days 23(11,62)

Variability & Correlation Between Lumbar Spine and Lateral Ventricular CSF.

a Detailed in Table 2, Table 3, Fig. 2, and Fig. 3. Fig. 2A, B, 2C, 2D, 2E, 2F, and 2G represent the overall differences in LDH, Glu, Cl-, protein, WBC, RBC, and tBC in ventricular versus lumbar CSF for all patients respectively. Fig. 3A, B, 3C, 3D, 3E, 3F, and 3G represent the correlation of LDH, Glu, Cl-, protein, WBC, RBC, and tBC in the patients' ventricular versus lumbar CSF.
b Variability: LDH ($t = 0.486, p = 0.623$, 95%Cl = [-10.176, 16.747]); Glu ($t = 3.268, p = 0.002$, 95%Cl = [0.084, 0.359]); Cl- ($t = 4.726, p = 0.001$, 95%Cl = [0.671, 1.683]); protein ($t = 4.447, p = 0.000$, 95%Cl = [412.746, 1107.596]); WBC ($Z = -1.159, p = 0.247$); RBC ($Z = -2.606, p = 0.009$); total blood cell ($Z = -2.342, p = 0.019$); Pandy's test ($Z = -3.017, p = 0.003$); OB ($Z = 0.000, p = 1.000$); clot ($Z = 0.000, p = 1.000$); transparency ($Z = -1.000, p = 0.317$); Color ($Z = -1.000, p = 0.317$).
c Correlation: LDH ($r = 0.833$); Glu ($r = 0.927$); Cl- ($r = 0.958$); protein ($r = 0.702$); WBC ($r = 0.627$); RBC ($r = 0.741$); total blood cell ($r = 0.735$); Pandy's test ($r = 0.790$); OB ($r = 1.000$); clot ($r = 1.000$); transparency ($r = 0.804$); Color ($r = 0.983$). All of the above items have a p-value of 0.000.

Differences in ventricular CSF and lumbar CSF at different times.

aPresented in Fig. 4. Fig. 4A, B, 4C, 4D, and 4E represent the differences in RBC, tBC, WBC, LDH, and protein in ventricular versus lumbar CSF from the same patient.

Regression Model Curves & Equations.

aIllustrated in Fig. 3 and detailed in Table 4.
bGoodness of fit: LDH ($R2 = 0.838$); Glu ($R2 = 0.859$); Cl- ($R2 = 0.921$); protein ($R2 = 0.785$); WBC ($R2 = 0.649$); RBC ($R2 = 0.826$); total blood cell ($R2 = 0.826$)

Clinical outcomes.

a rate of infection:7.4 % (2/27), follow-up date up to present.
b Shunt-dependent hydrocephalus: 54.5 % (12/22), the deadline for shunt evaluation is set at 6 months corrected age for the infants, of which 5 cases have not yet reached the deadline.
c Mortality: 0(2/27), follow-up date up to present.

Table 1
Demographic and clinical variables.

Variable	Data
No. of patients	27
No. of cerebrospinal fluid samples	70
Percentage of females, %	28.6(10/35)
Gestational age at birth, weeks	30.96 ± 4.95
Unadjusted age at the time of sampling, months	1(1,5)
Sampling time after surgery, days	23(11,62)
GMH(germinal matrix hemorrhage) grade, %	
Papile grade III	74.07(20/27)
Papile grade IV	25.93(7/27)

Count data are expressed as examples (%), and measurement data are expressed using ($\bar{x} \pm s$) when normally distributed and M(P_{25}, P_{75}) when not normally distributed.

