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Clinical Utility of CSF Correction Factors for Traumatic Lumbar Puncture in Adults

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Abstract

Objectives

To identify indicators of false pleocytosis in adults with traumatic lumbar puncture (LP), and determine specificities and sensitivities of commonly used CSF correction factors.

Methods

Adults who underwent 4-tube CSF collection were reviewed. Study inclusion required elevated tube 1 red blood cell (RBC) count, tube 1 pleocytosis, and normalized tube 4 RBC count. Tube 4 white blood cell (WBC) count served as the reference standard. Specificities and sensitivities of 3 correction factors (1 WBC:500 RBC, 1 WBC:1000 RBC, and 1 WBC:1500 RBC) were calculated.

Results

One hundred ninety-five adults were included. Among them, 106 (54%) had false tube 1 pleocytosis; these patients had a significantly higher median CSF RBC count and lower median CSF WBC count than those with true tube 1 pleocytosis. Specificities and sensitivities of correction factors ranged from 71.7% to 29.2% and 84.3% to 97.8%, respectively; 1 WBC:500 RBC had highest specificity for pleocytosis, while 1 WBC:1500 RBC had highest sensitivity. Irrespective of correction factor used, false-positive and false-negative determinations of pleocytosis were usually mild (≤20 WBCs/μL).

Discussion

Indicators of false pleocytosis in adults with traumatic LP include bloodier CSF and milder pleocytosis, suggesting that correction factors are most useful in such cases. Across correction factors, an expected specificity/sensitivity tradeoff is observed. Corrected CSF WBC counts suggesting only mild pleocytosis should be interpreted cautiously.

PRACTICAL IMPLICATIONS

When applying commonly used CSF correction factors in adults with traumatic LP, clinicians should be aware that corrected CSF WBC counts suggesting only mild pleocytosis merit cautious interpretation to avoid patient misdiagnosis.

Introduction

Lumbar puncture (LP) to assess for CSF pleocytosis is a cornerstone of the diagnostic evaluation for infectious, inflammatory, and malignant CNS diseases. A traumatic LP, which introduces extra red blood cells (RBCs) and white blood cells (WBCs) from the peripheral blood into the CSF because of needle trauma, commonly occurs in clinical practice and can confound CSF WBC interpretation.[1-3] To estimate the "true" CSF WBC in such cases, calculators incorporating peripheral and CSF cell counts are available; however, if the peripheral RBC and WBC counts are not abnormally low or high, convenient CSF correction factors have been proposed that are in widespread clinical use and are commonly taught to

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medical trainees.[4,5] These correction factors, which range from subtracting 1 WBC for every 500 RBCs (1 WBC:500 RBC correction factor) to subtracting 1 WBC for every 1500 RBCs (1 WBC:1500 RBC correction factor), are considered to be a "good rule of thumb" for estimating the true CSF WBC count following traumatic LP.[4,5] Yet, despite their ubiquitous use in clinical practice, evaluations of these correction factors are sparse and focus primarily on meningitis diagnosis in children.[1,6] Given the routineness with which LP is performed to help diagnose a variety of CNS diseases in adults, it would be valuable to examine the clinical utility of these correction factors in this population. At our institution, we commonly perform 4-tube CSF collections and send both tube 1 and tube 4 for determination of CSF RBC and WBC counts. In cases of traumatic LP with tube 1 pleocytosis, tube 4 is considered to reflect the true CSF WBC count if the peripheral blood introduced in tube 1 has cleared by the time of tube 4 collection; in such cases, the true tube 4 CSF WBC count could intuitively serve as the reference standard against which one could compare uncorrected and corrected tube 1 CSF WBC counts. We therefore identified adults who had tube 1 pleocytosis in the context of traumatic LP and clearance of peripheral blood in tube 4, to evaluate the clinical utility of commonly used CSF correction factors.

Methods

All patients who underwent CSF collection by LP between January 2012 and July 2023 at London Health Sciences Centre were included in this retrospective study if they had (1) age at time of LP ≥18 years, (2) normal peripheral RBC count (defined as 4.00–6.50 × 10^6 RBCs/μL), (3) normal peripheral WBC count (defined as 4.0–10.0 × 10^3 WBCs/μL), (4) 4-tube CSF collection with CSF RBC and WBC counts from both tubes 1 and 4, (5) elevated tube 1 CSF RBC count (defined as ≥500 RBCs/μL) compatible with traumatic LP, (6) tube 1 pleocytosis (defined as >5 WBCs/μL) that would merit consideration of a CSF correction factor, and (7) normalized tube 4 CSF RBC count (defined as <500 RBCs/μL) that would be compatible with peripheral blood clearance. Normal peripheral WBC and RBC counts were based on institutional reference ranges for adults. In patients who had multiple peripheral blood cell counts performed, only the one performed closest to time of LP was considered. Determinations of WBC and RBC counts were performed using the Beckman Coulter DxH 800 Hematology Analyzer (January 2012–March 2018) and Sysmex XN-1000 Hematology Analyzer (April 2018–July 2023). Severity of pleocytosis was stratified into mild (6–20 WBC/μL), moderate (21–99 WBC/μL), or severe (≥100 WBC/μL). The presence or absence of pleocytosis in tube 4 was treated as the reference standard against which tube 1 pleocytosis was compared and was used to determine the specificities and sensitivities of different CSF correction factors. Continuous and categorical variables were compared using the Mann-Whitney *U* test and Fisher exact test, respectively. A *p* value less than 0.05 was considered statistically significant. This study was approved by the Western University Research Ethics Board.

