The Effect of the Rapid Antigen Test for Influenza on Clinical Practice in the Emergency Department: A Comparison of Periods before and After the 2009 H1N1 Influenza Pandemic

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Abstract

Introduction. The rapid antigen test (RAT) plays an important role in the Emergency Room (ER). In this study, we investigated the effect of the RAT for influenza on clinical practice in an emergency department.

Methods. A retrospective chart review was conducted considering two

periods, namely before and after the 2009 influenza pandemic. The rate of antibiotic administration, the use of blood sample tests, the use of simple chest X-rays, the rate of antibiotic administration according to the result of the RAT, and the duration of ER stay in the case of influenza-like illnesses were investigated for the two study periods considered.

Results. The use of the RAT increased from 23.9% to 39.8% in influenza-like pediatric patients ($p<0.05$) and from 4.9% to 67.6% in adult patients ($p<0.001$). After the 2009 influenza pandemic, the number of cases of antibiotic administration, blood sample test and simple chest X-ray decreased by 19.0%, 46.2%, and 27.4%, respectively, in pediatric patients with the use of RAT. Among RAT-positive patients, after the 2009 influenza pandemic, none of the pediatric patients and only 3 of the adult patients (17.6%) were administered antibiotics. The duration of ER stay was longer in patients who underwent RAT than in those who did not.

Conclusion. The increased use of RAT for influenza has led to a decrease in antibiotic administration and a reduction in additional diagnostic tests in influenza-like illnesses. However, the use of RAT has not contributed to a decrease in the duration of ER stay.

Key words: influenza, rapid antigen test, antibiotic, duration of stay

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Introduction

A novel H1N1 influenza virus was discovered in April 2009 and spread around the world rapidly; this led to a declaration of a pandemic outbreak by the World Health Organization in June 2009. (1)

With the 2009 influenza pandemic, the overcrowding of patients with influenza-like symptoms led to a chaotic crisis in emergency departments (EDs). (2,3) The signs and symptoms of influenza cannot be differentiated from those caused by other respiratory pathogens, which makes it challenging to diagnosis influenza accurately in the ED. (4-6)

The rapid antigen test (RAT) played an important role in EDs during this time for a quick diagnosis of influenza.

However, its sensitivity shows wide variations in comparison with polymerase chain reaction (PCR)-based methods. Lucas et al. reported that the sensitivity and specificity for the detection of H1N1 was 20.0% and 99.0%, respectively, using the QuickVue Influenza A+B Test (Quidel), while other investigators have found its sensitivity to be higher than this value. (7-9) In one study, the Actim Influenza A&B kit (Medix Biochemica, Joensuu, Finland) has been shown to be 90.0% sensitive for the detection of influenza A virus. (10)

Some small studies have shown that a positive RAT spurs changes in clinical practice. (11-13) In this study, we investigated the effect of RAT for influenza on the proportion of antibiotic administration, additional diagnostic tests, and the length of stay (LOS) in the ED.

Materials and methods

This study was conducted at the Korea University Guro Hospital Emergency Department as a retrospective chart review. It was approved by the Institutional Review Board of the hospital (IRB No.: KUGH 14018). The study periods were from December 15, 2008, to January 11, 2009 (before the 2009 influenza pandemic) and from February 9, 2013, to March 8, 2013 (after the 2009 influenza pandemic); each period was reported to have the peak seasonal flu activity by the Korea Centers for Disease Control and Prevention in the corresponding years. (14,15) All patients who presented with influenza-like illnesses during the study periods were included in this research. Influenza-like illness included a fever of ≥38°C or afebrile state in the case of antipyretic use in the previous 8 h and at least one of the following respiratory symptoms: cough, sore throat, rhinorrhea, and/or nasal congestion. The data collected were gender, age, body temperature, symptoms, duration of symptoms, use of a RAT kit, antibiotic administration, use of blood sample tests, use of X-rays, and duration of emergency room (ER) stay.

The symptoms investigated included shivering, rhinorrhea, headache, sore throat, malaise, cough, sputum, myalgia, and gastrointestinal symptoms. Two emergency specialists reviewed the patient charts. The mean value of the above mentioned data was used when the two chart reviewers were presented with conflicting data for continuous variables. For conflicting data with categorical variables, a third investigator reviewed the charts and determined which data were to be used.