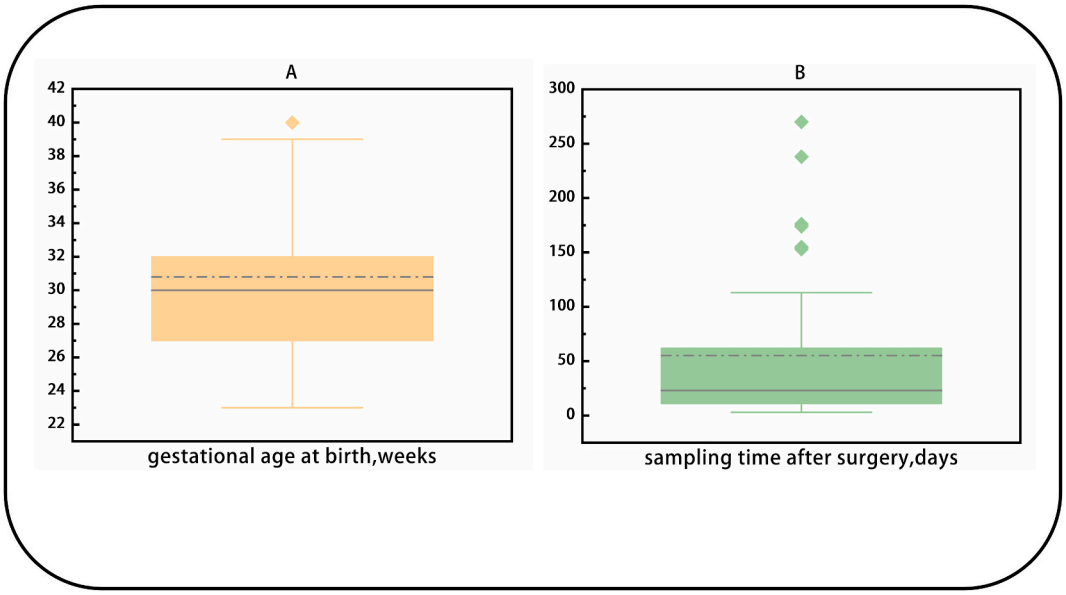

Fig. 1. Figure A shows the gestational age of the child at birth; Figure B shows the sampling time after surgery; Within the boxes, dashed lines represent the means, while solid lines denote the medians.

Table 2
Differences and correlations between lumbar and ventricular CSF.

Item	Sampling site		test value of Difference	P value of Significant difference	Correlation coefficient, r	P value of Significant Correlation
	lumbar	ventricular				
LDH,U/L	89.14 ± 61.832	85.86 ± 70.615	0.486	0.623	0.833	0.000
Glu,mmol/L	2.198 ± 0.855	1.977 ± 1.032	3.268	0.002	0.927	0.000
Cl-,mmol/L	119.189 ± 4.973	118.011 ± 5.145	4.726	0.001	0.958	0.000
protein,mg/L	1829.657 ± 1387.562	1069.486 ± 759.935	4.447	0.000	0.702	0.000
WBC,10^6/L	5 (1 , 15)	6 (2 , 12)	−1.159	0.247	0.627	0.000
RBC,10^6/L	36 (1 , 300)	100 (1 , 1890)	−2.606	0.009	0.741	0.000
total blood cell,10^6/L	58 (3 , 308)	102 (8 , 1896)	−2.342	0.019	0.735	0.000
Pandy's test , %			−3.017	0.003	0.790	0.000
	28.6 %(10/35)	37.1 % (13/35)				
+	37.1 % (13/35)	51.4 % (18/35)				
++	17.1 % (6/35)	8.6 % (3/35)				
+++	17.1 % (6/35)	2.9 % (1/35)				
OB , %			0.000	1.000	1.000	0.000
-	2.7 % (1/35)	2.7 % (1/35)				
+	97.3 % (34/35)	97.3 % (34/35)				
clot , %			0.000	1.000	1.000	0.000
	100 % (35/35)	100 % (35/35)				
+	0 % (0/35)	0 % (0/35)				
transparency , %			−1.000	0.317	0.804	0.000
Clear	94.3 % (33/35)	91.4 % (32/35)				
turbid	5.7 % (2/35)	8.6 % (3/35)				
Color , %			−1.000	0.317	0.983	0.000
Colorless	40 % (14/35)	37.1 % (13/35)				
Light color	20 % (7/35)	22.8 % (8/35)				
Dark color	40 % (14/35)	40 % (14/35)				

Count data are expressed as examples (%), and measurement data are expressed using ($\bar{x} \pm s$) when normally distributed and M(P_{25}, P_{75}) when not normally distributed. $p < 0.05$ is statistically significant.

Table 3
Correlation and molecular weight of components between two sites.

Item	Correlation, r	molecular weight	P value
Cl^-	0.958	35.5	0.000
Glu	0.927	180.16	0.000
LDH	0.833	135~140*10^3	0.000
protein	0.702	150~450*10^3	0.000
total blood cell	0.735	2~20*10^8	0.000

The correlation strength is roughly inversely proportional to the molecular weight.

