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Evaluation of Three Covid-19 Antigen Assay Versus PCR Detection in Routine Practice

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ABSTRACT

According to WHO, molecular testing is the "Gold Standard" for the diagnosis of SARS-CoV-2 infection. However, these tests have some limitations in practice (well trained staff, specific equipment requirements, organization of area and time frame for reporting results). Thus, rapid antigen test (RAT) for the detection of one or several SARS-CoV-2 antigens have emerged. We evaluated the analytical performance of 3 RAT used in our laboratory : FREND® Ag COVID-19 (NanoEntek) (FA), STANDARD Q COVID-19 Ag (SD Biosensor) (BA), PANBIO™ COVID-19 Ag RAPID TEST DEVICE (Abbott) (PA) in comparaison to rRT-PCR results. Our study indicates that PA and SA antigen tests have a very good sensitivity to identify infected patients with COVID-19 specifically between in the 0-5 days time-window post onset of symptoms. Nevertheless, one out of three antigen tests (FA) showed very poor clinical performance.

KEYWORDS: Antigenic test, SARS-CoV-2, Analytical performance.

INTRODUCTION

In December 2019, pneumonia with viral appearance emerged in the city of Wuhan (Hubei province, China). January 9th, 2020, the discovery of a new coronavirus (first called 2019-nCoV and then officially SARS-CoV-2) has been officially announced by the Chinese health authorities and the World Health Organization (WHO). This new virus is the agent responsible for the Covid-19 disease (for CoronaVIrus Disease). There is currently no treatment or vaccine that is effective in treating or preventing the disease is proven. According to WHO, molecular testing is the "Gold Standard" for the diagnosis of SARS-CoV-2 infection [1]. However, these tests have some limitations in practice (well trained staff, specific equipment requirements, organization of area and time frame for reporting results).

Thus, rapid antigen test (RAT) for the detection of one or several SARS-CoV-2 antigens have emerged. They are easy to perform and results are available after 10-30 min. Specificity is consistently reported to be high. Sensitivity compared to rRT-PCR is highly variable (0-94%) and related to the viral load, with higher sensitivity reported on samples with higher viral load [2]. They would be useful for screening and diagnosis on a large scale as well as in countries with limited resources. We evaluated the analytical performance of 3 RAT used in our laboratory : FREND® Ag COVID-19 (NanoEntek) (FA), STANDARD Q COVID-19 Ag (SD Biosensor) (BA), PANBIO™ COVID-19 Ag RAPID TEST DEVICE (Abbott) (PA) in comparaison to rRT-PCR results.

MATERIELS AND METHODS

Eighty (80) samples were taken from symptomatic patient in the first 5 days after the onset of symptoms (S1 group) and 80 samples were taken from symptomatic patient who have symptoms more than 5 days ago (S2 group). Patient was considered symptomatic when he presented one or more of the following signs: fever, dry cough, rhinorrhea, chest pain, dyspnea, myalgia, fatigue, anosmia, ageusia, odynophagia, diarrhea, conjunctivitis, and cephalea). In the other hand, 80 nasopharyngeal samples from asymptomatic patients without recent exposure to the virus were collected for screening (S3 group). All samples were processed immediately upon receipt. rRT-PCR assay was performed on RNA extracts to

detect viral RNA by using GeneFinder™ COVID-19 PLUS RealAmp Kit targeting the RNA dependant RNA polymerase (RdRp) gene, Nucleocapsid gene (N) and Envelop gene (E). The amplification was performed on a QuantStudio 5 instrument (Applied Biosystem)) according to the manufacturer's recommendations. For RAT, there were used as recommended by the manufacturers, using only materials provided in the kit. To read FA RAT result, we used fluorimeter suppleid with the test. However, BA and PA RAT were manually read. The criteria used for the performance assessment of COVID-19 RAT were sensitivity, specificity, negative and positive predictive value (NPV and PPV). RT-qPCR was considered as the gold standard for this evaluation. The Cohen's kappa coefficient (κ) were used to evaluate assay agreement. Analyses were performed using SPSS® Statistics 27.0. All subjects have given their written informed consent.

RESULTS

The median age of the study population was 47.5 (range: 0–72) with a sex ratio of 0.6 (151 men and 89 women). According to rRT-PCR results, 72 samples were positive in S1 group and 51 in S2 group. In S3 group, one rRT-PCR was positive. For S1 and S2 group, the results are reported in Table 1. RAT was negative for all participants of S3 group with the three kits.

Table 1: Comparaison between RAT and rRT-PCR results for S1 and S2 groups.