Results

We identified 195 adults with tube 1 pleocytosis in the context of traumatic LP who met criteria for study inclusion (Figure). The median age was 48 years (range: 18–93 years), and 93 (48%) were female. When compared against the tube

Figure Frequencies of True and False Tube 1 Pleocytosis Following Use of Cerebrospinal Fluid Correction Factors for Traumatic Lumbar Puncture

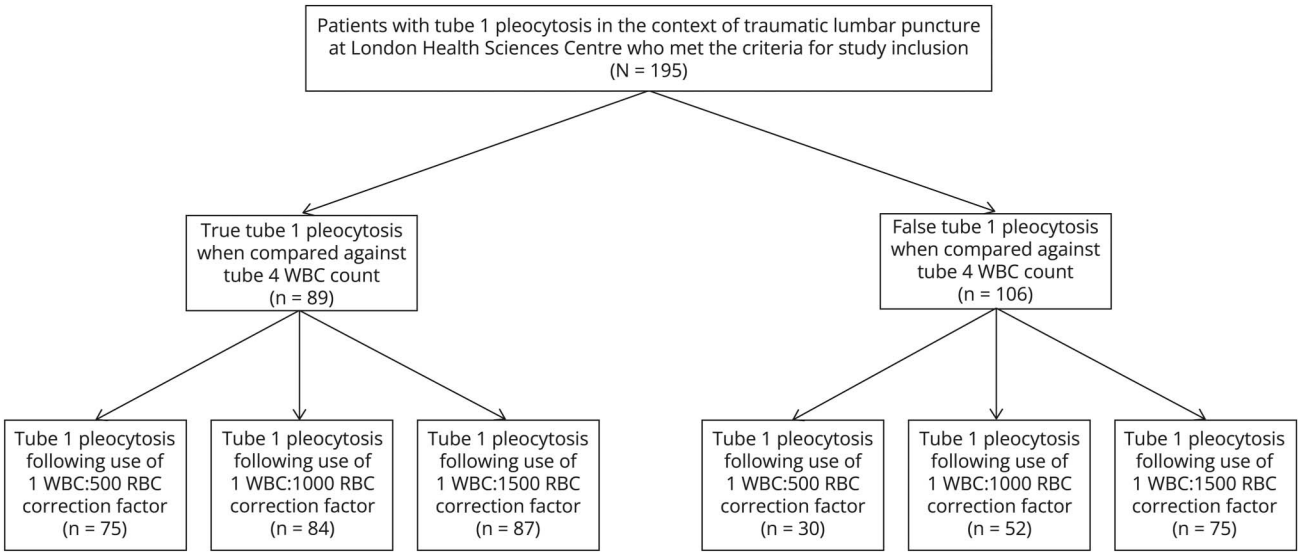

Table 1 Comparison of True vs False Tube 1 Pleocytosis in Adults With Traumatic Lumbar Puncture

	All adults with traumatic LP and tube 1 pleocytosis (N = 195)	Adults with traumatic LP and true tube 1 pleocytosis (N = 89)	Adults with traumatic LP and false tube 1 pleocytosis (N = 106)	*p* Value
Median age in years (range)	48 (18–93)	45 (18–89)	53 (18–93)	0.16
Female (%)	93 (48)	40 (45)	53 (50)	0.57
Median tube 1 CSF RBC count/μL (range)	1500 (503–234000)	1210 (513–234000)	2091.5 (503–77500)	0.006
Median tube 1 CSF WBC count/μL (range)	13 (6–3408)	32 (6–3408)	8 (6–65)	<0.001

Abbreviations: LP = lumbar puncture; RBC = red blood cell; WBC = white blood cell.

