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BRIEF REPORT

Sensitivity of Nasopharyngeal Swabs and Saliva for the Detection of Severe Acute Respiratory Syndrome Coronavirus 2

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We enrolled 91 consecutive inpatients with COVID-19 at 6 hospitals in Toronto, Canada, and tested 1 nasopharyngeal swab/saliva sample pair from each patient using real-time RT-PCR for severe acute respiratory syndrome coronavirus 2. Sensitivity was 89% for nasopharyngeal swabs and 72% for saliva ($P = .02$). Difference in sensitivity was greatest for sample pairs collected later in illness.

Keywords. COVID-19; SARS-CoV-2; nasopharyngeal swab; saliva.

Rapid and accurate detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patient specimens is critical to controlling the coronavirus disease 2019 (COVID-19) pandemic. As yet, there are few data comparing sensitivity of different specimen types for SARS-CoV-2 detection.

In Canada, nasopharyngeal (NP) swabs are the preferred collection site for SARS-CoV-2 testing [1, 2], and preliminary data suggest that they may be more sensitive than oropharyngeal swabs for SARS-CoV-2 detection [3, 4]. However, collection of both NP and oropharyngeal swabs is uncomfortable for patients and may pose a risk to healthcare workers. Moreover, recent global supply-chain shortages have resulted in limited access to various swab types. Saliva, in contrast, can be easily self-collected by most adolescents and adults. Other groups have demonstrated successful detection of SARS-CoV-2 in saliva specimens and use of saliva for serial sampling [5–7]. We aimed to compare the sensitivity of NP swabs and saliva for SARS-CoV-2 detection in hospitalized patients.

METHODS

The Toronto Invasive Bacterial Disease Network (TIBDN) performs population-based surveillance for select infectious diseases in metropolitan Toronto and the regional municipality of Peel (population base, 4.2 million in 2016), Ontario, Canada. For COVID-19, clinical microbiology laboratories report specimens testing positive for SARS-CoV-2 to the central study office. Starting on 16 March 2020, study staff enrolled consecutive inpatients at 6 TIBDN hospitals. Patient demographic, exposure, and medical data were collected by interview and chart review. An NP swab and saliva specimen were collected on the day of enrollment, and then 3 subsequent pairs of samples were obtained at 72-hour intervals if the patient remained hospitalized. The NP swabs were collected as per standard procedures and placed into UTM viral transport medium (COPAN Diagnostics, Murrietta, CA) [8]. For saliva specimens, patients were asked to spit 1 teaspoon (5 mL) of saliva into a sterile specimen container and then 2.5 mL of phosphate-buffered saline was added.

Samples were transported to the research microbiology laboratory, where they were aliquoted and frozen at −80°C within 8 hours of collection. On 14 April, we selected each patient's most recent NP swab/saliva sample pair for SARS-CoV-2 real-time reverse transcriptase–polymerase chain reaction (RT-PCR) testing. On 1 June, we repeated the selection for new patients enrolled since 14 April. Laboratory testing was with the Allplex 2019-nCoV Assay (100T) (Seegene Inc, Seoul, Korea) to detect RNA-dependent RNA polymerase (RdRp), envelope (E), and nucleocapsid (N) genes at Sinai Health System (Toronto, Canada).

RESULTS

Ninety-one inpatients were included; all were confirmed to have COVID-19 with an NP, midturbinate, or nasal swab tested in a clinical laboratory in Toronto. The median age was 66 years (range, 23–106 years), 39 (43%) were female, 70 (77%) had at least 1 comorbidity, and 12 (13%) were immunocompromised. Eighteen (20%) had a household contact as the suspected source of exposure. On admission, 66 (73%) had fever and 68 (75%) had cough. The median time from illness onset to hospital admission was 6 days (interquartile range [IQR], 2–9 days) and 27 (30%) required intensive care. The median time from illness onset to collection of the tested specimens was 12 days (IQR, 9–15 days). As of 5 June, 3 (3%) patients remained hospitalized, 82 (90%) were discharged, and 6 (7%) had died.

