

Effect of Rapid Diagnosis of Influenza Virus Type A on the Emergency Department Management of Febrile Infants and Toddlers

Vidya Sharma, MBBS, MPH; M. Denise Dowd, MD, MPH; Andrew J. Slaughter; Stephen D. Simon, PhD

Background: Evidence shows that the rapid detection of influenza using an enzyme-linked immunosorbent assay decreases antibiotic use in the treatment of pediatric patients. To our knowledge, the effect on other diagnostic testing in an emergency department (ED) has not been examined.

Objective: To determine the effect of rapid diagnosis of influenza virus type A on the clinical management of febrile infants and toddlers in a pediatric ED at an urban children's hospital.

Materials and Methods: A retrospective review of ED records from an electronic database was performed. All children 2 to 24 months of age, with a temperature higher than 39°C who had a positive influenza virus type A test result using an enzyme-linked immunosorbent assay from November 1, 1998, through April 30, 2000 (n=72), were included in this study. Two groups were compared—those who had positive test results reported before dis-

charge from the ED (early diagnosis) and those who had positive test results after discharge (late diagnosis).

Results: Forty-seven patients (65%) were in the early diagnosis group and 25 (35%) in the late diagnosis group. The groups were similar for age, temperature, and triage category. Fewer patients in the early diagnosis group received ceftriaxone sodium compared with those in the late diagnosis group (2% vs 24%, $P=.006$); there were fewer urinalyses (2% vs 24%, $P=.006$) and complete blood cell counts performed (17% vs 44%, $P=.02$).

Conclusions: Rapid confirmation of influenza virus type A infection seems to decrease ancillary tests and antibiotic use in febrile infants and toddlers in the ED. A prospective study with a larger group is needed to confirm these findings.

Arch Pediatr Adolesc Med. 2002;156:41-43

From the Departments of Pediatrics (Drs Sharma, Dowd, and Simon) and Information Services (Mr Slaughter), Children's Mercy Hospital, Kansas City, Mo; and the University of Missouri School of Medicine at Kansas City (Drs Sharma, Dowd, and Simon).

INFLUENZA VIRUS type A (IVTA) infections are a common cause of illness in infants and children in the winter. Attack rates in healthy children are estimated to be between 10% and 40% each year.¹ Approximately 1% of young children with IVTA are hospitalized, rates in children with chronic diseases are higher.² Influenza virus type A infection may mimic bacterial sepsis in early infancy owing to its nonspecific presentation with fever and/or irritability.³ To distinguish viral infections from bacterial infections, diagnostic testing, including chest radiographs, urinalysis (UA) and culture, complete blood cell count (CBC), and blood culture and cerebrospinal fluid examination are frequently performed in children younger than 24 months. Additionally, the empirical use of antimicrobial agents and hospitalizations are not uncommon. Various diagnostic guidelines for fever without focus have been studied but none include the use of a rapid viral test.⁴ A rapid, specific test for viral infection has the potential to reduce the amount of diagnostic test-

ing, empirical antibiotic usage, and decrease hospitalization. This should ultimately result in a reduction of complications associated with empirical treatment as well as financial cost.

Neuraminidase inhibitors, such as zanamivir and oseltamivir phosphate, with activity against both influenza virus types A and B, have been approved by the Food and Drug Administration for influenza.^{4,5} When started early in the course of the disease amantadine hydrochloride and rimantadine hydrochloride have been shown to decrease the severity of symptoms in patients with influenza.^{6,7} For antiviral therapy to have an effect on the course of the disease, a rapid, specific diagnosis, shortly after the onset of the disease is essential.

Rapid diagnostic testing for the detection of IVTA is available. The rapid detection of influenza virus type A infection by enzyme-linked immunosorbent assay (ELISA) is a sensitive and specific test compared with a viral culture for the diagnosis of IVTA in children.^{8,9} The effect of rapid diagnosis of viral infections on patient care