We divided the included patients into the adult (>= 16 years) and pediatric (<16 years) group. In each group, the rate of antibiotic administration, the use of blood sample tests, and the use of simple chest X-rays, according to the use of a RAT kit, were investigated in patients with influenza-like illness by comparing the periods before and after the 2009 H1N1 influenza pandemic. The proportion of cases that received antibiotic administration according to the result of RAT in both pediatric and adult patients with influenza-like illness was also investigated for both study periods. The duration of ER stay, according to the use of a RAT kit, was analyzed in the cases of patients discharged after ER care for both the groups within each of the two periods separately,

Statistics

Using SPSS Statistics for Windows 17.0 software package (SPSS 17.0, IBM, Chicago, USA), we conducted an independent t test to compare the mean value of the continuous variables; the Mann-Whitney test was used to compare continuous variables that did not show a normal distribution. A chi-squared analysis or Fisher's exact test was used for the categorical variables. Continuous variables are presented as mean ± standard deviation.

Results

A total of 474 patients with influenza-like illnesses were included during the 8-week study periods. 146 pediatric patients visited the ER between December 15, 2008, and January 11, 2009 (before the 2009 influenza

pandemic) and 196 between February 9, 2013 and March 8, 2013 (after the 2009 influenza pandemic). The number of adult patients visiting the ER for influenza-like illnesses was 61 for the former period and 71 for the latter period. The clinical data of the included patients are presented in table 1. In the case of pediatric patients, the patients in the latter study period were younger than the patients in the former study period. Some of the symptoms such as shiverings, rhinorrhea, sore throat sputum, and gastrointestinal symptoms were different in both groups. In contrast, the adult patients before the 2009 influenza pandemic were younger than the adult patients after the 2009 influenza pandemic. Otherwise, there were no differences in clinical data between the two adult groups. Among the pediatric patients, 128 (87.7%) were discharged after ER care before the 2009 influenza pandemic and 166 (84.7%) after the pandemic. Among the adult patients, 53 (86.9%) were discharged after ER care before the 2009 influenza pandemic and 62 (87.3%) after the pandemic. Among pediatric patients with influenza-like illnesses, 35 (23.9%) were provided with RAT before the 2009 influenza pandemic and 78 (39.8%) after the pandemic. Among adults with influenza-like illnesses, 3 patients (4.9%) were provide with RAT before the 2009 influenza pandemic and 48 (67.6%) after the pandemic (figure 1).

Changes in clinical practice according to the use of RAT in pediatric patients with influenza-like illnesses

Before the 2009 influenza pandemic, the number of cases that underwent antibiotic administration, blood sample test and simple chest X-ray was 21 (60.0%), 22 (62.9%), and 28 (80.0%) in patients with the use of RAT; it was 40 (36.0%), 24 (21.6%), and 34 (30.6%) in patients without RAT. After the pandemic, the number of cases of antibiotic administration, blood sample test and simple chest X-ray was 32 (41.0%), 13 (16.7%), and 41 (52.6%) in patients with the use of RAT; it was 74 (62.7%), 30 (25.4%), and 57 (48.3%) in patients without RAT (figure 2). Before the pandemic, antibiotics were administered in 3 patients (42.9%) with RAT-positive results, while none were provided

with antibiotics in RAT-positive patients after the pandemic (figure 4A).

The duration of ER stay in discharged patients was 286.3 ± 171.5 min in patients with the use of the RAT kit and 182.4 ± 129.6 min in patients with no use of the RAT kit before the 2009 influenza pandemic (p=0.001). After the pandemic, the duration of ER stay in discharged patients was 133.5 ± 100.7 min in patients with the use of RAT and 103.3 ± 93.1 min in patients without RAT (p=0.048) (figure 5A).

Changes in clinical practice according to the use of the RAT kit in adult patients with influenza-like illnesses

Only 3 patients (4.9%) underwent RAT for influenza before the 2009 influenza pandemic; therefore, we omitted the analysis comparing RAT use before and after the pandemic. In patients who received RAT, the number who underwent antibiotic administration, blood sample test and simple chest X-ray was 21 (43.8%), 46 (95.8%), and 48 (100.0%), respectively; it was 13 (56.5%), 18 (78.3%), and 18 (78.3%) in patients who did not receive RAT (figure 3). Antibiotics were administered in 3 patients (17.6%) with RAT-positive results, while 31 RAT-negative patients (57.4%) were provided with antibiotics after the 2009 influenza pandemic (figure 4B). The duration of ER stay in discharged patients was 268.9 ± 144.2 min in patients with the use of a RAT kit and 210.5 ± 205.3 min in patients with no use of a RAT kit after the 2009 influenza pandemic (figure 5B).

