Testing for Meningitis in Children with Bronchiolitis

Michael Stefanski, MD, MPH; Ronald Williams, MD, FAAP, FACP; George McSherry, MD; Joseph Geskey, DO, MBA

Perm J 2014 Fall;18(4):16-19

http://dx.doi.org/10.7812/TPP/14-015

Abstract

Viral bronchiolitis accounts for almost 20% of all-cause hospitalizations of infants (ie, children younger than age 1 year). The annual incidence of fever in viral bronchiolitis has been documented at 23% to 31%. However the incidence of concurrent serious bacterial infections is low (1%-7%), with meningitis occurring in less than 1% to 2% of cases, but lumbar puncture is performed in up to 9% of viral bronchiolitis cases. To our knowledge, no study has examined clinical factors that influence a physician's decision to perform a lumbar puncture in the setting of viral bronchiolitis.

We present a retrospective, case-control study of hospitalized infants younger than one year diagnosed with viral bronchiolitis who underwent lumbar puncture as part of an evaluation for meningitis. The objective of the study was to determine clinical factors that influence a physician's decision to perform a lumbar puncture in the setting of viral bronchiolitis. Although the presence of apnea, cyanosis, meningeal signs, positive urine culture results, and young age were factors found to be preliminarily associated with the performance of a lumbar puncture in the setting of bronchiolitis, young age was the only significant clinical factor found after multivariable regression; no other demographic, clinical, laboratory, or radiologic variables were found to be significant.

Introduction

Viral bronchiolitis is the most common cause of lower respiratory tract infection in children younger than age 1 year, accounting for almost 20% of all-cause infant hospitalizations.[1,2] The burden of disease is most prevalent in the fall and winter months, with peak incidence occurring in children between ages 2 to 6 months.[3,4] The clinical course of viral bronchiolitis is characterized by an upper respiratory prodrome and subsequent lower respiratory tract symptoms and signs, including cough, wheeze, increased respiratory rate (RR), and increased effort. The incidence of fever in the setting of bronchiolitis has been documented at 23% to 31%.[5]

When fever develops, so too does the dilemma of determining whether the fever is a consequence of the viral infection or a superimposed serious bacterial infection (SBI). In bronchiolitis patients, the incidence of concurrent SBI is low (1%-7%), with most being urinary tract infections (1%-5.5%).[5-9] Although the sequelae of bacterial meningitis are well documented and carry substantial morbidity and mortality rates, the incidence of concurrent meningitis in infants and children with clinical viral bronchiolitis has been reported to be less than 1% to 2%.[5-13]

In the appropriate clinical setting, performance of a lumbar puncture (LP) is necessary to make the diagnosis of meningitis and to ensure appropriate treatment, but this must be weighed against the adverse effects and potential yield of the study. The performance of an LP is anxiety provoking to parents[14] and has been reported to contribute to parental dissatisfaction with the care their infant receives.[15] Moreover, physicians must balance the very small chance of meningitis occurring in viral bronchiolitis against the possible iatrogenic complications, including morbidity of LP, intravenous line placement, and unnecessary use of broad-spectrum antibiotics. We examined clinical factors that may influence a physician's decision to perform an LP in the setting of viral bronchiolitis.

Methods

Study Design and Setting

A retrospective, case-control study of 42 hospitalized infants younger than age 1 year who had International Classification of Diseases, Ninth Revision (ICD-9) codes of bronchiolitis (ICD-9: 466.11 or 466.19) and underwent LP were matched 1:4 with children who had ICD-9 codes of bronchiolitis without LP (168 controls) from January 1, 2001, through December 31, 2011 (Figure 1). The study was conducted at Penn State Children's Hospital, an academic tertiary care children's hospital located in Hershey, PA. The Penn State Milton S Hershey Medical Center's institutional review board approved this study with waiver of informed consent.

Data and Study Definitions

A standardized abstraction form was used to collect the following data from both cohorts of hospitalized patients: age; sex; prematurity; chronic lung disease; insurance type; admitting service (critical care vs general pediatrics); presence or absence of apnea, cyanosis, tachypnea, fever, and meningeal signs; results of urine culture, blood culture, chest radiographs, respiratory syncytial virus (RSV) testing, cerebrospinal fluid culture, and white blood cell count if obtained; and hospital length of stay.

