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Antigen Rapid Test is Expected to Accelerate the Detection Efficiency of the COVID-19 Epidemic

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Abstract

Objective: Explore the performance and strength & weakness of antigen rapid test methods in detecting COVID-19 epidemic.

Methods: Selected 7 different companies' antigen rapid test (nasal swab) product test data for comparison and the clinical results (sensitivity, specificity and accuracy) of each company's swab rapid antigen test product are obtained. Different onset time samples were tested with RT-PCR and COVID-19 antigen tests. Total 421 specimens were used in clinical study and the research will respect the autonomy of participants and conducts follow-up assessment of the rapid test to determine whether the COVID-19 is associated with the results. The sample used for rapid detection of COVID-19 antigen was nasal swab.

Results: Through clinical research show that the detection rate of COVID-19 antigen was decreased gradually, it was corresponding to the nature of antigen in the human body.

Conclusion: The emergence of various COVID-19 rapid tests (especially nasal swab) enables health professional to complete the preliminary screening. Antigen detection method has own advantages in COVID-19 epidemic. In antigen detection, we use products of different companies (Abbott, Roche, Healgen, Acro, Siemens, Lepu, Wondfo) to predict the advantages of convenient and sample collection, high throughput, low workload, high reproducibility and low cost in practical applications.

Keywords: COVID-19; Rapid test; Antigen; Nasal swab

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Introduction

Coronaviruses are a large family of viruses which may cause illness in animals or humans. In humans, several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recently discovered coronavirus in 2019 causes coronavirus disease COVID-19 [1]. Currently, the COVID-19 is occurring in many areas of the world. COVID-19 is a disease that is caused by infection with the coronavirus known as *SARS-CoV-2*, it can cause severe complications including acute respiratory distress syndrome, acute myocardial injury and metabolic acidosis, which cause irreversible damage, even lead to death. This virus is transmitted between humankind and has spread rapidly and due to the rapid spread of *SARS-CoV-2*, COVID-19 is now a pandemic affecting many countries globally [2]. As of September 18, 2021, more than 226 million confirmed cases have been reported in countries and regions around the world, and more than 4.666 million patients have died. The spread is still ongoing. The estimated value of the fatality rate of this disease varies greatly among countries in the world. As of February 8, 2021, the observed fatality rate of this disease in most countries is between 0.5% and 5.0%, and the global preliminary revised case fatality rate is about 2.9%. The impact of COVID-19 on human health may vary greatly. Some infected people have no obvious symptoms and may not have adverse reaction. Other infected patients have mild or severe symptoms and may be life-threatening. Therefore, there is giant demand for the COVID-19 rapid tests.

There are three main types of COVID-19 diagnostic or screening tests: nucleic acid amplification tests, antigen tests and antibody tests. Virus antigen detection not only has all the advantages of antibody detection, but also has most advantages of nucleic acid detection [3]. So the article mainly focuses on antigen testing for research and discussion. The England Public Health Bureau has evaluated some advanced antigen rapid test kit with NCV mutation samples [4]. Abbott, Healgen, Roche, Acro and other companies have developed Novel coronavirus antigen and antibody rapid

test kit. In order to further clarify the inspection performance of different products, the measurements of different manufacturers had been compared and analyzed.

Literature Review

PCR

The most common method for detecting the specific sequence of the novel coronavirus is fluorescent quantitative PCR (polymerase chain reaction). It has the characteristics of early diagnosis, high sensitivity and specificity [5], and is the "gold standard" for diagnosing novel coronavirus. Currently, the most widely used mehod is Real-time fluorescent quantitative PCR technology [2]. Generally, the two targets located on the ORF1ab and N genes of the virus are detected. The same sample must meet the double target positive or the repeated test as the single target positive, or the two samples must meet the single target at the same time to confirm the positive of the *SARS-CoV-2* virus nucleic acid. The unique gene sequence of the virus is used as the detection target [6]. Through PCR amplification, the target DNA sequence we choose increases exponentially. Each amplified DNA sequence can be combined with a fluorescent-labeled probe that we added in advance, produce fluorescent signal, the more target genes amplified, the stronger the accumulated fluorescent signal display [6]. In samples without infected, since there is no target gene amplification, no increase in fluorescence signal can be detected. Therefore, nucleic acid detection is actually to determine whether there is novel coronavirus nucleic acid in the sample by detecting the accumulation of fluorescent signals.