Discussion

Historically, influenza has been well known to physicians. The most devastating worldwide influenza pandemic broke out in 1918. After that, influenza pandemics were not so devastating, killed fewer people than previous pandemics, and broke out in a restricted area or with limited spread. (16,17) The cause of influenza is the RNA virus of the family Orthomyxoviridae. (18) However, influenza cannot be confirmed by

clinical symptoms and is difficult to distinguish from other viral diseases. (19,20) Prior to the 2009 influenza pandemic, when patients were diagnosed with influenza, most of the diagnoses were clinical diagnosis, not laboratory diagnoses in South Korea.

In 2009, everything changed with the influenza pandemic outbreak. Emergency physicians suffered from overcrowding and had to take countermeasures to solve this problem. (21) Since then, RAT for influenza has been widely used for rapid diagnosis of this disease. Figure 1 shows that the use of RAT for influenza has increased significantly in both pediatric and adult patients after the 2009 influenza pandemic. A variety of methods for detecting the influenza virus, such as cell culture and real-time polymerase chain reaction (RT-PCR), can be used. While RT-PCR and cell culture are the most sensitive methods for an influenza diagnosis, they require specialized equipment and need a considerable amount of time. The RAT is valuable for its ease of use and laboratory independence. Further, RAT for influenza has fast turnaround times (10–30 min), which makes it a useful tool for an influenza diagnosis in the ED. (22-24) Thus, since 2009, RAT for influenza-like illnesses has been used increasingly by emergency physicians in Korea.

There were some differences in symptoms in patients before and after the 2009 influenza pandemic. These may be due to the differences in the subtype of the influenza virus. The main subtype of influenza was H1N1 in the study period before the 2009 influenza pandemic and H3N2 in the study period after the 2009 influenza pandemic. (14,15) Further, pediatric patients after the 2009 influenza pandemic were younger than those before the influenza pandemic, and adult patients after the 2009 influenza pandemic were older than those before the influenza pandemic. It is thought that the learning effect of the 2009 influenza pandemic has led high-risk patients to visit the ED.

First, we analyzed clinical practice in EDs with respect to pediatric patients before and after the 2009 influenza pandemic. Before the 2009 influenza pandemic, pediatric patients with influenza-like illnesses who underwent RAT experienced higher antibiotic administration, use of

blood sample tests, and use of simple chest X-rays than those who did not undergo RAT. However, after the 2009 influenza pandemic, patients who did not undergo RAT experienced higher antibiotic administration than those who underwent the RAT. The use of blood sample tests and simple chest X-rays did not differ according to the use of a RAT kit after the 2009 influenza pandemic (figure 2). Furthermore, the result of RAT did not have a decisive effect on antibiotic administration before the 2009 influenza pandemic (figure 4A). This implies that before the 2009 influenza pandemic, physicians administered RAT in influenza-like illness patients as a routine laboratory test. It also means that after the 2009 influenza pandemic, RAT became a guideline test for influenza and many patients did not received further evaluation or antibiotic administration, based on the result of RAT.

The duration of ER stay according to the use of the RAT kit was compared only in discharged patients and within each of the two periods separately. This was because most patients were discharged, and ER length of stay is influenced by many factors (ER crowding, availability of rooms in the ward, the ER attending physician's individual practice pattern, etc.).

In fact, we expected that the use of RAT for influenza would decrease the duration of ER stay by supporting clinical decision making. Rather, our data showed an increase in the duration of ER stay in patients who underwent RAT. A previous study has reported that the use of point-of-care-test (POCT) for influenza did not appear to significantly reduce the length of stay in a pediatric ED. However, a significant reduction in requests for urinalyses and urine cultures was associated with a positive result of POCT in this previous study. (25)

Next, we analyzed the effect of RAT for influenza on clinical practice in EDs with respect to adult patients before and after the 2009 influenza pandemic. However, RAT was rarely used in adult patients with influenza-like illnesses before the pandemic (figure 1). We found only 3 patients (4.9%) who underwent RAT for influenza during the study period before the 2009 influenza pandemic and hence, did not compare

the effect of RAT for influenza on the clinical practice in EDs for adult patients before and after the 2009 H1N1 influenza pandemic. However, although the rate of antibiotic administration did not differ between the group of patients who did not undergo RAT and those who did after the 2009 influenza pandemic, the rate of antibiotic prescription was lower in RAT-positive patients than in RAT-negative ones (figure 4B). Judging from this result, the use of RAT for influenza-like illnesses decreased the frequency of antibiotic administration. The duration of ER stay was also increased in adult patients with use of RAT (figure 5B).