The presence of prematurity and chronic lung disease were noted from the medical history. Insurance type was classified as commercial or governmental. Patients who were admitted to either the neonatal intensive care unit or the pediatric intensive

Michael Stefanski, MD, MPH, is an Internist and Pediatrician at Penn State University Hershey Medical Center in PA. E-mail: mstefanski@hmc.psu.edu. **Ronald Williams, MD, FAAP, FACP,** is a Professor of Pediatrics and Internal Medicine at Penn State Hershey Children's Hospital in PA. E-mail: rwilliams@hmc.psu.edu. **George McSherry, MD,** is a Pediatrician in the Division of Infectious Diseases at Penn State Hershey Children's Hospital in PA. E-mail: gmcsherry@hmc.psu.edu. **Joseph Geskey, DO, MBA,** is Vice President of Medical Affairs at Doctors Hospital in Columbus, OH. E-mail: joseph.geskey@ohiohealth.com.

care unit were classified as critical care; otherwise, patients were classified as general pediatrics. The presence of apnea and cyanosis were noted as present if these terms were noted in the medical record. The definition of tachypnea was based on age-defined RR of the World Health Organization guidelines: (< 2 months, RR ≥ 60/min; 2-12 months, RR ≥ 50; 1-5 years, RR ≥ 40). Fever was defined as a temperature of 38.0˚C or greater. Meningeal signs were considered present if there was a notation of neck stiffness, bulging fontanel, inconsolable irritability/crying, Kernig sign, or Brudzinski sign.

A urinary tract infection was defined by the presence of more than 50,000 colony-forming units of a single pathogenic organism from a urine culture obtained by transurethral catheterization or more than 1000 colony-forming units obtained by suprapubic aspiration. A bloodstream infection was defined as a known bacterial pathogen from the blood whereas bacterial meningitis was defined as the isolation of a bacterial pathogen from the cerebrospinal fluid. Chest radiographs that were interpreted as having an alveolar infiltrate, air bronchogram, or consolidation were classified as having pneumonia (World Health Organization criteria).[16] Bronchiolitis was classified as RSV if a positive result was obtained from either antigen testing or culture from nasal secretions.

Statistical Analyses

Descriptive statistics were prepared for all variables including frequencies and percentages for categorical variables (eg, sex, apnea) and means, standard deviations, and quartiles for quantitative variables (eg, white blood cell count, length of stay). Age was considered as both a quantitative (age in days) and categorical (< 30, 30-59, 60-179, and ≥ 180 days) variable. Bivariate analyses were conducted to assess the relationship between each variable and LP using χ^2 or Fisher exact tests for categorical variables and logistic regression for quantitative variables. All variables showing a marginal ($p < 0.10$) or significant ($p < 0.05$) relationship with LP were included in a multivariable regression model, and backward elimination was used to arrive at a final model, keeping all significant variables. To further examine the effect of age on the findings, cases were matched on age category to controls in a 1:1 ratio using a greedy algorithm. Generalized estimating equations, an extension of logistic regression that takes into account the matching, were used to examine the relationship of LP to the remaining variables.[17,18] All analyses were conducted using SAS, version 9.2 (SAS Institute Inc, Cary, NC).

Results

None of the patients with acute bronchiolitis had documented meningitis. However, the presence of apnea, cyanosis, meningeal signs, positive urine culture results, and young age were factors associated with the performance of an LP in bronchiolitis (Table 1). The presence of a fever and tachypnea were not associated with testing for meningitis. RSV status also did not influence the decision to perform an LP, nor did admission to a critical care service. There was a significant difference in the mean age (44 days) of the LP cohort compared with the mean age of the control group (141 days [$p < 0.001$]).

