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Evaluation of rapid antigen detection kit from the WHO Emergency Use List for detecting SARS-CoV-2

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ABSTRACT

Background: Currently, there are two rapid antigen detection (RAD) kits from the WHO Emergency Use List for detecting SARS-CoV-2.
Objective: The Panbio COVID-19 Ag Rapid Test Device was selected to evaluate the performance for detecting SARS-CoV-2.
Study Design: Analytical sensitivity for the detection of SARS-CoV-2 virus was determined by limit of detection (LOD) using RT-PCR as a reference method. Clinical sensitivity was evaluated by using respiratory specimens collected from confirmed COVID-19 patients.
Results: The LOD results showed that the RAD kit was 100 fold less sensitive than RT-PCR. Clinical sensitivity of the RAD kit was 68.6 % for detecting specimens from COVID-19 patients.
Conclusions: The RAD kit evaluated in the present study shared similar performance with another kit from the WHO Emergency Use List, the Standard Q COVID-19 Ag. Understanding the clinical characteristics of RAD kits can guide us to decide different testing strategies in different settings.

1. Introduction

RT-PCR is the gold standard for detection of SARS-CoV-2 virus. The application of a rapid antigen detection (RAD) kit is limited by its sensitivity [1]. However, among the currently available RAD kits, lateral flow antigen assay is fast, low cost, and can be performed by healthcare professional without intensive training and specialized instrument. The principle is based on the movement of a liquid sample [2]. RAD kits would be helpful for the diagnosis of COVID-19 patients either as mass-screening or first aid tests at the emergency room who are most likely to be in the early and contagious phase of the illness [3,4]. A few minutes to results have the potential to satisfy the demand for an early SARS-CoV-2 infection diagnosis [5].

Currently, there are two RAD kits under the 'WHO Emergency Use Listing for In vitro diagnostics (IVDs) Detecting SARS-CoV-2' [6]. They are Standard Q COVID-19 Ag (SD Biosensor, Korea) and Panbio COVID-19 Ag Rapid Test Device (Abbott Rapid Diagnostics, Germany). For the ease of communication, 'Standard Q' and 'Panbio' stand for these two kits respectively. We have evaluated different RAD kits before October 2020 and found that the Standard Q kit might satisfy the demand for an early SARS-CoV-2 infection diagnosis [7,8]. The Panbio kit was commercially available in Hong Kong at the end of October 2020. We are interested to know if the Panbio kit showed comparable performance with the Standard Q kit.

2. Methods

2.1. Limit of detection

The intended use for the Panbio kit is for the detection of SARS-CoV-2 virus in nasopharyngeal swabs. As our specimens were placed in viral transport media or phosphate-buffered saline, a fixed amount of specimen was mixed with the extraction buffer. The subsequent procedures were carried out according to the manufacturer's instructions. We evaluated two specimen volumes, 100 μL and 350 μL.

In an effort to compare the performance of these two specimen volumes, limit of detection (LOD) was determined using a serial tenfold dilution of a nasopharyngeal swab and throat swab (NPS & TS) which was obtained from the Hong Kong COVID-19 patient, hCoV-19/Hong Kong/VM20031164/2020. The results were then compared with RT-

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PCR.

The Standard Q kit was also tested as a reference method simultaneously. The kit was gifted by Roche. Virus concentrations in each dilution were estimated from cycle threshold (Ct) value as described [7].

2.2. Respiratory specimens used for accessing clinical sensitivity

From April 3, 2020 to October 20, 2020, respiratory specimens from COVID-19 patients collected by the Public Health Laboratory Services Branch in Hong Kong were retrieved for this evaluation. All of the specimens were confirmed with SARS-CoV-2 infection by RT-PCR as described [7].

The types of specimens selected and the total number tested were identical to the previous study [8]. Since the nasopharyngeal aspirate and throat swab (NPA & TS) were used up in our previous evaluations, this type of specimen cannot be included in the present study. In brief, three types of specimens were selected: (1) NPS & TS, (2), NPS and (3) throat saliva. A total of 105 archive specimens were tested. These comprised 35 NPS & TS, 35 NPS and 35 throat saliva. The Ct values for the two cutoffs <18.57 and >28.67 were utilized to classify specimens as 'high viral load' and 'low viral load' respectively. Ct values between 18.57 and 28.67 were classified as 'normal viral load' [8]. Of the 105 specimens tested, 24, 54 and 27 specimens were classified as 'high viral load', 'normal viral load' and 'low viral load' specimens respectively. This viral load distribution was similar to the previous study [8].

2.3. Respiratory isolates used for evaluating cross-reactivity

To evaluate the cross-reactivity of the RAD kit, 13 non-SARS-CoV-2 respiratory virus isolates were tested. They were influenza A (H1pdm09), influenza A(H3), influenza B, adenovirus, coronavirus type OC43, coronavirus type 229E, parainfluenza virus type 1, parainfluenza virus type 2, parainfluenza virus type 3, parainfluenza virus type 4, respiratory syncytial virus, rhinovirus and enterovirus.

3. Results

The LOD of the Panbio kit was 10^{-4}. There were no marked differences when using 100 µL and 350 µL specimen volumes. However, the test bands were more intense when using 350 µL specimen volume. Since the specimen volume utilized for the Standard Q kit was also 350 µL, this specimen volume was selected for accessing clinical sensitivity of the Panbio kit.