There are other limitations of this study. Our data apply to a single center and are not nationally representative, which might generate a bias of faulty generalization. The other limitation is that this study was carried out using retrospective chart review. We were unable to record the exact time when physicians decided to use RAT in each patient. If we had more information on whether RAT was administered with a blood sample test and a simple X-ray in a bundle or whether RAT was used as a guideline for further evaluation, the effect of the use of RAT in influenza-like illnesses could be investigated in more detail.

Conclusion

The RAT for influenza has been increasingly used in an ED setting after the 2009 influenza pandemic. This has led to a decrease in antibiotic administration and a reduction in additional diagnostic tests in influenza-like illnesses since the 2009 influenza pandemic. However, it did not contribute to a decrease in the duration of ER stay.

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Table 1. Clinical data on included patients.

	Pediatric patients			Adult patients		
	Before the 2009 influenza pandemic (n = 146)	After the 2009 influenza pandemic (n = 196)	*p*	Before the 2009 influenza pandemic (n = 61)	After the 2009 influenza pandemic (n = 71)	*p*
Male gender (%)	82(56.2)	93(47.5)	0.111	25(41.0)	29(40.8)	0.987
Age(mean ± SD, years)	3.3±3.0	2.6±2.3	0.042	36.2±16.9	48.1±19.5	0.000
Body temperature (mean ± SD, °C)	38.8±0.6	38.7±0.6	0.102	38.6±0.5	38.6±0.5	0.694
Symptoms (%)	25(17.1)	75(38.3)	0.000	41(67.2)	54(76.1)	0.259
Chill	65(44.	118(60	0.004	29(47.5)	24(33.8)	0.108
						0.4

Rhinorrhea	5)	.2)	0.252	11(18.1)	17(23.9)	080
Headache	5(3.4)	3(1.5)	0.050	9(14.8)	19(26.8)	0.093
Sore throat	6(4.1)	19(9.7)	0.482	3(4.9)	7(9.9)	0.285
Loss of appetite	9(6.2)	16(8.2)	0.463	44(72.1)	53(74.6)	0.744
Cough	92(63.0)	131(66.8)	0.026	34(55.8)	40(56.3)	0.945
Sputum	35(24.0)	69(35.2)	0.125	18(29.5)	30(42.3)	0.129
Myalgia	1(0.7)	6(3.1)	0.000	7(11.5)	14(19.7)	0.197
Gastrointestinal symptoms	34(23.3)	10(5.1)				
Onset time before ER visit (mean ± SD, days)	1.8 ± 1.5	2.0 ± 2.2	0.648	2.74 ± 1.5	2.4 ± 2.4	0.015
Patients discharged after ER care (%)	128(87.7)	166 (84.7)	0.197	53(86.9)	62(87.3)	0.940