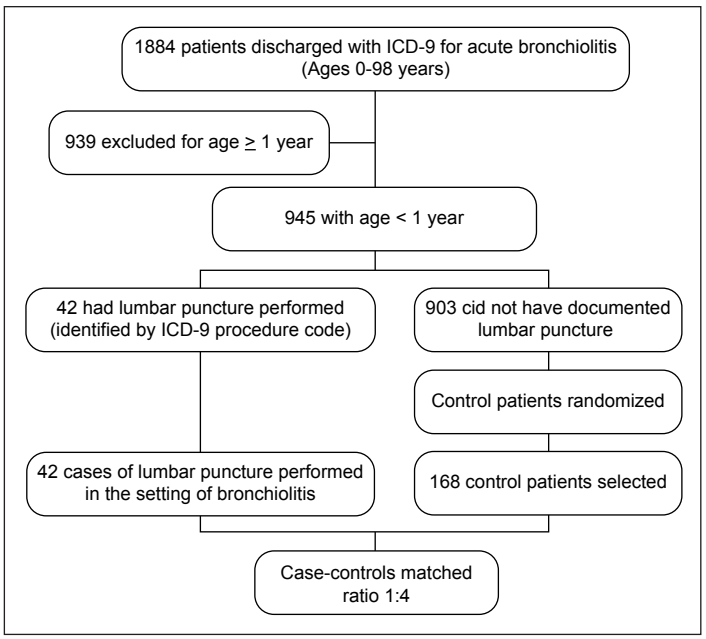

Figure 1. Selection of case-control participants. A total of 42 patients were selected as cases on the basis of International Classification of Diseases, Ninth Revision (ICD-9) procedure code of lumbar puncture. Each case was matched with 4 control patients who were selected at random from the remainder of the cohort meeting inclusion criteria of an ICD-9 discharge diagnosis of acute bronchiolitis without documentation of a lumbar puncture being performed during the hospitalization. The total number of patients studied was 210.

Table 1. Bivariate analysis of factors associated with lumbar puncture in acute bronchiolitis

Variable	Controls, n = 168 (%)	Cases, n = 42 (%)	p value[a]
Clinical features			
Apnea	18 (10.7)	14 (33.3)	0.0003
Cyanosis	22 (13.1)	14 (33.3)	0.0019
Tachypnea	99 (59.3)	23 (54.8)	0.5953
Fever	78 (46.4)	21 (50.0)	0.6783
Meningeal signs	2 (1.2)	5 (11.9)	0.004
Diagnostic studies			
Positive urine culture	2/41[b] (3.9)	6/32[b] (18.8)	0.0501
Positive blood culture	5/69[b] (7.2)	1/37[b] (2.7)	0.6625
Positive chest radiograph	14/148[b] (9.5)	4/40[b] (10.0)	> 0.99
Positive RSV	74/143[b] (51.7)	25/42[b] (59.5)	0.3744
WBC count	12.6 (0.50-49.00[c])	11.2 (4.00-28.40)	0.1915
Demographic characteristics			
Age in days	141 (1-336[d])	44 (7-210[d])	< 0.0001
Male sex	102 (60.7)	25 (59.5)	0.8878
Prematurity	44 (26.2)	14 (33.3)	0.3544
Chronic lung disease	18 (10.7)	3 (7.1)	0.4902
Commerical insurance	86 (51.2)	24/41[e] (58.5)	0.699
Admit service critical care	16 (9.5)	8 (19.0)	0.1026

[a] p value ≥ 0.10 included in multivariable regression model.
[b] Positive results out of number tested.
[c] Range of WBC counts in the tested population.
[d] Age range in days.
[e] 24 cases of 41 total cases with documented insurance had commercial insurance.
RSV = respiratory syncytial virus; WBC = white blood cell count.

Table 2. Adjusted multivariable regression model for performance of lumbar puncture in acute bronchiolitis

Variable	95% CI	p value
Apnea	0.232-4.303	0.3883
Cyanosis	0.421-8.344	0.999
Meningeal signs	0.277-79.57	0.2838
Positive urine culture result	0.558-17.776	0.1940
Age in days	0.964-0.994	0.0058

CI = confidence interval.