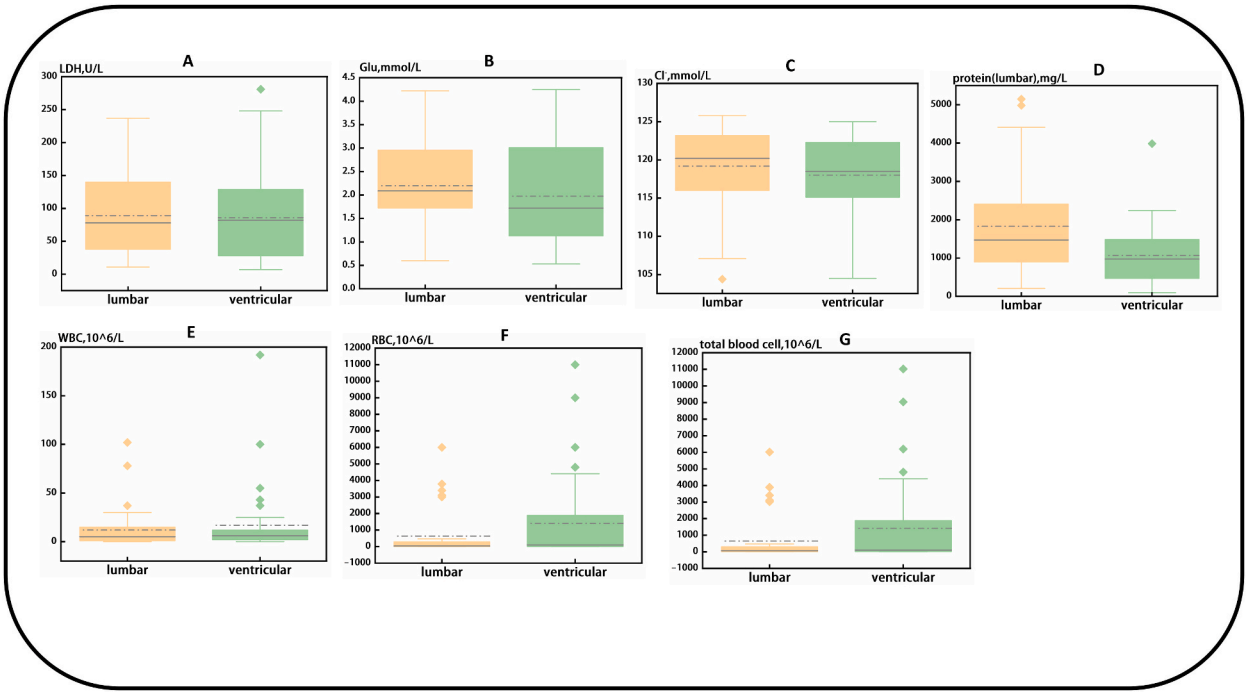

Fig. 2. Figures A, B, C, D, E, F, and G represent the overall differences in LDH, Glu, Cl-, protein, WBC, RBC, and tBC in ventricular versus lumbar cerebrospinal fluid for all patients, respectively. Presented using box-and-line plots. Within the boxes, dashed lines represent the means, while solid lines denote the medians.

Description and interpretation.

a **In the demographic aspect:** We analyzed 70 samples from 27 patients. The population was 28 % female, with an average gestational age of 31 weeks. The median time for sample collection was on the 21st day post-operation. The majority of the patients were preterm infants.

b **Regarding correlation:** All cerebrospinal fluid components showed a high degree of correlation, with the correlation coefficient appearing to be inversely proportional to the component's molecular weight.

c **In terms of differences:** The concentration of lactate dehydrogenase in the ventricles was higher than in the lumbar region early on, while in the later stages, its concentration in the lumbar region exceeded that in the ventricles. Cells were consistently higher in the ventricles than in the lumbar region. Protein levels were always higher in the lumbar region than in the ventricles. This may be due to the restrictive effect caused by the foramina of Magendie and Luschka and the effect of gravity.

d **Regarding regression equations:** With the exception of WBC, good regression equations were obtained for other metrics, consistent with the high correlation. The WBC may be an exception due to the sample population, as patients' WBC levels were extremely low, hindering mathematical modeling.

e **In terms of clinical outcomes:** All patients have survived to date, with 54.5 % of the patients undergoing ventriculoperitoneal shunting due to shunt dependency, and 7.4 % of the patients developed intracranial infections. Among these, one case was due to improper handling of the Ommaya reservoir post-discharge, and another was due to poor healing of a scalp surgical incision during hospitalization.