ER, emergency room

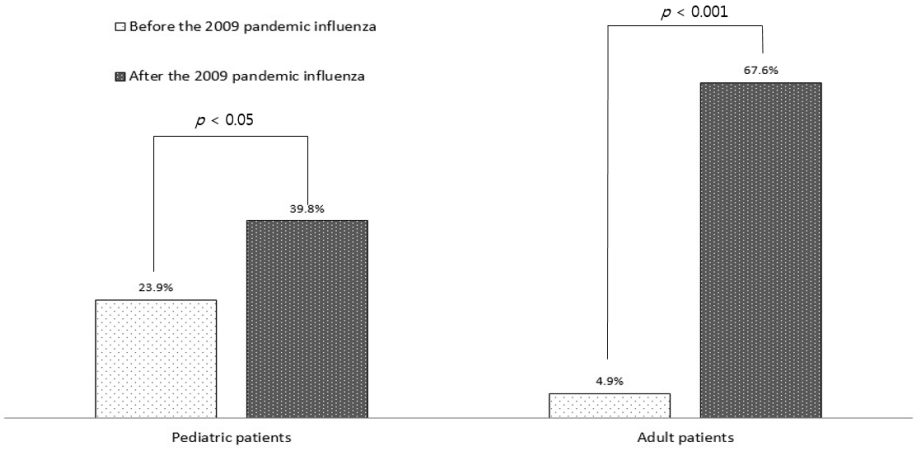

Figure 1. The use of RAT (Rapid Antigen Test) for influenza in patients who visited the emergency room for influenza-like illnesses during study periods before and after the 2009 influenza pandemic.

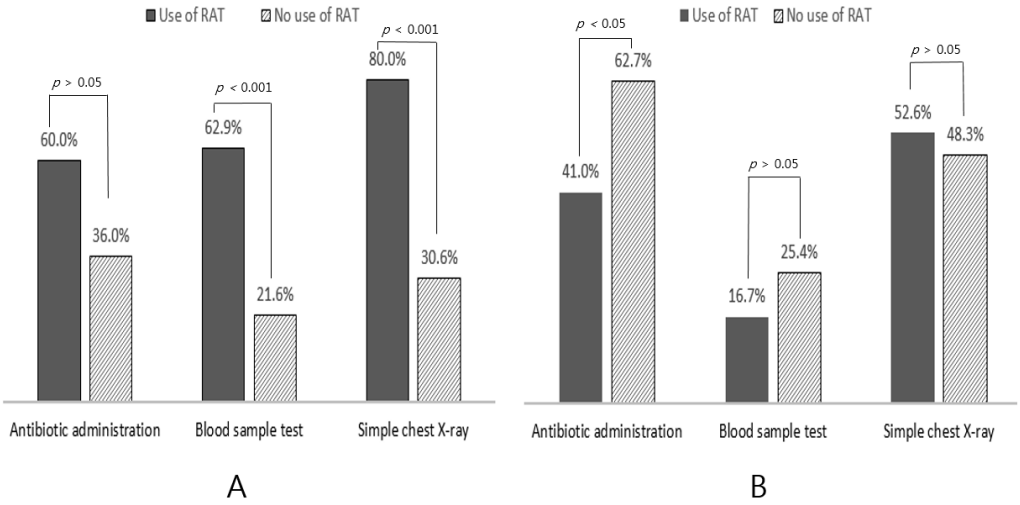

Figure 2. The rate of antibiotic administration, use of blood sample tests and simple chest X-rays in pediatric patients with influenza-like illnesses (A Before the 2009 influenza pandemic; B After the 2009 influenza pandemic).

RAT, Rapid Antigen Test.

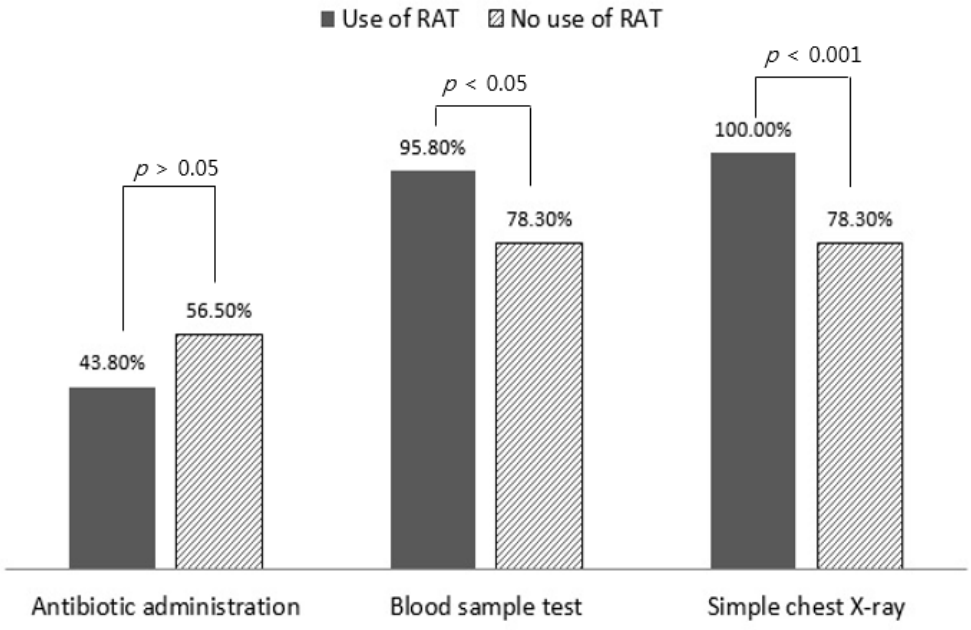

Figure 3. Rate of antibiotic administration, use of blood sample tests, and simple chest X-rays in adult patients with influenza-like illnesses after the 2009 influenza pandemic.

