

## SHORT REPORT

## Effect of a rapid influenza diagnosis

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Managing children with influenza-like illness is associated with costly and painful interventions because, in order to distinguish viral from bacterial infections, diagnostic tests (including routine blood examinations and chest radiographs) are frequently performed,<sup>1,2</sup> and the empirical use of antimicrobial agents is common.<sup>3</sup>

Various rapid diagnostic techniques for the detection of influenza viruses have been developed, but few data are available on their impact on child care.<sup>2,4,5</sup> The aim of this study was to assess the effect of a rapid diagnosis of influenza infection on the management of children with influenza-like illness in an emergency department.

## METHODS

All patients seen for influenza-like illness from 6 January to 27 February 2002, at the paediatric emergency department of the University of Milan, Italy, were enrolled and blindly randomly assigned in a 1:1 ratio to undergo a rapid test for the detection of influenza viruses or no rapid test. Influenza-like illness was defined as an axillary temperature of  $\geq 37.8^{\circ}\text{C}$  and at least one symptom of acute upper or lower respiratory tract disease.<sup>6</sup> The patients who underwent the test had their throats swabbed after vigorously rubbing both tonsillar surfaces and the posterior pharynx; the swab was then immediately

submitted to the Quickvue influenza test (Quidel, Milan, Italy) for the rapid detection of influenza A and B viruses. The test, which has an overall sensitivity of 74–95% and an overall specificity of 76–98%,<sup>5,7,8</sup> was performed by a postgraduate student in accordance with the manufacturer's recommendations. The results were available after 10 minutes; the emergency department paediatrician then prescribed diagnostic and therapeutic procedures.

The medical records of the children with a positive Quickvue test were evaluated and compared with those of two control groups: the first consisted of the patients with a negative test result, and the second of children who did not undergo the test. The comparison covered demographic and clinical data, as well as the likelihood of routine blood examinations, chest radiographs, antibiotic use, and hospital admission.

The study protocol was approved by the University of Milan's Institutional Review Board, and written informed consent was obtained from the parents or legal guardians of each child.

Categorical variables were compared using the  $\chi^2$  test with Yates's correction or Fisher's exact test, and continuous variables by means of the Mann-Whitney U test. All statistical tests were based on two tailed alternatives, with p values of 0.05 or less being considered significant. The statistical analysis was performed using SPSS 8.0 for Windows statistical software (SPSS Inc., Chicago, IL).

**Table 1** Comparison of children with a positive (cases) or negative rapid influenza test result (control group 1) and those who did not undergo the test (control group 2)

Characteristic	Cases (n=43)	Control group 1 (n=435)	p value	Control group 2 (n=479)	p value
Gender					
Male	23 (53.5)	242 (55.6)	0.913	254 (53.0)	0.919
Female	20 (46.5)	193 (44.4)		225 (47.0)	
Age (y)					
Median	2.5	2.3	0.643	2.6	0.706
Range	0.3–14.5	0.1–14.7		0.1–14.8	
Underlying illness	2* (4.6)	21† (4.8)	1.000	24‡ (5.0)	1.000
Previous influenza vaccination	0	9 (2.1)	1.000	11 (2.3)	0.611
Diagnosis					
Rhinitis	14 (32.6)	105 (24.1)	0.301	137 (28.6)	0.709
Pharyngitis	16 (37.2)	163 (37.5)	0.133	164 (34.2)	0.821
Acute otitis media	9 (20.9)	72 (16.6)	0.605	86 (18.0)	0.725
Croup	1 (2.3)	8 (1.8)	0.575	15 (3.1)	1.000
Wheezing	1 (2.3)	20 (4.6)	0.709	19 (4.0)	1.000
Acute bronchitis	2 (4.7)	41 (9.4)	0.408	34 (7.1)	0.757
Pneumonia	0	26 (6.0)	0.153	24 (5.0)	0.246
Routine blood examination	1 (2.3)	63 (14.5)	0.045	72 (15.0)	0.038
Chest radiograph	2 (4.6)	50 (11.5)	0.207	56 (11.7)	0.208
Antibiotic use	14 (32.6)	282 (64.8)	<0.0001	296 (61.8)	0.0003
Days of antibiotics					
Median	7	7	0.944	7	0.961
Range	4–10	3–20		5–14	
Admitted	0	20 (4.6)	0.240	28 (5.8)	0.154
Antiviral use	0	0		0	

Percentages in parentheses.

\*Includes one child with congenital heart disease and one with asthma.

†Includes seven children with congenital heart disease, five with asthma, four with malignancy, three with neurological deficits, and two with cystic fibrosis.