MATERIALS AND METHODS

DATA COLLECTION

This study was exempted from review by the pediatric institutional review board at the University of Missouri at Kansas City because no patient identifiers were collected and clinical care was not affected. The setting was an urban children's hospital ED with an annual census of 55 000. Approximately 2000 febrile infants and toddlers are evaluated in the ED each year. Clinical data were accessed through the central data repository at the hospital where all patient encounters data are stored. Electronic medical records of all infants and toddlers 2 to 24 months old, with a temperature higher than 39°C, who presented to the ED or the urgent care clinic between November 1, 1998, through March 30, 1999, and November 1, 1999, through March 30, 2000, were retrospectively identified. All patients who had an ELISA test to detect IVTA and tested positive were included herein. The decision to perform an IVTA test was made at the discretion of the individual treating physician; no specific set of criteria was used, including the timing of the testing during the ED visit. The hospital laboratory used the same ELISA to detect IVTA infection in each of the 2 study periods. The test used was commercially available (Directigen FLU-A; Becton Dickinson, Franklin Lakes, NJ). Using cell culture and blocking results as the reference, the manufacturer estimated this test to have an overall sensitivity of 91% and a specificity of 95%.⁸ Variables recorded included triage status (emergent, urgent, or nonurgent); date and time the patient was seen; date and time the influenza virus type A test was ordered; date and time of the influenza virus type A test results; other ancillary tests ordered such as UA, CBC, and chest radiographs with their results; whether the patient was admitted to the hospital; length of inpatient stay; and total charges.

DATA ANALYSIS

Data were first analyzed using descriptive methods. All of the categorical variables were tested using the Fisher exact test. All continuous outcomes were compared using an independent samples *t* test. All tests were 2-sided at an α level of .05. Statistical analysis was conducted using SPSS Version 9 for Windows (SPSS Inc, Chicago, Ill).

has been studied for enterovirus and IVTA infections.^{10,11} Rapid diagnosis of enteroviral infections was shown to decrease unnecessary diagnostic and therapeutic interventions such as the administration of intravenous antibiotics, chest radiographs, and computed tomographic scans.¹⁰ A study by Noyola and Demmler¹¹ demonstrated that rapid diagnosis of influenza virus type A resulted in a positive effect on medical management by decreasing antibiotic use both in the emergency department (ED) and for hospitalized pediatric patients.

Febrile infants and toddlers are a sizable proportion of patients evaluated in pediatric EDs. During influenza epidemics the numbers of infants and toddlers

Diagnostic Tests Ordered and Antibiotics Given to 72 Infants and Toddlers Having the Diagnosis of Influenza Virus Type A Infection

Variable	Diagnosis Group, No. (%) of Patients		P Value
	Early (n = 47)	Late (n = 25)	
Complete blood cell count	8 (17)	11 (44)	.02
Urinalysis	1 (2)	6 (24)	.006
Chest radiograph	22 (47)	17 (68)	.14
Ceftriaxone sodium given	1 (2)	6 (24)	.006
Admitted to the hospital	8 (17)	6 (24)	.54
Time in ED, mean, min*	187	204	.31
ED charges, mean, \$	650	747	.25

*ED indicates emergency department.

evaluated for fever increases dramatically. For a test to have an effect on clinical management in the ED, the result should be available at the time diagnostic and treatment decisions are made. The virology laboratory at the study hospital established a rapid test for IVTA in 1998. During the 1998-1999 influenza season, this test was unavailable as a 24-hour test but rather as a convenience test that was performed on weekdays between 8 AM and 4 PM. During the 1999-2000 season, the test was available around the clock 7 days a week with results provided to the physician within 2 hours.

This study was undertaken to determine the effect of this procedural change in rapid IVTA testing on the clinical management of febrile infants and toddlers, specifically other diagnostic testing performed and treatment with broad-spectrum antibiotics. We compared patients having a confirmed diagnosis of IVTA infection before discharge from the ED (early diagnosis) to patients in whom the diagnosis was confirmed after discharge from the ED (late diagnosis).

RESULTS

During the 2-year study period there were a total of 2772 infants and toddlers between ages 2 and 24 months with a temperature of higher than 39°C who presented to the ED for urgent care. Of these 183 (6.6%) were tested for IVTA, a total of 72 infants and toddlers had a positive test result and were included in the study; 47 (65%) had test results available before discharge from the ED (early diagnosis) and 25 (35%) had test results available after discharge (late diagnosis). For all patients, the mean age was 9 months; mean temperature, 39.8°C; and the white blood cell count ranged from 5200 to 18300 cells/ μ L (mean of 11800 cells/ μ L). Early and late diagnosis groups did not significantly differ for age, triage categories, temperature, white blood cell count, chest radiographs performed, mean (SD) length of stay in the ED 187 (58.9) vs 204 (80.6) minutes, mean (SD) charges \$650 (339.5) vs \$747 (337.6), or admission to an inpatient unit.

As given in the **Table** fewer patients in the early diagnosis group received ceftriaxone sodium compared with the late diagnosis group (2% vs 24%, $P = .006$). Similarly, fewer UAs (2% vs 24%, $P = .006$) and CBCs (17% vs 44%, $P = .02$) were performed in the early vs late diagnosis groups.