RAT, Rapid Antigen Test.

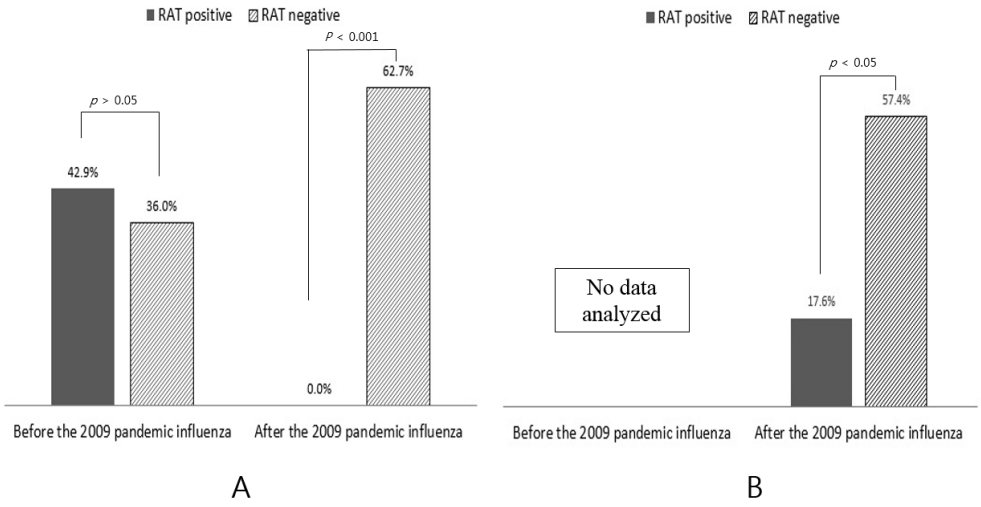

Figure 4. The rate of antibiotic administration according to the result of RAT in patients with influenza-like illnesses (A pediatric patients and B adult patients).

RAT, Rapid Antigen Test.

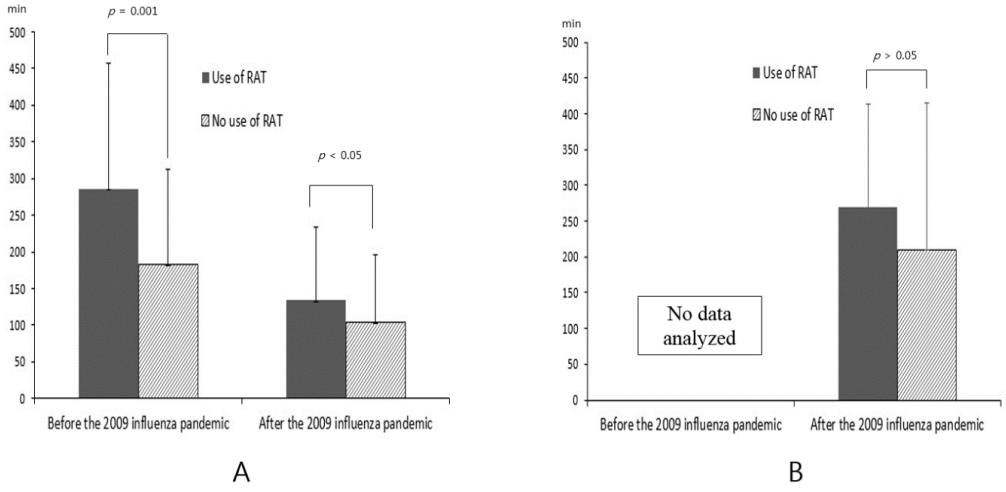

Figure 5. The duration of ER stay in patients with influenza-like illnesses according to the use of RAT (A pediatric patients and B adult patients).

RAT, Rapid Antigen Test.

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