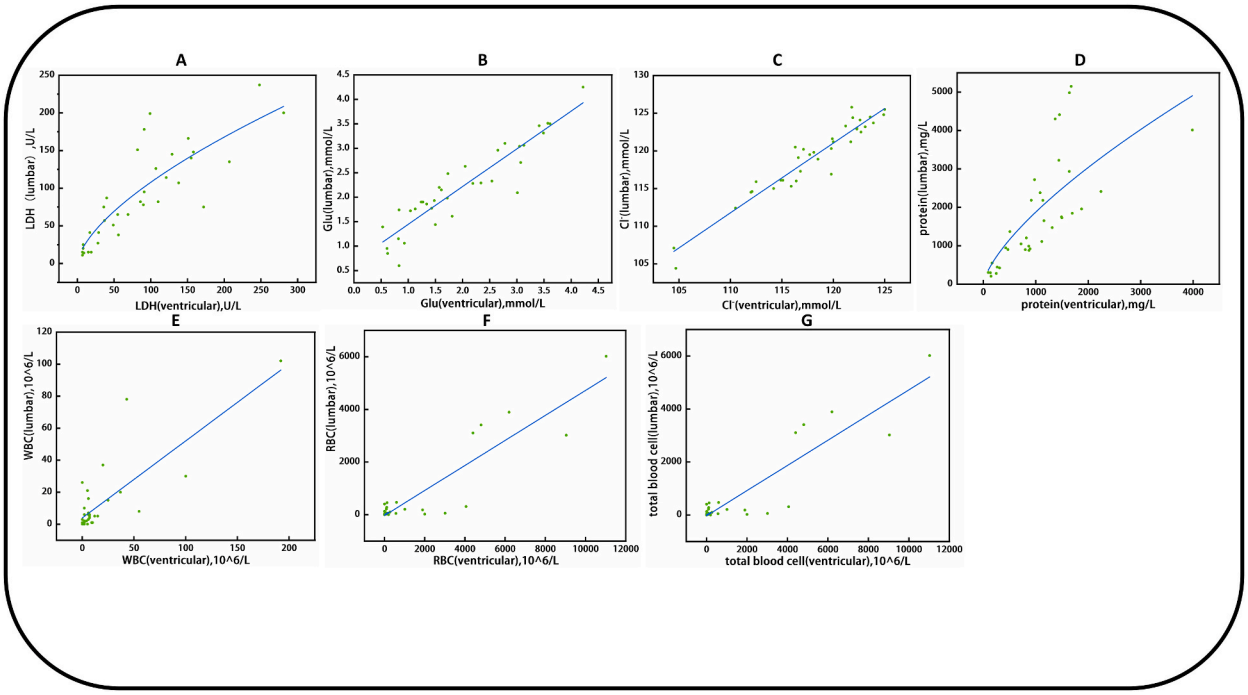

Fig. 3. Figures A, B, C, D, E, F, and G represent the correlation of LDH, Glu, Cl-, protein, WBC, RBC, and tBC in the patients' ventricular versus lumbar cerebrospinal fluid, respectively. Scattered points are the values corresponding to lumbar versus ventricular cerebrospinal fluid for each patient, solid lines correspond to the best-fit equations.