The reference Standard Q kit shared the same LOD with the Panbio kit, both of them were 10^{-4} (Table 1). The LOD of the Standard Q kit was 100 fold less sensitive than RT-PCR which was concordant to our previous study [8].

Of the 105 specimens tested, the Panbio kit showed high sensitivity for both high viral load and normal viral load specimens (83.3 %–100 %) but low sensitivity for low viral load specimens (0–11.1 %) (Table 2). The corresponding Ct values for the specimens tested by Panbio kit were shown in Fig. S1.

In the cross-reactivity test using virus isolates, all were tested negative by the Panbio kit.

4. Discussion

In this study, we determined the performance characteristics of the Panbio kit for detecting SARS-CoV-2 virus. Clinical sensitivity was 68.6 % (72/105) for detecting specimens from COVID-19 patients. Although archived specimens were tested in the present study, our results were inline with other studies using in-field nasopharyngeal swabs. The overall sensitivity of the Panbio kit ranged from 73.3%–75.5% [9–11].

The main objective of this study is to see if the Panbio kit showed comparable performance with the Standard Q kit that we performed previously [8]. Parallel comparison between these two kits has not been performed. It is difficult to compare RAD kits due to the number of confounding factors that can affect the reliability of results, these include: site of testing, type of specimen processed, volume of specimen input, viral load distribution among specimens selected, variation of method to quantify viral load. In the present study, a more controlled method was employed to limit these confounding factors. In terms of analytical sensitivity, the Panbio kit shared the same LOD with the Standard Q kit, both of them were 100 fold less sensitive than RT-PCR. In terms of clinical sensitivity, both kits shared similar sensitivity for detecting specimens from COVID-19 patients, Panbio kit: 68.6 %; Standard Q kit: 65.7–71.4 % (Table S1). In our previous study, we recommended specimens obtained within 7 days after symptom onset for use with the Standard Q based on the prevalence of specimens of certain viral load. Since both Panbio kit and Standard Q kit shared similar clinical characteristics, the recommendation of testing specimens obtained within 7 days after symptom onset was also valid for the Panbio

Table 1
Comparison of RT-PCR and rapid antigen detection kits for the limit of detection of SARS-COV-2 virus.

Dilution[b]	Test results[a]			
	RAD test			RT-PCR[e]
	Panbio (100 µL)[c]	Panbio (350 µL)[d]	Standard Q	
10^{-1}	POS	POS	POS	16.41
10^{-2}	POS	POS	POS	19.80
10^{-3}	POS	POS	POS	23.15
10^{-4}	POS	POS	POS	26.29
10^{-5}	NEG	NEG	NEG	28.80
10^{-6}	NEG	NEG	NEG	33.58
10^{-7}	NEG	NEG	NEG	NEG

[a] POS, positive; NEG, negative.
[b] Serial tenfold dilution of the respiratory specimen, NPS & TS, obtained from the Hong Kong COVID-19 patient, hCoV-19/Hong Kong/VM20031164/2020.
[c] Specimen volume of 100 µL was mixed with the extraction buffer. The subsequent procedures were carried out according to the manufacturer's instructions.
[d] Specimen volume of 350 µL was mixed with the extraction buffer. The subsequent procedures were carried out according to the manufacturer's instructions.
[e] RT-PCR were tested twice with identical results. The Ct values shown were the mean of both runs.

Table 2
Performance characteristics of the rapid antigen detection kit for the presence of SARS-CoV-2 virus in 105 respiratory specimens.

Specimen type[a]	Specimens used for testing the Panbio kit and the results				
	Ct value		No. of specimens		sensitivity
	mean	range	tested	positive	
NPS & TS					
High	15.30	12.98–18.08	8	8	100 %
Normal	22.85	18.91–28.41	18	15	83.3 %
Low	31.43	29.30–34.59	9	1	11.1 %
All	23.33	12.98–34.59	35	24	68.6 %
NPS					
High	16.54	13.02–18.50	8	8	100 %
Normal	24.17	18.75–28.65	18	16	88.9 %
Low	34.85	33.42–35.88	9	0	0 %
All	25.17	13.02–35.88	35	24	68.6 %
throat saliva					
High	14.77	11.45–18.26	8	8	100 %
Normal	24.22	19.13–28.24	18	15	83.3 %
Low	31.73	29.25–34.42	9	1	11.1 %
All	23.99	11.45–34.42	35	24	68.6 %

[a] 'High', means specimens with Ct values <18.57 of SARS-CoV-2 virus RT-PCR; 'Normal', Ct values between 18.57 and 28.67; 'Low', Ct values >28.67.

kit. Our observation was also concordant to the recent study that 'Panbio antigen rapid test is reliable to diagnose SARS-CoV-2 infection in the first 7 days after the onset of symptoms' [9].

In conclusion, understanding the performance of RAD kits can guide us to implement the test appropriately. During the pandemic, it is not known whether the increased demand for an early SARS-CoV-2 infection diagnosis will lead to the limited availability of test kits. Alternatives have to be sought for test kits shared similar operating procedures and similar performance. Our information can provide implementation guidance when deciding different testing strategies in different settings [12].

Declaration of Competing Interest

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jcv.2020.104712.

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