Group/RAT Kits	S1 group (Symptoms < 5j)		S2 group (Symptoms > 5j)	
	rRT- PCR +	rRT- PCR -	rRT- PCR +	rRT- PCR -
PA test +	72	0	51	0
PA test -	0	8	12	17
SA test +	71	0	49	0
SA test -	1	8	14	17
FA test +	56	0	31	0
FA test -	16	8	32	17

In S1 group, sensitivity of PA, SA and FA COVID-19 RAT is 100%, 98% and 77% respectively, NPV is 100%, 89% and 33% respectively. In S2 group, sensitivity of PA, SA and FA COVID-19 RAT is 81%, 78% and 49% respectively, NPV is 58%, 54% and 34% respectively. Finally, specificity and PPV are around 100% for the 3 kits in this group. The agreement κ index in S1 group between PA / SA and PCR was around 1, the κ index between FA and PCR was 0.7 indicating a moderate agreement. The agreement κ index in S2 group between PA / SA and PCR was around 0,6, the κ index between FA and PCR was 0.29 indicating a fair agreement.

DISCUSSION

At present, the confirmation of COVID-19 exclusively depends on the "gold standard" method, RT-qPCR for virus nucleic acid detection due to their high sensitivity and specificity. However, these tests requires a particular organization of the premises, dedicated equipment and experienced personnel. In addition, the delay in rendering results varies between 6 and 8 hours, which could delay the treatment of the patient and promote the spread of the virus. Thus, other alternatives have been developed such as antigen tests as an aid in the diagnosis of SARS-CoV-2 infection. Antigen tests are immunoassays that detect the presence of a specific viral antigen, which implies current viral infection. Several studies have evaluated the analytical performance of these tests. The specificity of antigen tests is generally as high as most NAATs but the sensitivity of antigen tests varies but is generally lower than most NAATs. The antigen level in specimens collected either before symptom onset, or late in the course of infection, may be below the limit of detection of virus of the test. The WHO recommends RAT tests to reach a minimum performance of ≥80% sensitivity and ≥97% specificity compared to rRT-PCR [3]. In this single-center study, we present a clinical evaluation and comparison of three commercially available COVID-19 antigen tests in nasopharyngeal swab, using RT-PCR as a reference Our study indicates that PA and SA antigen tests have a very good sensitivity to identify infected patients with COVID-19 specifically between in the 0-5 days time-window post onset of symptoms, which has already been shown for other antigen tests than those used by us [4]. Nevertheless, one out of three antigen tests (FA) showed very poor clinical performance.

In a recent study, sensitivity numbers (75–93 %) equal to that for symptomatic patients was found for patients with presymptomatic or early asymptomatic infections. However, for asymptomatic patients late in the course of disease, the sensitivity was very low (26 %) [3]. This is in line with other studies of the Panbio RAT, where sensitivity ranged from 77.2 % to 95.8 % when only patients with symptom duration of less than one week were considered [5]. The Standard Q Ag-RDT (SD Biosensor) was validated in 529 participants, with 170 positive Ag-RDT results out of 191 positive RT-PCR individuals, yielding a sensitivity of 89.0% [6]. One false positive result was obtained in 338 RT-PCR negative individuals, yielding a specificity of 99.7% [6]

Because most of the currently available Ag-RDTs have a considerable false-negative rate, health-care professionals should be aware that a single negative test cannot conclusively rule out SARS-CoV-2 infection; this is

particularly true in low-prevalence settings, where the typically excellent NPV of Ag-RDTs is misleading. Negative results must be combined with clinical observations, patient history, and epidemiological information. For the American Control Disease center (CDC), for the symptomatic patient, a negative test deserves to be controlled by PCR which is not the case for the asymptomatic patient [7]. It's also possible that antigen tests can be used for screening testing in high-risk congregate settings in which repeat testing could quickly identify persons with a SARS-CoV-2 infection to inform infection prevention and control measures, thus preventing transmission. With regular testing (daily or 3 times a week) infectious individuals can be quickly identified and removed from circulation.

CONCLUSION

Although the number of tests is small and the study may not provide by itself a conclusive assessment, it adds to other data that suggest that antigen tests may provide a reasonable testing alternative. Testing criteria focusing on patients with typical symptoms in their early symptomatic period onset could further increase diagnostic value.

Statement of Ethics

All subjects have given their written informed consent.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

TAGAJDID Mohamed Rida : Testing and redaction

EL KOCHRI Safae, ELANNAZ Hicham, ABI Rachid : Bibliography

AKHOUAD Youssef and REGGAD Ahmed and KASSMI Zhour and ENNIBI Khalid : Review

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