COMMENT

Managing febrile infants and toddlers in EDs or urgent care is associated with costly and painful interventions, which may be decreased if a definitive diagnosis is readily available. Test results must be available at the time clinical decisions are made, for the ED, on a 24-hour basis. This study confirms a decrease in antibiotic and ancillary test use in febrile infants and toddlers presenting to the ED where the diagnosis of IVTA infection was confirmed rapidly.

We show that a preliminary diagnosis of influenza virus type A, when an obvious bacterial source was not present, did decrease antibiotic use. Patients in whom the diagnosis of influenza was confirmed before ED discharge were less likely to receive ceftriaxone therapy than those with the same disease but in whom the diagnosis was not confirmed before ED discharge. This suggests that physician decision making was influenced by the test results. Bacterial and viral infections have been shown to coexist.¹² But, the incidence of serious bacterial infections in infants and toddlers with other viral infections such as viral syndromes and bronchiolitis with respiratory syncytial virus infection has been shown to be low.¹³⁻¹⁶

We observed statistically significant differences in the use of ancillary tests such as UAs and CBCs. Data from the rapid diagnosis of enteroviral meningitis by enteroviral-specific reverse transcriptase polymerase chain reaction suggest that the test must be ordered early in the evaluation process to have a maximum effect on patient management.¹⁰ In busy EDs many tests may be ordered at the same time; however, further reductions are likely in ancillary test use, such as chest radiographs, if the IVTA tests are ordered early in the evaluation process in the IVTA season. A cost analysis of enteroviral-specific reverse transcriptase polymerase chain reaction demonstrated significant cost savings especially if the test was limited to use in the enteroviral season.¹⁷ The length of stay in the ED was not different between the groups whose conditions were diagnosed prior to discharge compared with those whose conditions were diagnosed later, which suggests that the test did not prolong the time the infant spent in the ED.

This observational study has clear limitations. Most importantly, the group of children being tested was chosen at the discretion of the physician and not randomly selected. While it seems early testing has the potential of decreasing antibiotic usage and ancillary testing, future studies examining a comparison of randomly selected children will be necessary to generalize these findings. Other limitations include the small sample size. This study had only limited power to detect large effects. For an outcome such as chest radiograph use, which had 68% use in the patients in the late diagnosis group, we would have 81% power for detecting a decline to 31% in the early diagnosis group. Thus, this research design only had enough precision to detect very large differences between the 2 groups. Another limitation is the retrospective nature of the study, because of this, it cannot be concluded that the positive test result was the sole cause of the significant reductions in antibiotic and ancillary tests

What This Study Adds

Influenza virus type A infections, a common cause of illness in children in the winter, may mimic bacterial sepsis in young infants and toddlers owing to its nonspecific presentation with fever and irritability. Rapid diagnosis of influenza virus type A has been shown to decrease antibiotic use in both ED-treated and hospitalized pediatric patients.

This study confirms decreased antibiotic use in febrile infants and toddlers presenting to the ED who have rapid confirmation of influenza virus type A infection. In addition, this study also found decreased empirical testing of infants and toddlers who present with fever without a focus. A larger prospective study is needed to confirm these results. Should this be confirmed, future guidelines for fever without a focus in infants and toddlers may need to consider the use of rapid viral diagnostic tests to decrease empirical testing and antibiotic use in these infants and toddlers.

that we observed; other factors may have played a role in management. We did not examine the effect of the influenza test on other aspects of the patients' management, for example, other viral tests done or the use of intravenous fluids. Lastly, we only examined the use of ceftriaxone but not other broad-spectrum antibiotics. We believe this is unlikely to introduce bias since in our ED only ceftriaxone is used in the vast majority of cases and it is our impression that this practice did not change during the study period.

CONCLUSION

We demonstrated decreases in ceftriaxone therapy use and the number of UAs and CBCs ordered in a group of febrile infants and toddlers with IVTA infection presenting to the ED in whom the results of the ELISA for IVTA was available before discharge from the ED compared with infants and toddlers for whom the test results were available later. A prospective larger study is needed to confirm our findings and to test the effects on other factors such as patient satisfaction with care and return visits to the ED or primary care physician offices.

Accepted for publication August 30, 2001.

Corresponding author and reprints: Vidya Sharma, MBBS, MPH, Department of Pediatrics, Children's Mercy Hospital, 2401 Gilham Rd, Kansas City, MO 64108 (e-mail: vsharma@cmh.edu).

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