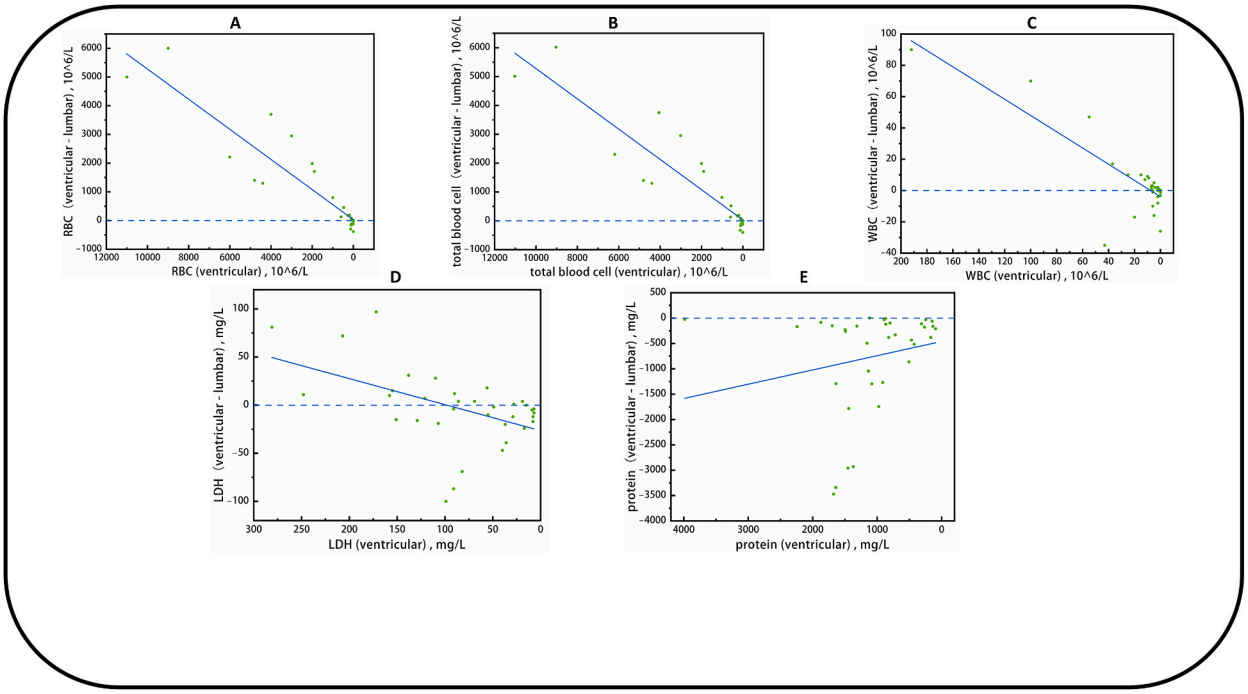

Fig. 4. Figures A, B, C, D, and E represent the differences in RBC, tBC, WBC, LDH, and protein in ventricular versus lumbar cerebrospinal fluid from the same patient, respectively. Scatter presentation was used for each corresponding value subscale. The solid line represents the linear fit. As all enrolled cases are patients with intraventricular hemorrhage (IVH), higher levels of cerebrospinal fluid blood cells, LDH, and protein indicate a shorter time since the bleeding event occurred.

Table 4
Regression equation between lumbar and ventricular CSF.

Item	R [2]	Regression equation	P value
LDH,U/L	0.838	Y = 3.382*x**0.740	0.000
Glu,mmol/L	0.859	Y = 0.768*x+0.680	0.000
Cl^-,mmol/L	0.921	Y = 1.480*x**0.920	0.000
protein,mg/L	0.785	Y = 3.940*x**0.872	0.000
WBC,10^6/L	0.649	Y = 0.481*x+3.960	0.000
RBC,10^6/L	0.826	Y = 0.476*x-34.762	0.000
total blood cell,10^6/L	0.826	Y = 0.476*x-30.203	0.000

Set the ventricular CSF data to x and the lumbar CSF data to Y, where x and Y are not less than 0. And set Y = f(x), if f(x) < 0, then Y = 0.

4. Key findings

1. Differences between Lateral Ventricle and Lumbar Spine:
   a **Higher in Lumbar Spine:** Chloride ion, glucose, protein, and Pandy's test.
   b **Lower in Lumbar Spine:** Erythrocytes and total cells.
2. No Significant Differences between Lateral Ventricle and Lumbar for:
   a Lactate dehydrogenase, leukocytes, occult blood, clots, clarity, and color.
3. Significant Correlations between Lateral Ventricles and Lumbar Vertebrae:
   a Observed for lactate dehydrogenase, glucose, chloride, protein, erythrocytes, leukocytes, total cells, Pandy's test, occult blood, clots, clarity, and color.
   b The correlation strength and equation fit degree were generally inversely related to the molecule's weight.
4. Regression Equations:
   a Well-fitted equations were derived for lactate dehydrogenase, glucose, chloride, protein, leukocytes, erythrocytes, and total cells.
5. Differences in ventricular CSF and lumbar CSF at different times and their relationship with the degree of obstruction:
   a As treatment progresses and time passes, the obstruction caused by the hematoma gradually diminishes, leading to a gradual reduction in the differences between the cerebrospinal fluid in the ventricles and lumbar spine.

5. Discussion

5.1. Correlation

Cushing's "classical bulk flow theory" provided a foundational understanding of cerebrospinal fluid (CSF) dynamics. This theory proposes the choroid plexus as the primary site of CSF secretion, leading to its flow through various brain structures and eventually its passive absorption into venous sinuses [12]. However, as with many classical models, limitations arise with advancing research and technological capabilities.

