No detection of SARS-CoV-2 RNA on urethral swab in patients with positive naso-pharyngeal swab

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Research

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Abstract

Background

The recent SARS-CoV-2 infection is the cause of one of the most important pandemics that history has ever experienced. SARS-CoV-2 can lead to a MOF (Multiple Organ Failure) that is critical for life of patients. Viral RNA is found in human tissues as lung, intestine, testicle, kidney, etc. and it is the reason to theorize different ways of transmission of the virus in addition to respiratory droplets. The aim of our study was to evaluate the presence of SARS-CoV-2 in urethral swabs.

Methods

We enrolled 10 patients with SARS-CoV-2 infection who attended the Infectious Diseases Unit of the A.O.U. Federico II of Naples, from March 2020 to April 2020. For each patient, one urethral swab was collected at the time of SARS-CoV-2 infection.

Results

All ten patients had a negative urethral swab for SARS-CoV-2 RNA when the rhino-oropharyngeal swab was found to be positive for SARS-CoV-2 RNA. Our data show for the first time that the virus would not affect the urinary tract and therefore would not be found in the urine and even less would it be transmissible through the urine. This result was independent of the stage of the disease, in fact, regardless of the severity of the clinical conditions, all patients had a negative urethral swab for SARS-CoV-2 RNA.

Conclusion

This observation, which needs to be further investigated with further studies and a larger sample, could be the cornerstone for understanding the role of SARS-CoV-2 in relation to the genitourinary system.

Introduction

The recent SARS-CoV-2 infection is the cause of one of the most important pandemics that history has ever experienced. SARS-CoV-2 is the causative agent of COVID-19 (1, 2). The main manifestations of COVID-19 are fever, dry cough and asthenia. Rapid progression to ARDS (Acute Respiratory Distress Syndrome), septic shock, metabolic acidosis, coagulation deficiency and lastly MOF (Multiple Organ Failure) is possible in critically ill patients (3). Most patients have a good prognosis, while a small part of them develops a severe disease. The virus can be transmitted from person to person, directly or indirectly, via the respiratory, oro-fecal and probably sexual routes. (4, 5) Rapid development and serious consequences of the infection prompted authorities to contain the pandemic and the researchers to study

the transmission pathways. (6) Human receptor of SARS-CoV-is the angiotensin converting enzyme (ACE2). This is expressed in human tissues as lung, intestine, testicle, kidney, etc. Viral RNA has also been identified in other biological samples such as feces, blood, semen (7), tears (8) and urine. However, the ways of transmission of the infection are not fully understood. The evolution of the pandemic worldwide pushes research to find answers to questions about attitudes in real life such as sexual behavior. For example, is it safe for a patient with SARS-CoV-2 infection after negative naso-pharyngeal swab to have sex? And in the end, is Sars-CoV-2 a Sexually Transmitted Disease (STD)? The aim of our study was to evaluate the presence of SARS-CoV-2 in urethral swabs collected in 9 consecutive patients with COVID-19

Materials And Methods

We enrolled patients with SARS-CoV-2 infection who consecutively attended the Infectious Diseases Unit of the A.O.U. Federico II of Naples, from March 2020 through April 2020. The SARS-CoV-2 RNA infection was defined by the positivity of the rhino-oropharyngeal swab for SARS-CoV-2 RNA by reverse polymerase chain reaction (rRT-PCR). Diagnosis of COVID-19 was defined by the positivity of the rhino-oropharyngeal swab for SARS-CoV-2 RNA by reverse polymerase chain reaction (rRT-PCR) and from clinical-laboratory-instrumental manifestations characteristic of this infection. In particular, as regards the clinical manifestations, they were fever, dry cough, asthenia, nasal obstruction, rhinorrhea, pharyngodynia, myalgia, diarrhea, dyspnea, hypoxemia, ARDS (Acute Respiratory Distress Syndrome), septic shock, acidosis metabolic, coagulation deficiency and MOF (Multiple Organ Failure). As for blood chemistry tests, lymphopenia, elevated transaminases, lactate dehydrogenase (LDH), creatine kinase (CPK), myoglobin, troponin T elevation (TnT), increased D-dimer, an increase in reactive protein C (PCR) and erythro-sedimentation rate (ESR). Regarding instrumental diagnostics, in the initial phase of the disease a nodular and / or interstitial pattern occurs, especially in the periphery of the parenchyma. Subsequently, frosted glass patterns develop bilaterally, infiltrative patterns. (9) In turn, patients with SARS-CoV-2 infection were distinguished by the stage of the disease, in particular they distinguished: patients with an asymptomatic form, patients with a mild-moderate form (symptoms, no pneumonia), patients with non-severe pneumonia (patient with pneumonia and no signs of severe pneumonia and no need for oxygen therapy), patients with severe pneumonia (fever or suspected respiratory infection, and at least one of the following: respiratory rate > 30 acts / min, severe breathing difficulty or SpO2 < 93% in ambient air), patients with Acute Respiratory Distress Syndrome (ARDS). (10) For each patient, a urethral swab and a rectal swab were collected at the time of SARS-CoV-2 infection. Detection of SARS-CoV-2 was conducted on each sample by reverse polymerase chain reaction (rRT-PCR). For patients who presented with a urethral swab and / or a rectal swab positive at the time of diagnosis, the swab was performed again at the time of the patient's virological recovery. The patient was defined as virologically cured, when she/he presented two rino-oropharyngeal swabs for SARS-CoV-2 RNA, performed at least 24 hours apart, negative. (11) Subjects with the following inclusion and exclusion criteria were enrolled:

- Inclusion criteria: patient with positivity of the rhino-oropharyngeal swab for SARS-CoV-2 RNA; age > 18 years; intention to participate in the study and to sign the informed consent.