Antigen detection

The novel coronavirus antigen test can directly detect whether the human sample contains the novel coronavirus, and its diagnosis is efficient, accurate, and less equipment and personnel. Antigens such as the N protein, E protein and S protein of the novel coronavirus can be used as immunogens to stimulate plasma cells to produce specific antibodies after the virus infects the human body. According to the principle of double-antibody sandwich ELISA, using two antigen-specific antibodies to recognize and bind to different epitopes of a target antigen can greatly reduce the probability of cross-reaction, thereby effectively improving its specificity [2]. The type of antigen test sample is generally a sample from the site of infection, such as oropharyngeal swabs, nasal swabs, sputum, etc. [7]. The *SARS-CoV-2* Antigen Rapid Test (nasal swab) is a rapid chromatographic immunoassay for the qualitative detection of *SARS-CoV-2* nucleocapsid protein antigens in nasal swab specimen from individuals with suspected *SARS-CoV-2* infection in conjunction with clinical presentations and the results of other laboratory tests. Results are for the detection of *SARS-CoV-2* Antigens. An antigen is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient clinic history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Negative results do not preclude SARS -CoV-2 infections and should not be used as the sole basis for treatment or patient management decisions. Negative results should be treated a presumptive and confirmed with a molecular assay, if necessary for patient management. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and symptoms consistent with COVID-19. In areas with widespread transmission, rapid antigen testing can be used to detect the virus early and isolate positive cases. It is widely used in health facilities, COVID-19 testing centers/sites, nursing homes, prisons, schools, frontline and health care workers [7]. Rapid antigen detection is easy operating, high precision, convenient sample collection, and quick results. This allows medical personnel to perform testing with less training and explanation of the principles, and to provide patients with rapid novel coronavirus testing services, which can greatly reduce the overload of the medical system.

Research Methodology

Sampling techniques: Now, in view of the advantages of antigen detection, for example easy sample collection, high throughput, low workload, high reproducibility and low cost, we were compared with the data of products (Abbott, Roche, Healgen, Acro, Siemens, Lepu, Wondfo) to conduct methods of COVID-19 detection. The aim of the clinical study is to determine whether the rapid test is safe and effective and provide an accurate and reliable result. The study tracks samples from multiple subjects and conducts follow-up assessment of the rapid test to determine whether the new coronavirus is associated with the results. As the research progresses, the results of participants will be measured and recorded, compare the performance of antigen rapid test methods on samples from novel coronavirus pneumonia patients, randomly select some of the confirmed samples after gradient dilution to detect the sensitivity of the testing products, thus the relationship with the specific characteristics of the new coronavirus will also be determined. The sample used for rapid detection of COVID-19 antigen was nasal swab.

Ethics: Ethical approval is of great significance to the whole research. Without ethical approval, it means that if participants make a claim regarding the research, the researcher will assume personal responsibility [12]. This research will respect the autonomy of participants, which includes four parts. Firstly, to provide sufficient information for the research participants. For example, the significance of research and learning objectives. Make participants to make an informed decision as to whether to take part in research. Secondly, ensuring that participants are not subject to coercion to take part or not taking part [12], the survey is entirely dependent on the wishes of the participants. Thirdly, ensuring that participants are free to withdraw from the research at any time and that there can be no reason. Fourthly, all samples are anonymous, research will strictly confidential and respect personal information by participants provided, and that information will not be disclosed to the outside world. In addition, this research paper has an obligation to conduct research with sincere and impartial attitude, ensuring that research maximize to get the useful results and appropriate and effective dissemination. However, research will not have practical or potential interests and will be honest and transparent

in the whole process. When rejecting any participants, this research paper will give a reasonable ethical interpretation in the application, and that research does not discriminate against certain individuals or groups.

Limitations: All researches have limitations [13]. The research project also has many limitations, the researcher will discussion to limitations related to the research problems. Those research limitation as follows. In the first place, sample size. Researchers only collected 421 samples for analysis in clinical studies, so the sample size was small, which can not estimate precisely the performance of antigen rapid test in COVID-19 epidemic. As we know, clinical results require a large number of samples and data (tens of thousands) as support. However, due to the limitations of the clinical samples of this research, the rigor is slightly lacking. Next, the age of people group is not evenly distributed. The age of most participants is between 20 years to 40 years, which was 69.3%, and thus dominate in samples. The age of participants is between 15 years to 20 years, 40 years to 50 years and over 50 years was little. In the second place, lack of previous research studies, lead to the lack of research results to support the research project, to cause shortcomings of the results.