Bulat and colleagues introduced a nuanced understanding, the Bulat-Orešković-Klarica CSF hypothesis. This model proposed a distributed mechanism for CSF production and absorption, suggesting that CSF is not just produced by the choroid plexus (CP) but also results from fluid filtration between capillaries and the interstitial fluid [13,14].

Technological advancements, like the Time-SLIP technique employed by Yamada and team, have further refined our understanding of CSF dynamics [15–17]. Their research demonstrated an active exchange of CSF and emphasized the pulsatile nature of CSF flow, synchronized with cardiac rhythms [15,16]. More fascinatingly, they noted the significant impact of respiratory dynamics on CSF flow, sometimes even more influential than cardiac pulsations [17]. It was understood that CSF does not follow a simple unidirectional path like blood flow but exhibits a more oscillatory movement pattern [15]. Furthermore, inertia and gravity are also important driving forces for cerebrospinal fluid, and they also have a significant impact on the movement of cerebrospinal fluid [15].

Neeta and colleagues' PET imaging study further added a layer of intricacy to this understanding. Their work highlighted the potential role of the foramens Magendie and Luschka as restrictive bottlenecks, especially for larger molecules like antibodies [18].

Our research complements these insights. We observed high correlations across CSF tests, indicative of the pulsatile and interactive nature of CSF flow within the ventricles and the lumbar vertebrae. Interestingly, the correlation values declined with increasing molecular weights. This could be attributed to the challenges faced by larger molecules (like cellular structures and proteins) when navigating the restrictive foramens Magendie and Luschka [18]. This could potentially explain the variations in distribution patterns and concentrations across the CSF.

5.2. Difference

The understanding of cerebrospinal fluid (CSF) has long been rooted in textbook definitions, which were primarily centered around the secretion and reabsorption model. Recent revelations, spearheaded by the studies of Jeffrey et al., have provided intriguing insights into the sophisticated pathways involved in CSF circulation. This, along with the findings from the present study, creates a complex picture that helps us understand the behavior and movement of different cells, proteins, and molecules within the CSF.

1. **Challenging Traditional Models**:
   a The Jeffrey et al., 2012 study has been instrumental in emphasizing the recirculation of subarachnoid CSF within the brain parenchyma. This movement takes place in paravascular spaces, intermingling with the interstitial fluid (ISF) [19].
   b CSF flows into the brain using para-arterial pathways, exchanging contents with the ISF. This exchanged ISF is then expunged from the brain along para-venous channels [19].
   c This fluid movement, particularly within paravascular spaces and the brain interstitium, is made efficient via the AQP4 water channels in astrocytes, underscoring the importance of astrocytes in waste clearance [19].
2. **Contrast-enhanced MRI Findings**:
   a In their 2013 study, contrast-enhanced MRI became a tool to visualize CSF-ISF exchange. The team's innovative use of contrast agents allowed them to understand that molecular characteristics, especially molecular weight, significantly influenced the movement patterns of substances in the brain [20,21].
3. **Findings of the Present Study:**
   a **Cellular Level**: There were more red blood cells (erythrocytes), white blood cells (leukocytes), and overall cells in the brain's ventricles than in the lumbar pool. This significant difference in erythrocytes and total cells is due to the primary hemorrhage occurring in the brain's ventricles. The blood cells' movement is restricted through the foramen of Magendie and the foramen of Luschka [18], causing more cells in the ventricles than the lumbar spine. However, because there were no intracranial infections, the leukocyte count was consistently lower, and its difference wasn't statistically significant.
   b **Protein Level**: In Fig. 4 of this study, we have observed that the protein levels in the lumbar spine consistently surpass those in the cerebral ventricles. However, lactate dehydrogenase (LDH) levels in the lumbar spine are initially lower than those in the cerebral ventricles, but become higher in later stages. Logically, one would expect large-molecule proteins to be elevated in the cerebral ventricles compared to the lumbar spine due to the obstructive effect of hematoma on the cerebral aqueduct. However, infants with intraventricular hemorrhage (IVH) undergoing our treatment protocol undergo several stages before obtaining cerebrospinal fluid samples: 1. Transfer of patients to our hospital for treatment shortly after birth; 2. Improvement of coagulation function before surgery; 3. Postoperative management involving at least 3 days of Ommaya ventricular drainage. During this period, erythrocytes comprising the hematoma gradually lyse, and cerebrospinal fluid pathways reopen. The combined effects of gravity and the clearance of the paravascular pathways result in consistently higher protein levels in the lumbar spine compared to the cerebral ventricles [19]. Concurrently, erythrocyte lysis and release of LDH from brain tissue injury within the ventricles contribute to the initial elevation of LDH levels in the ventricles compared to those in the lumbar spine.
   c **Small Molecules**: The elevated levels of glucose and chloride ions in the lumbar spine over the cerebral ventricles are intriguing. This might be influenced by the distribution of transport proteins, the role of gravity [22,23], and the effective of the ability to traverse the Foramen of Magendie and the Foramen of Luschka effortlessly as small molecules.
   d **Assays and Appearance**: The lumbar Pandy's test results are in line with the observed CSF protein concentrations, validating its reliance on CSF protein levels. Observable features like blood presence, clots, transparency, and color did not exhibit significant differences between the two regions, possibly due to the difference that was not so great as to be recognized by the naked eye in RBC, protein, and hemoglobin concentrations.