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Table 1. Results of Testing of Nasopharyngeal Swab and Saliva for SARS-CoV-2 RNA in Hospitalized Patients With COVID-19, by Time From Illness Onset to Collection of Sample Pair

Time From Illness Onset to Specimen Collection	No. of Patients (%)			
	With NP Swabs and Saliva Both Positive	With NP Swab Only Positive	With Saliva Only Positive	With NP Swab and Saliva Both Negative
0–7 days (n = 18)	14 (78)	2 (11)	1 (6)	1 (6)
8–14 days (n = 43)	21 (49)	13 (30)	4 (9)	5 (12)
≥15 days (n = 30)	9 (30)	5 (17)	3 (10)	13 (43)
Any (n = 91)	44 (48)	20 (22)	8 (9)	19 (21)

N = 91.

Abbreviations: COVID-19, coronavirus disease 2019; NP, nasopharyngeal; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Of 91 patients with paired samples tested, 72 (79%) had at least 1 positive specimen. In 44 (61%) of these 72 patients, both NP swab and saliva were positive, in 20 (28%) only the NP swab was positive, and in 8 (11%) only saliva was positive ($P = .02$) (Table 1). Thus, using NP swabs only would have detected 64 of 72 (89%) patients with at least 1 positive specimen and using saliva only would have detected 52 of 72 (72%) patients with at least 1 positive specimen. Using NP swabs only would have detected 16 of 17 (94%), 34 of 38 (89%), and 14 of 17 (82%) patients in their first, second, and third/fourth week of illness, respectively (Table 1). Using saliva only would have detected 15 of 17 (88%), 25 of 38 (66%), and 12 of 17 (71%) patients in their first, second, and third/fourth week of illness, respectively (Table 1).

The median N gene cycle threshold (Ct) for NP swabs was 30 (IQR, 26–35) when the saliva specimen in the pair was positive (n = 44) versus 34 (IQR, 31–37) when the saliva specimen in the pair was negative (n = 20) ($P = .003$). N gene Ct values were higher if samples were collected later in illness (Spearman's $\rho = 0.3$, $P = .0003$). Results were similar when Ct values of the E and RdRp genes were used (data not shown).

DISCUSSION

In this sample of 91 inpatients, NP swabs were 17% more sensitive than saliva overall. Sensitivity of both types of specimens was highest in the first week of illness, when viral concentrations have been reported to be highest [4, 9]. The difference in sensitivity between NP swabs and saliva was 6% if collected in the first week of illness and 20% if collected in the second week of illness or later. Our data suggest that NP swabs are more sensitive than saliva for SARS-CoV-2 detection, especially if the patient is later in illness.

Our data also suggest that neither a single NP swab nor a single saliva specimen is 100% sensitive for the detection of COVID-19. This is consistent with prior literature [10], emphasizing that a single negative test does not rule out disease in patients with a high pretest probability of COVID-19. Repeated samples may improve yield. For example, among patients with a high pretest probability for COVID-19 and a negative NP swab, repeating the NP swab and also collecting a saliva sample may be considered, as saliva sampling is noninvasive and 11% of patients in this study with at least 1 positive specimen were only positive in their saliva.

There are several limitations to this analysis. As these patients were originally diagnosed using NP, midturbinate, or nasal swabs, it is possible that there is a bias towards subsequent NP swabs versus other specimens being positive. We used a single detection system (Seegene), and other platforms may have yielded different results. We simply asked patients to spit a teaspoon of saliva into a specimen container; many patients were unable to provide a full teaspoon of saliva, and this may in part explain the gap in sensitivity between NP swabs and saliva. It is also possible that other methods, such as throat washing with normal saline, would have improved yield. One small study found throat washing to be significantly more sensitive than NP swabs for SARS-CoV-2 detection, possibly enabling the acquisition of more epithelial cells [11]. Throat washing is easy to self-collect and should be further investigated as a noninvasive alternative to NP swabs and other invasive swabs such as oropharyngeal swabs.

In conclusion, NP swabs were more sensitive than saliva for SARS-CoV-2 detection, particularly among patients beyond the first week of illness. Notably, however, NP swabs were only 6% more sensitive than saliva among the 18 sample pairs collected in the first week of illness in this study. This raises the possibility that NP swabs and saliva are equivalent early in illness, but this requires study in a larger sample. More data are also needed to assess testing on different platforms and to assess the sensitivity of different specimen types in asymptomatic patients or those whose illness does not require hospitalization.

Notes

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