‡Includes eight children with congenital heart disease, seven with asthma, four with neurological deficits, three with cystic fibrosis, and two with malignancy.

## RESULTS

During the study period, of the 957 patients aged 0–15 years attending the emergency department because of influenza-like illness, 478 (49.9%) underwent the Quickvue test and 43 (8.9%) proved to be positive for influenza viruses.

Table 1 presents the demographic characteristics, clinical information, and outcome data of the study population. No significant difference was observed between the groups in terms of gender and age distribution, medical history, or clinical diagnosis. However, the patients with a positive Quickvue test were significantly less likely than those with a negative or no test result to undergo routine blood examinations (2.3% v 14.5% and 15.0%;  $p = 0.045$  and  $p = 0.038$ ) or receive antibiotics (32.6% v 64.8% and 61.8%;  $p < 0.0001$  and  $p = 0.0003$ ). There was also a tendency towards lower incidence (although statistically not significant) in the proportion of chest radiographs (4.6% v 11.5% and 11.7%;  $p = 0.207$  and  $p = 0.208$ ) and the likelihood of admission (0% v 4.6% and 5.8%;  $p = 0.240$  and  $p = 0.154$ ) among the children with a positive Quickvue test. On the contrary, when an antibiotic was prescribed, the duration of use was comparable in the three groups. Moreover, none of the patients received antiviral therapy because in Italy no antiviral drug is approved for use in the therapy of influenza in children.

## DISCUSSION

The results of this study show that rapid influenza diagnostic tests have a positive impact on medical management by decreasing ancillary tests and antibiotic use in children evaluated for influenza-like illness in an emergency department. This is highlighted by the fact that the paediatrician behaviour was similar in children with a negative test and those who did not undergo the test. Moreover, both situations were significantly different from what was observed in the cases positive for influenza viruses. Although the clinical characteristics were similar in all groups, the early availability of a positive result influences paediatrician decision making and may help in containing the costs of care.

In children positive for influenza we observed a significant reduction in the number of routine blood examinations and, although not statistically significant, clinically relevant reductions in the number of chest radiographs and the likelihood of admission. The absence of a significant difference in these last two parameters may be explained by the low absolute number of chest radiographs and the low admission rate in our population.

The costs of large scale rapid influenza testing would also be substantial, and in order to reduce them it may be useful to use the rapid tests only during the peak of the influenza season. However, the saving of indirect costs also has to be considered. The benefits of decreasing unnecessary antibiotic use include fewer side effects and a decrease in the emergence of antibiotic resistant bacteria.<sup>3</sup> The emergence of penicillin and macrolide resistant strains of *Streptococcus pneumoniae* as well as  $\beta$  lactamase producing isolates of *Haemophilus influenzae* has been reported in children and has been related to antibiotic use.<sup>9–12</sup> In an era of increasing antibiotic resistance, it is imperative to avoid unnecessary antibiotic use. The impact of confirming a specific diagnosis on parental understanding of the nature and expected course of an illness should not be underestimated, and may play a key role in allowing physicians to avoid antibiotic therapy.<sup>3</sup>

Neuraminidase inhibitors, such as zanamivir and oseltamivir, which are active against influenza A and B viruses, have recently been approved for the treatment of influenza.<sup>6</sup> Zanamivir is approved for treatment for persons aged  $\geq 7$  years, and oseltamivir is approved for treatment for persons aged  $\geq 1$  years.<sup>14</sup> Few studies of the efficacy of neuraminidase inhibitors have been conducted among paediatric populations. One study of oseltamivir therapy documented a decreased incidence of

acute otitis media among treated children, which would further reduce the use of antibiotics.<sup>6</sup> The possibility of starting effective antiviral therapy early has to be considered when evaluating the impact of rapid influenza tests on patient management.<sup>13</sup>

As viral respiratory infections have been associated with bacterial respiratory and invasive infections, concern about the potential misdiagnosis of a concomitant bacterial infection in a patient with a positive rapid influenza test is valid,<sup>4</sup> but although viral and bacterial infections do coexist, the incidence of serious bacterial infections in paediatric patients with viral infections and influenza-like symptoms is low.<sup>15</sup> The rapid diagnosis of influenza therefore retains its usefulness in reducing the indiscriminate use of ancillary tests and antibiotics when there is no obvious bacterial focus of infection.

In conclusion, the provision of a rapid influenza diagnosis for children with influenza-like illness affects patient care and reduces medical interventions. These results should be taken into account at the time clinical decisions are made in an emergency department and also in future guidelines for the management of influenza-like illness.

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