GEBRUIK VAN SPEEKSELSTALEN VOOR HET TESTEN MET EEN SNELLE ANTIGEEN TEST

RAG subgroep Testing – 17 mei 2021

Opmerking: De huidige aanbevelingen zijn onderhevig aan veranderingen afhankelijk van nieuwe wetenschappelijke gegevens en/of de evolutie van de epidemie.

Aanbevelingen:

- Er zijn momenteel nog teveel twijfels over de betrouwbaarheid van speekselstalen voor het testen met snelle antigeentesten, en het is daarom ten sterkste afgeraden deze te gebruiken.
- Dit dient duidelijker gecommuniceerd te worden aan huisartsen en andere zorgverstrekkers.

De volgende personen hebben deelgenomen aan dit advies:

Emmanuel André (KU Leuven); Emmanuel Bottieau (ITG/IMT) ; Achille Djiena (AVIQ); Herman Goossens (UAntwerpen); Marie Pierre Hayette (CHU-Liège); Yves Lafort (Sciensano); Barbara Legiest (ZG); Tinne Lernout (Sciensano); Romain Mahieu (COCOM); Elizaveta Padalko (UZGent); Olivier Vandenberg (LHUB-ULB); Ann Van den Bruel (KU Leuven); Steven Van Gucht (Sciensano); Pieter Vermeersch (UZ-Leuven).

CONTEXT

The current recommendation with regards to what specimen to use for rapid Ag testing is that it should always be done on swab samples. The preferential swab is a nasopharyngeal swab, although that combined nose-throat swabs and nasal swabs (in a context of self-testing) are also acceptable. However, the list of rapid Ag tests approved for use in Belgium by the Federal Agency for Medicines and Medical Products (FAGG/AFMPS) includes several test kits intended for saliva specimens (1). This creates confusion among some general practitioners who conclude that rapid Ag tests can be used on saliva specimens. The RAG Testing therefore reviewed the evidence of the performance of rapid Ag tests on saliva.

DISCUSSION

- Studies evaluating the performance of rapid Ag tests using saliva specimens find sometimes very discordant results. However:
    - Most studies found a low sensitivity, and some alarmingly low sensitivity (4%!).

- One study compared the same rapid Ag test when performed on saliva and on a nasopharyngeal swab, and found that sensitivity on saliva was about 10 times lower than on an NPS. This study used a rapid Ag test currently distributed in Belgium for self-testing (SD Biosensor).

- There is thus some evidence that saliva might have a greater negative impact on sensitivity in rapid Ag tests than it has in RT-PCR.

RECOMMENDATIONS

- Until the reasons for the sometimes very low performance of rapid Ag tests on saliva is clarified: maintain the recommendation not to use rapid Ag tests on saliva specimens.
- Communicate this message clearly to all stakeholders involved.

BACKGROUND LITERATURE

Several studies evaluated the performance of rapid Ag tests on saliva samples, with sometimes discordant results. The table below summarizes the findings of these studies.

Study	Population	Saliva specimen	N positive	Sensitivity	N negative	Specificity
Azzi et al. (2)	Hospitalized patients and asymptomatic health care workers	drooled	55	91%*	57	60%
Nagura-Ikeda et al. (3)	Hospitalized patients and asymptomatic high-risk contacts	spitted	103	11.7%**	-	-
	Early symptomatic (<=9 days)		61	13.1%**	-	-
	Asymptomatic		15	13.3%**	-	-
Yokota et al. (4)	Symptomatic in-patients	spitted	17	59%**	-	-
			17	24%*	-	-
Agullo et al. (5)	Symptomatic and asymptomatic adults and children	spitted	59	23.1%**	575	100%
Kannian et al. (6)	Stored saliva samples of patients	?	20	45%*	10	100%
Kritikos et al. (7)	Hospitalized patients	?	58	4%***	-	-
Igloi et al. (8)	Test center attendees (symptomatic and asymptomatic)	drooled cough discharge	44	66.1%*	745	99.6%
			62	75.0%**	727	99.3%
	Ct value <30		38	88.6%*	-	-
			45	86.1%**	-	-

* Compared to RT-PCR on saliva

** Compared to RT-PCR on nasopharyngeal swab

*** Compared to RT-PCR on either saliva or nasopharyngeal swab

Some studies showed very disappointing results with regard to the sensitivity of rapid Ag tests on saliva. Kritikos et al. evaluated the performance of the SD Biosensor rapid Ag test (Roche) on

both nasopharyngeal (NP) and saliva samples, and of RT-PCR on NP and saliva samples. The highest sensitivity (using samples positive with PCR on either sample as reference) was RT-PCR on NP (98%), followed by RT-PCR on saliva (69%) and a rapid Ag test on NP (35%/47% depending on the transport medium). Sensitivity of the rapid Ag test on saliva was only 4% (only 2 positive samples out of 58 detected). Also the studies by Agullo et al. and Nagura-Ikeda et al. found extremely low sensitivity. Part of the explanation for the lower sensitivity of the RT-PCR on saliva than on NPS was that the sample included also patients with a lower viral load, which were not detected in the saliva sample. A possible explanation given by Kritikos et al. for the much lower sensitivity of the rapid Ag test on saliva than the rapid Ag test on a NPS, is the presence of mucosal secretory immunoglobulins targeting SARS-CoV-2 antigens and thus competing with the rapid Ag test for the same target.

Igloi et al, on the other hand, evaluated the same test (SD Biosensor) and found a much higher sensitivity, although still rather low. Using samples that tested positive with an RT-PCR on a NPS as reference, sensitivity was 75%, using positive RT-PCR on saliva as reference, sensitivity was 66%. Among samples with a higher viral load (Ct<30), sensitivity was 86% and 89%, respectively. Also Azzi et al. found higher sensitivity.

INTERNATIONAL GUIDELINES

ECDC

In its recent technical report on the use of rapid antigen detection (including self-) tests for SARS-CoV-2 in occupational settings, ECDC states that there are very few clinical validation studies on the use of saliva as sample material for rapid Ag tests and data on the sensitivity of the tests are lacking (9). Self-sampling using saliva is not clinically validated for rapid Ag tests.

CDC

In its testing for SARS-CoV-2 overview (updated 17 Mars 2021), CDC recommends to perform rapid Ag tests on nasal or nasopharyngeal specimens (10), as does the FDA (11). However, on its site on self-testing CDC mentions the possibility to use tests that require a saliva specimen (12). The FDA has, on the other hand, not yet approved a rapid Ag test kit using saliva (13).

The Netherlands

RIVM (26 April) states that saliva samples are only suitable for molecular detection of virus in saliva, not for antibody detection or culture (14). It does not specifically state that it cannot be used for rapid Ag testing, although this is indirectly implied.

France

The French Haute autorité de santé has not yet approved the ue of saliva specimens for rapid Ag testing (15).

United Kingdom

The UK currently only distributes swab self-sampling kits (16).

Germany

As in Belgium, the German agency for medicines and medical products (BfARM) has approved some rapid Ag tests using saliva (17).

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