Data Quality Assurance

Comparison of different *SARS-CoV-2* antigen rapid test data

From **table 1** below, we can see the performance data comparison of COVID-19 antigen rapid detection reagents from different companies. Wondfo *SARS-COV-2* Antigen rapid test detects the virus antigen, indicating that the virus infection is active. The sensitivity of antigen detection is 96.18%, and the specificity is 99.72%. The rapid detection kit of *SARS-CoV-2* antigen developed by Lepu is used for qualitative detection of *SARS-CoV-2* antigen in clinical samples (nasal lining). The antigen test showed a sensitivity of 92.00% and a specificity of 99.26%. Siemens Rapid COVID-19 Antigen Test is an in vitro immunochromatographic test for qualitative testing. The sensitivity and specificity of the detection were 96.72% and 99.22% respectively. The COVID-19 antigen detection (Swab) developed by Acro aims to qualitatively detects SARS-CoV-2. The sensitivity and specificity of the detection were 94.6% and 99.4% respectively. *SARS-CoV-2* antibody is applied to the test line area. In the test, the sample will react with *SARS-CoV-2* aniline coated particles. Then the mixture migrates upward on the membrane by capillary action, and reacts with *SARS-CoV-2* antibody in the test line area. If the sample contains *SARS-CoV-2* antigen, the result will appear as a colored line in the test line area. If the specimen does not contain *SARS-CoV-2* antigen, no colored line appears in the test line area, which indicates a negative result. In order to be used as a program control, a colored line will always appear in the control line area, indicating that an appropriate volume of sample has been added and film wicking has occurred and also it's a valid result. Besides, the COVID-19 antigen rapid test (Swab) has been evaluated with specimens obtained from the patients. The sensitivity has been tested with 111 independent samples that have been measured as positive by real-time PCR up to the 33rd cycle, while the specificity has been tested with 310 independent samples that have been measured negative by real-time PCR. 111/421 pcs yielded correct positive results. 310/421 pcs yielded correct negative results. The sensitivity of the product is 94.6% and the specificity of the product is 99.4% based on the results. Abbott's rapid test is one of the most widely used in the United States. Since April 2021, it has completed more than 300 million rapid tests. The clinical performance of this rapid test is determined by testing 60 *SARS-ClV-2* antigen (Ag) positive samples and 181 *SARSClV-2* antigen (Ag) negative samples. These samples are based on the RT-PCR reference method recommended by FDA EUA confirm. The sensitivity is 93.33% (95% Cl: 83.8-98.2%), and the specificity is 99.45% (95% Cl: 97.0-100%). The *SARS-CoV-2* rapid antigen detection developed by Roche is a rapid chromatographic immunoassay method for the qualitative detection of *SARS-CoV-2* specific antigens present in the human nasopharynx. The sensitivity of *SARS-CoV-2* rapid antigen detection is 96.52%, and the specificity is 99.68%. The novel coronavirus antigen detection developed by Healgen aims to qualitatively detects *SARS-CoV-2*. The sensitivity and specificity of detection were 98.32% and 99.60%, respectively.

Conclusion

PCR method

Initially, PCR is used for the qualitative and quantitative diagnosis of the new coronavirus, because it directly detects the viral nucleic acid in the specimens we collected, so it has strong specificity and relatively high sensitivity, even the early infected patients can be diagnosed well. However, the source of the sample is difficult to standardize. Samples include pharynx, nasopharynx secretions, sputum, bronchus, lavage fluid, lung biopsy, conjunctiva, stool, etc. [14]. The copy number of the virus in an individual and in different parts is not the same, so it is hard to standardize the sample. The testing condition is high. The laboratory needs a high levels hospital, P3 level protection, and a certified gene amplification laboratory. It requires PCR-certified personnel to operate, and the steps are cumbersome, during which it requires multiple centrifugation, repeated operations such as opening the lid and adding samples, and the whole process takes 5 to 8 hours, and it takes a long time to complete a batch of tests. It is difficult to avoid aerosol pollution. The storage conditions of nucleic acid samples are harsh, and RNA is easily lysed. It can only be stored for 24 hours at 4°C, but samples for antibody detection such as serum can be stored for 72 hours [14]. In the case of gene sequencing, although the accuracy is higher, it needs to be interpreted by professionals, and the expenditure is obvious.

Table 1 The performance of different COVID-19 Antigen Rapid Tests has been compared and the data are shown in the Table below.

Test	Wondfo	Lepu	Siemens	Acro	Abbott	Roche	Healgen
Relative Sensitivity	96.18%	92.00%	96.72%	94.6%	93.33%	96.52%	98.32%
Relative Specificity	99.72%	99.26%	99.22%	99.4%	99.45%	99.68%	99.60%
Accuracy	97.67%	96.67%	98.74%	98.6%	97.93%	98.83%	99.42%

Timely testing is crucial, and long distances and slow turnaround times will limit the clinical and public health impact of COVID-19 molecular testing. So this method is not suitable for large-area screening.

Antigen rapid test

So far, the emergence of various COVID-19 rapid tests enables us to complete the preliminary screening. Sensitivity and specificity are the two indexs used to evaluate the accuracy of a test. They are important parameter for rapid test product, as they determine the extent to which the test results can be used to draw clinical and epidemiological conclusions, and to understand other evidence that might be needed. This study was designed for COVID-19 Antigen Test Cassette performance with clinical specimen. Total 421 specimens (111 COVID-19 positive specimens and 310 COVID-19 negative specimens confirmed by RT-PCR) were used in clinical study at different locations. Commercial PCR served as the reference method for the COVID-19 Antigen Test Cassette (Nasal swab). The result shows the COVID-19 Antigen Rapid Test has a high restive sensitivity and high relative specificity. The *SARS-CoV-2* diagnostic tests: Antigen (Ag) tests that directly detect the *SARS-CoV-2* virus antigen produced by the host immune response against the virus. The antigen detection method is simple and the detection time is short, but the false negative rate is high. Antigen rapid test (especially nasal swab) with is easy to operate, high precision, convenient sample collection, and quick results. This allows medical personnel to perform testing with less training and explanation of the principles, and to provide patients with efficient novel coronavirus testing services, which can greatly reduce the overload of the medical system. The tests are easy-to-use, antigen rapid test that can be used at or near the point of care, without the need for laboratory infrastructure or expensive equipment. Only a better portfolio and by using suitable detection methods in different situations can be more effective in preventing the COVID-19 virus.

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