4 CSF WBC count, 106/195 (54%) were classified as having false tube 1 pleocytosis. Compared with those with true tube 1 pleocytosis, patients with false tube 1 pleocytosis had a significantly higher median CSF RBC count (2091.5 RBCs/μL vs 1210 RBCs/μL, $p = 0.006$) and a significantly lower median CSF WBC count (8 WBCs/μL vs 32 WBCs/μL, $p < 0.001$) (Table 1). The specificities and sensitivities of different CSF correction factors for pleocytosis, as well their proportions of false-positive and false-negative determinations of pleocytosis stratified by severity, are shown in Table 2. Specificities and sensitivities ranged from 71.7%–29.2% and 84.3%–97.8%, respectively; the 1 WBC:500 RBC correction factor had highest specificity for pleocytosis, while the 1 WBC:1500 RBC correction factor had highest sensitivity. Irrespective of the correction factor used, false-positive and false-negative determinations of pleocytosis were usually mild (Table 2).

Discussion

We found that 54% of pleocytosis occurring in the context of traumatic LP was false. Those with false pleocytosis had significantly higher median CSF RBC counts and lower median CSF WBC counts than those with true pleocytosis, indicating that correction factors are of greatest utility when applied to patients with traumatic LP who have bloodier CSF and milder pleocytosis. On calculating specificities and

Table 2 Specificities and Sensitivities of CSF Correction Factors for Traumatic Lumbar Puncture

	1 WBC:500 RBC correction factor applied to tube 1 pleocytosis in the context of traumatic LP	1 WBC:1000 RBC correction factor applied to tube 1 pleocytosis in the context of traumatic LP	1 WBC:1500 RBC correction factor applied to tube 1 pleocytosis in the context of traumatic LP
Specificity for true pleocytosis (95% CI)	71.7% (62.1%–80.0%)	50.9% (41.1%–60.8%)	29.2% (20.8%–39.9%)
Proportion of false-positives that suggested mild pleocytosis (%)	27/30 (90%)	46/52 (88%)	67/75 (89%)
Proportion of false-positives that suggested moderate pleocytosis (%)	3/30 (10%)	6/52 (12%)	8/75 (11%)
Proportion of false-positives that suggested severe pleocytosis (%)	0/30 (0%)	0/52 (0%)	0/75 (0%)
Sensitivity for true pleocytosis (95% CI)	84.3% (75.0%–91.1%)	94.4% (87.4%–98.2%)	97.8% (92.1%–99.7%)
Proportion of false-negatives that missed mild pleocytosis (%)	13/14 (93%)	5/5 (100%)	2/2 (100%)
Proportion of false-negatives that missed moderate pleocytosis (%)	1/14 (7%)	0/5 (0%)	0/2 (0%)
Proportion of false-negatives that missed severe pleocytosis (%)	0/14 (0%)	0/5 (0%)	0/2 (0%)

Abbreviations: LP = lumbar puncture; RBC = red blood cell; WBC = white blood cell.

sensitivities of commonly used correction factors, an expected tradeoff between specificity and sensitivity was observed. Yet, irrespective of the correction factor used, false-positive and false-negative determinations of pleocytosis were usually mild. This is reassuring about use of correction factors when evaluating for CNS diseases typically associated with severe pleocytosis, such as bacterial meningitis. However, the potential for false-positive and false-negative determinations of mild pleocytosis when using correction factors is a concern when evaluating for CNS diseases typically associated with mild-to-moderate elevations in CSF WBC count, such as autoimmune encephalitis.[7,8] Much like how overinterpreting nonspecific serum antibodies has been found to contribute to autoimmune encephalitis misdiagnosis in adults,[9] overinterpretation of mild pleocytosis following use of correction factors could be similarly problematic. For this reason, corrected CSF WBC counts in such scenarios should be viewed critically, particularly if discordant with other clinical or ancillary test data. If uncertainty persists surrounding the clinical relevance of a corrected CSF WBC count, then repeat LP should be considered, ideally with 4-tube collection so that the tube 4 WBC count is available if traumatic LP reoccurs.

Limitations to our study include that it is single-center, which may limit generalizability. We did not attempt to determine an "optimal" CSF correction factor because preference may be given to either specificity or sensitivity of a diagnostic tool depending on the clinical context; for this reason, we instead chose to illustrate the specificity/sensitivity tradeoff of commonly used correction factors to help inform their selection in clinical practice. Despite normalized RBC counts, tube 4 WBC counts may still be an imperfect reference standard for the presence or absence of pleocytosis, due to the potential for natural variability of CSF WBC count across tubes and the imperfect accuracy of hematology analyzers.[10] Recognizing these limitations, our study indicates that CSF correction factors for traumatic LP are of greatest utility in patients with bloodier CSF and milder pleocytosis. Although correction factors are unlikely to misclassify moderate-to-severe pleocytosis, corrected WBC counts suggesting only mild pleocytosis should be interpreted with caution.

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