Table 3. Multivariable analysis with backward elimination based on age categories for performance of lumbar puncture in children with acute bronchiolitis

Variable	95% CI	p value
Apnea	0.179-4.085	0.8455
Cyanosis	0.526-12.126	0.2470
Meningeal signs	0.238-72.473	0.3287
Positive urine culture result	0.475-15.711	0.2603
Age 30-59 days vs < 30 days	0.169-2.062	0.4092
Age 60-179 days vs < 30 days	0.026-0.452	0.0023
Age ≥ 180 days vs < 30 days	0.011-1.032	0.0533

CI = confidence interval.

In addition to the significant quantitative difference in age between the 2 groups, there was a significant difference in the categorical age variable. The number (and percentage) of the 42 infants who underwent lumbar testing at less than age 30 days, 30-59 days, 60-179 days, and 180 days or older were 18 (42.8%), 13 (31.0%), 10 (23.8%), and 1 (2.4%), respectively ($p < 0.001$). However, the presence of fever combined with age as either a quantitative variable (age in days) or a categorical value (< 30 days, 30-59 days, 60-179 days, and ≥ 180 days) was not associated with performance of an LP (data not shown).

After the multivariable regression model and backward elimination were performed, the only variable that remained significant was age (Table 2). Similarly, when categorical values of age were used, younger infants were more likely to undergo performance of an LP than were older infants (Table 3).

… the most accurate diagnostic combination is unclear, particularly in this young age group.

When cases were matched on age category to controls and general estimating equations were used to examine the relationship of LP to the remaining variables, there were no significant results.

Case controls were well matched regarding age as there was no significant difference in the age of the 168 controls versus the remaining 777 infants who met control criteria but were not selected for the study. The median length of stay for patients who underwent an LP was 5 days versus 4 days for those who did not undergo the procedure, though this difference was not found to be statistically significant.

Discussion

Although the likelihood of having meningitis in acute bronchiolitis is negligible, infants still undergo LP testing to exclude a serious infection. To our knowledge, no previous studies have examined why hospitalized young infants with bronchiolitis undergo LP to exclude meningitis. A recent study reported that children with influenza were more likely to undergo LP testing than children with other respiratory illnesses, but the percentage of children with RSV was not reported.[19] The only other significant predictor of an LP in this study was age 3 months or younger; there were no cases of meningitis.

Despite its low yield, a common reason for screening for SBI in infants is the presence of fever. A systematic review of 11 studies reporting rates of SBIs in infants younger than 90 days reported a weighted rate of urinary tract infection of 3.3%, with no cases of reported bacteremia in 8 of 11 studies and no reported cases of meningitis at all.[9] As a result, these authors and others have suggested a more selective approach to screening for SBI in young infants with bronchiolitis,[20,21] particularly if they are RSV-positive.[7,8] However, there have been at least 2 case reports of infants with RSV bronchiolitis and meningitis.[11,22] To understand the reasons that physicians elect to perform a procedure for a condition with such an infrequent occurrence, we sought to ascertain whether there were any demographic, clinical, laboratory, or radiologic variables that would be associated with the clinical decision to perform an LP.

Our results suggest the most significant factor associated with performing an LP is young age. The presence of fever in young infants and a positive RSV test result did not influence the decision to perform an LP. Although the study was not designed to determine whether a clinician should perform an LP in hospitalized children with bronchiolitis, it is reassuring that despite a high rate of urinary tract infection and bacteremia no child had documented meningitis.

However, there are several limitations to our study. Even though we used clinical variables that might influence a clinician to perform an LP, the most accurate diagnostic combination is unclear, particularly in this young age group.[23] We also did not assess whether these specific demographic, clinical, and laboratory variables would lead physicians to perform more or fewer LP procedures compared with other screening tools that physicians in academic centers use in the evaluation of young febrile infants, such as the Rochester, NY;[24] Philadelphia, PA;[25,26] Boston, MA;[27] or Pittsburgh, PA[28] criteria. These screening tools use the presence of fever to determine further evaluation, but there have been reports of infants with meningitis who either do not have a fever or do not appear sick.[20] Another limitation of our study is that we retrospectively analyzed administrative data so we cannot exclude the possibility that cases of bronchiolitis, meningitis, and LP were missed owing to inappropriate coding or incomplete documentation by the physician. These limitations portend further investigation, particularly expanding the case-control study to a multicenter evaluation with other children's hospitals. Given that an infant's initial evaluation often occurs in the Emergency Department, cross-referencing inpatient data with emergency room data can further highlight the clinical factors that determine the performance of an LP in the setting of viral bronchiolitis.