In conclusion, this study, combined with the insights from Jeffrey et al., offers a deeper understanding of CSF dynamics. The findings can significantly impact clinical approaches to brain diseases and conditions and provide a strong foundation for future research in the field.

5.3. Simulate the distribution of compositions in the CSF of infants with IVH

For infants, previous studies have found that, under the influence of respiration and abdominal pressure, CSF exhibits synchronous pulsatile flow. Additionally, the foramens Magendie and Luschka have been shown to exert a restrictive effect on the flow of CSF [24].

Based on the data and conclusions from our study, we offer the following inferences about the distribution of CSF constituents in infants after IVH: Following IVH, a substantial number of red and white blood cells coexist with other CSF components within the ventricles. Due to the oscillatory movement of CSF [15,24], these substances are dispersed throughout the entire CSF system. However, the presence of the foramens Magendie and Luschka poses some resistance to the passage of larger molecules [18,24], such as proteins and cells, compared to smaller molecules like chloride ions and glucose. This results in a more uniform distribution of smaller molecules, where the correlation between their concentrations in the ventricles and lumbar CSF is significantly higher than that of larger molecules.

Additionally, the distribution of CSF components is influenced by gravity [15]. For most of the infant's life, the plane where the ventricles are located is higher than the lumbar region, leading to higher concentrations of chloride ions, glucose, and proteins in the lumbar CSF compared to the ventricles. The differential distribution of cells and lactate dehydrogenase (LDH) stems from the fact that the initial site of hemorrhage is within the ventricles. The passage of cells is significantly restricted by the foramens Magendie and Luschka, maintaining a higher cell count in the ventricles compared to the lumbar region. Moreover, the extensive lysis of blood cells within the ventricles releases a significant amount of LDH, explaining its higher concentration in the ventricles during the early stages of hemorrhage. As the number of ventricular blood cells decreases over time, the LDH produced from cell lysis also diminishes. Owing to gravitational effects, LDH demonstrates a similar distribution pattern to proteins, with concentrations in the lumbar region exceeding those in the ventricles.

5.4. Clinical applications

This research provides significant insights into the properties and correlations of cerebrospinal fluid (CSF) obtained from different regions, especially the ventricles and the lumbar spine. Here are the clinical implications.