- Exclusion criteria: age < 18 years; inability to understand or sign informed consent; any other condition that in the opinion of the experienced person could make the patient unsuitable for enrollment or that could interfere with the patient's participation in the study and its completion.

Shapiro-Wilk test was used to check for Gaussian distribution. In case of non-Gaussian Distribution, Non-parametric tests (Wilcoxon-Mann-Whitney test, Kruskal-Wallis non-parametric ANOVA) were used in case of Gaussian distribution we used t-Student testù or ANOVA. Multivariate statistical analysis (Principal Components Analysis, hierarchical clustering, Principal Coordinates Analysis) were used to identify the groupings of the samples and the definition of the variables that allowed these groupings. All significance values are adjusted to take into account the effect of multiple comparisons, using the Benjamini-Hochberg correction and a False Discovery Rate value < 0.05 was considered statistically significant. A p-value < 0.05 was considered statistically significant for all tests conducted in the study.

Results

Ten patients were enrolled (7 male and 3 females). (Table 1) Of these, six had pneumonia (one severe), the others had mild to moderate symptoms. Only one appeared to be asymptomatic. None of the patients were hospitalized in an intensive care unit. Eight were treated with hydroxychloroquine (200 mg 1 tablet x 2 / day), lopinavir / ritonavir (200/50 mg 2 tablets x 2 / day) and with azithromycin (500 mg 1 tablet / day). All therapies lasted 14 days. Two of these patients received treatment with Tocilizumab (8 mg / kg / day every 12 hours only twice). Only two patients did not receive therapy. All enrolled patients received low-weight heparin. All ten patients achieved clinical and virological cure. Seven of the 10 patients enrolled had comorbidities, in particular 3 were suffering from cardiovascular disease, 1 from anxiety-depressive syndrome, 1 from colon adenocarcinoma, 1 from cognitive decline and another from chronic pancreatitis. None of the patients had a history of disorders and / or pathologies attributable to the urinary genitourinary system.

Table 1
Anagraphic clinical features of enrolled patients

Age (median, IQR)	***64.9 (37–84)***
Gender	7 (70%)
M	3 (30%)
F	
Urethral swab	0 (0%)
Positive for SARS-CoV-2 RNA	10 (100%)
Negative for SARS-CoV-2 RNA	
D-dimer (mg/l, median, IQR)	2.198 (0.29–6.72)
Fibrinogen (mg/dl, median, IQR)	566.7 (327–828)
C-reactive protein (mg/l, median, IQR)	30.8 (7-119)
Albumin (g/dl; median, IQR)	3.9 (3-4.6)
Platelets (elements/μL; median, IQR)	218,000 (178,000-560,000)
INR (median, IQR)	0.9 (0.8–1.2)
ALT (IU/l, median, IQR)	23 (18–27)
AST (IU/l, median, IQR)	21 (15–29)
Tot. Bil. (mg/dl; median, IQR)	0.8 (0.6–1.3)
Staging COVID-19	1 (10%)
Asymptomatic	3 (30%)
Mild to moderate symptoms	5 (50%)
Non-severe pneumonia	1 (10%)
Severe pneumonia	
Antiviral therapy	8 (80%)
Hydroxychloroquine + Lopinavir / ritonavir + Azithromycin	2 (20%)
Tocilizumab	

All ten patients had a negative urethral swab for SARS-CoV-2 RNA in the active phase of the disease (COVID-19), i.e. when the rhino-oropharyngeal swab was found to be positive for SARS-CoV-2 RNA.

Discussion

We still have few data regarding pathophysiology of COVID-19, and data on presence of SARS-CO-V2 RNA in urethra are lacking. Our data show that the virus is not detected at the urethral level. In contrast, we do know that the virus has been detected in various biological samples. In particular, the virus has been detected in the ocular secretions, feces and seminal fluid of patients with COVID-19. These findings warned about the transmission modalities of the SARS-CoV-2, which may go beyond the respiratory route. Our data show for the first time that the virus is not found in urethral swab and this makes the transmission via urine unlikely. We underline that this result was independent of the stage of the disease, in fact, regardless of the severity of the clinical conditions, all patients had a negative urethral swab for SARS-CoV-2 RNA research during the active phase of the disease, i.e. when they were positive for SARS research -CoV-2 RNA on rhino-oropharyngeal swab.

Conclusion

We acknowledge that our study has several limitations, for example, the small sample size and the use of urethral swab as the only site of detection. However, this is first observation, which needs to be further investigated in larger studies, of the lack of detection of SARS-CoV-2 in urethral swabs from patients with COVID-19, during an active virological and clinical phase of the disease

Abbreviations

SARS-CoV-2: Severe Acute Respiratory Syndrome-CoronaVirus-2

COVID-19: COronaVIrus Disease 19

Declarations

-Ethics approval and consent to participate

The study has a statement on ethics approval and consent. The study involves human participants. The study was approved by the Federico II University Ethics Committee.

-Consent to publication

Not applicable

- Availability of data and material

There is an “Availability of data and materials” .

- Competing interests

There are not financial and non-financial competing interests.

- Funding

There are not fundings

- Authors' contributions

Lorenzo Spirito: the first author

Biagio Pinchera: the corresponding author

The others authors: co-authors

- Acknowledgements

Not applicable

I confirm I have provided a complete declarations section in my manuscript, in particular:

- I have the ethics approval and consent to participate.

- I have the consent for publication

- I have the availability of data and materials

- I have not competing interests

- I have not funding

- I have the authors' contributions

- I have the acknowledgements

The undersigned declares that what has been reported has been done and is true

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