Conclusion

Despite these limitations we can conclude that LPs are still performed in hospitalized children with acute bronchiolitis, particularly in young infants, despite an extremely low likelihood of having a positive result, which may lead to a longer hospital length of stay, increased parental anxiety, and unnecessary exposure to broad-spectrum antibiotics. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgment

Mary Corrado, ELS, provided editorial assistance.

References

1. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med 2009 Feb 5;360(6):588-98. DOI: http://dx.doi.org/10.1056/NEJMoa0804877.
2. Yorita KL, Holman RC, Sejvar JJ, Steiner CA, Schonberger LB. Infectious disease hospitalizations among infants in the United States. Pediatrics 2008 Feb;121(2):244-52. DOI: http://dx.doi.org/10.1542/peds.2007-1392.
3. Mansbach JM, Pelletier AJ, Camargo CA Jr. US outpatient office visits for bronchiolitis, 1993-2004. Ambul Pediatr 2007 Jul-Aug;7(4):304-7. DOI: http://dx.doi.org/10.1016/j.ambp.2007.03.006.
4. Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980-1996. JAMA 1999 Oct 20;282(15):1440-6. DOI: http://dx.doi.org/10.1001/jama.282.15.1440.
5. Melendez E, Harper MB. Utility of sepsis evaluation in infants 90 days of age or younger with fever and clinical bronchiolitis. Pediatr Infect Dis J 2003 Dec;22(12):1053-6. DOI: http://dx.doi.org/10.1097/01.inf.0000101296.68993.4d.
6. Levine DA, Platt SL, Dayan PS, et al; Multicenter RSV-SBI Study Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections. Pediatrics 2004 Jun;113(6):1728-34. DOI: http://dx.doi.org/10.1542/peds.113.6.1728.
7. Purcell K, Fergie J. Concurrent serious bacterial infections in 2396 infants and children hospitalized with respiratory syncytial virus lower respiratory tract infections. Arch Pediatr Adolesc Med 2002 Apr;156(4):322-4. DOI: http://dx.doi.org/10.1001/archpedi.156.4.322.
8. Titus MO, Wright SW. Prevalence of serious bacterial infections in febrile infants with respiratory syncytial virus infection. Pediatrics 2003 Aug;112(2):282-4. DOI: http://dx.doi.org/10.1542/peds.112.2.282.
9. Ralston S, Hill V, Waters A. Occult serious bacterial infection in infants younger than 60 to 90 days with bronchiolitis: a systematic review. Arch Pediatr Adolesc Med 2011 Oct;165(10):951-6. DOI: http://dx.doi.org/10.1001/archpediatrics.2011.155.
10. Geskey JM, Beck MJ, Brummel GL. Neonatal fever in the term infant: evaluation and management strategies. Curr Pediatr Rev 2008;4(2):84-95. DOI: http://dx.doi.org/10.2174/157339608784462052.
11. McGregor RS, Tung J. Concurrent meningitis/serious bacterial infection in an infant hospitalized with respiratory syncytial virus. Arch Pediatr Adolesc Med 2002 Oct;156(10):1055. DOI: http://dx.doi.org/10.1001/archpedi.156.10.1055.
12. Kuppermann N, Bank DE, Walton EA, Senac MO Jr, McCaslin I. Risks for bacteremia and urinary tract infections in young febrile children with bronchiolitis. Arch Pediatr Adolesc Med 1997 Dec;151(12):1207-14. DOI: http://dx.doi.org/10.1001/archpedi.1997.02170490033006.
13. Bilavsky E, Shouval DS, Yarden-Bilavsky H, Fisch N, Ashkenazi S, Amir J. A prospective study of the risk for serious bacterial infections in hospitalized febrile infants with or without bronchiolitis. Pediatr Infect Dis J 2008 Mar;27(3):269-70. DOI: http://dx.doi.org/10.1097/INF.0b013e31815e85b1.