1. **Estimation of Lumbar CSF Components**:
   a The high correlation between ventricular and lumbar CSF components suggests that tests on CSF obtained from the Ommaya reservoir can be used to approximate the attributes of lumbar CSF, reducing the need for direct lumbar puncture in many scenarios.
   b Critical components such as lactate dehydrogenase, glucose, chloride ions, protein, and cells have shown strong predictive regression equations, underscoring the reliability of these estimations.
   c Given the relationship between Pandy's test and protein concentration, Pandy's test can be effectively predicted using ventricular CSF.
2. **Consistency Over Time**:
   a Despite the study's focus on patients with intraventricular hemorrhage, the relationships between CSF components remained consistent for up to a year. This consistency suggests that fluid dynamics, rather than absorption, secretion, or pathology, may have a greater influence on CSF component distribution, especially for patients with unblocked CSF channels.
   b "The movement of CSF solutes by diffusion is much slower than CSF flow," a statement by Pardridge et al., which supports our conclusions [25].
3. **Generalizability**:
   a The CSF from the Ommaya reservoir mirrors that from other sources, including the extraventricular drain or ventriculoperitoneal shunt reservoir. This overlap ensures that the findings and applications are not confined to a single method of CSF extraction but can be applied across various medical procedures involving ventricular CSF retrieval.
4. **Real-time Monitoring and Treatment Efficacy**:
   a Regular CSF extraction through the Ommaya reservoir can serve as a diagnostic tool to gauge the tendency for infection to occur during the treatment of ventricular hemorrhage. For instance, an elevated leukocyte count, especially when it comprises a significant proportion, indicates a heightened risk of infection, allowing for proactive medical intervention.
5. **Advantages for Pediatric Patients**:
   a For children recovering from ventricular hemorrhage and facing potential hydrocephalus, the study's findings offer an alternative to invasive lumbar punctures. Since elevated CSF protein and cell levels can complicate ventriculoperitoneal shunt procedures, data from the Ommaya reservoir can guide clinical decisions, reducing associated pain and risks in pediatric patients.
6. **Refinement of Clinical Guidelines**:
   a Over the long term, understanding the CSF transformation equations between the lumbar spine and ventricles for diverse patient groups will aid in enhancing clinical guidelines. This clarity will help mitigate ambiguities and discrepancies arising due to different CSF source locations, ensuring standardized, informed medical decisions.

In essence, the research offers a promising avenue to refine CSF-associated medical practices, providing both direct clinical applications and broader implications for enhanced patient care, especially in scenarios where low-risk invasive methods are paramount.

6. Conclusion

In infants with intraventricular hemorrhage and unobstructed cerebrospinal fluid (CSF) channels, a robust correlation was noted between ventricular CSF sourced via the Ommaya reservoir and lumbar CSF. This correlation tended to be inversely related to molecular weight, with smaller molecular weights showing lesser disparities. Ventricular CSF data could anticipate lumbar CSF trends, and using regression equations with Ommaya-obtained CSF, one can derive approximate values for lumbar CSF.

Limitation

The findings of this study, centered on the cerebrospinal fluid (CSF) in infants with intracerebroventricular hemorrhage, are marked by several limitations.

1. **Specificity to Affected Infants**:
   a The study is anchored in data from infants with intracerebroventricular hemorrhage. Their CSF secretion and absorption patterns deviate from those observed in healthy children. Consequently, the derived transformation equation isn't universally adaptable and lacks applicability to the general infant population.
2. **Retrospective Design & Data Constraints**:
   a Operating with a retrospective methodology means potential biases stemming from pre-existing data without the advantage of real-time adjustments.
   b The data pool, being restricted in size, impedes the transformation equation's precision. The study, therefore, offers a broader approximation rather than pinpoint accuracy for CSF data.
3. **Gaps in Understanding CSF Dynamics**:

a The intricate processes of CSF secretion and absorption remain only partially understood in contemporary medical science. Current theories, while foundational, carry certain limitations. As such, pinning down the variability of CSF composition across diverse anatomical locales using a singular theoretical lens is problematic.

4. **CSF Volume Inconsistencies in Infants**:
   a Given the diminutive total CSF volume in infants, even minor volume variations can manifest as significant data discrepancies. As every milliliter of CSF can yield different lab results, subtle fluctuations in the extracted fluid volume can introduce inconsistencies, impacting the study's overall reliability.

Ethics statement

This retrospective study complies with all regulations and rules concerning the protection of human subjects and the committee review of clinical research. The research and its protocol were approved by the Medical Research Ethics Committee of Guangdong Women and Children Hospital (Approval No. 202401013) and conducted in accordance with the principles of the Declaration of Helsinki. Guardians (parents) of the patients from whom cerebrospinal fluid data were involved for the study provided written informed consent, agreeing to the use of clinical data and sample data for scientific research. Since the patients involved in the study were infants, lacking the capacity for autonomous communication and decision-making, it was not possible to obtain consent directly from the patients themselves.

Data availability statement

All data generated or analyzed during this study are included in this published article and its supplementary information file "raw data.xlsx".

CRediT authorship contribution statement

Xingyu Cao: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Data curation, Conceptualization. **Jiazhang Lu:** Writing – review & editing, Validation, Supervision, Investigation, Formal analysis. **Chengxian Chen:** Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Jian Gui:** Software, Resources, Methodology, Investigation, Funding acquisition, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32252.

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