14. Haimi-Cohen Y, Amir J, Harel L, Straussberg R, Varsano Y. Parental presence during lumbar puncture: anxiety and attitude toward the procedure. Clin Pediatr (Phila) 1996 Jan;35(1):2-4. DOI: http://dx.doi.org/10.1177/000992289603500101.
15. Kramer MS, Etezadi-Amoli J, Ciampi A, et al. Parents' versus physicians' values for clinical outcomes in young febrile children. Pediatrics 1994 May;93(5):697-702.
16. World Health Association Pneumonia Vaccine Trial Investigators' Group. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children. Geneva, Switzerland: Department of Vaccines and Biologicals, World Health Organization; 2001.
17. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73(1):13-22. DOI: http://dx.doi.org/10.2307/2336267.
18. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986 Mar;42(1):121-30. DOI: http://dx.doi.org/10.2307/2531248.
19. Khandaker G, Heron L, Rashid H, et al. Comparing the use of, and considering the need for, lumbar puncture in children with influenza or other respiratory virus infections. Influenza Other Respir Viruses 2013 Nov;7(6):932-7. DOI: http://dx.doi.org/10.1111/irv.12039.
20. Antonow JA, Hansen K, McKinstry CA, Byington CL. Sepsis evaluations in hospitalized infants with bronchiolitis. Pediatr Infect Dis J 1998 Mar;17(3):231-6. DOI: http://dx.doi.org/10.1097/00006454-199803000-00011.
21. Liebelt EL, Qi K, Harvey K. Diagnostic testing for serious bacterial infections in infants aged 90 days or younger with bronchiolitis. Arch Pediatr Adolesc Med 1999 May;153(5):525-30. DOI: http://dx.doi.org/10.1001/archpedi.153.5.525.
22. St Jacques DM, Barton LL, Rhee KH. Risk of serious bacterial infections in infants with bronchiolitis. Arch Pediatr Adolesc Med 1998 Aug;152(8):819-20.
23. Curtis S, Stobart K, Vandermeer B, Simel DL, Klassen T. Clinical features suggestive of meningitis in children: a systematic review of prospective data. Pediatrics 2010 Nov;126(5):952-60. DOI: http://dx.doi.org/10.1542/peds.2010-0277.
24. Dagan R, Powell KR, Hall CB, Menegus MA. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. J Pediatr 1985 Dec;107(6):855-60. DOI: http://dx.doi.org/10.1016/S0022-3476(85)80175-X.
25. Baker MD, Bell LM, Avner JR. Outpatient management without antibiotics of fever in selected infants. N Engl J Med 1993 Nov 11;329(20):1437-41. DOI: http://dx.doi.org/10.1056/NEJM199311113292001.
26. Baker MD, Bell LM, Avner JR. The efficacy of routine outpatient management without antibiotics of fever in selected infants. Pediatrics 1999 Mar;103(3):627-31. DOI: http://dx.doi.org/10.1542/peds.103.3.627.
27. Baskin MN, O'Rourke EJ, Fleisher GR. Outpatient treatment of febrile infants 28 to 89 days of age with intramuscular administration of ceftriaxone. J Pediatr 1992 Jan;120(1):22-7. DOI: http://dx.doi.org/10.1016/S0022-3476(05)80591-8.
28. Herr SM, Wald ER, Pitetti RD, Choi SS. Enhanced urinalysis improves identification of febrile infants ages 60 days and younger at low risk for serious bacterial illness. Pediatrics 2001 Oct;108(4):866-71. DOI: http://dx.doi.org/10.1542/peds.108.4.866.

Entitled

After nine months of pregnancy, a mother is entitled to have her baby get safe care.
To expose her newborn to infection is criminal.

— Béla Schick, 1877-1967, Hungarian-born American pediatrician, founder of the Schick test