



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

<http://dx.doi.org/10.3760/cma.jissn.0253-2727.2020.0006> [Epub ahead of print].

Áurea Redondo-Sendino*, Isabel Cristina González Sánchez, Beatriz de Victoria Fernández

Medicina de Familia, Centro de Salud Canillejas, Madrid, Spain

* Corresponding author.
E-mail address: aurearedondo@hotmail.com
(Á. Redondo-Sendino).

2387-0206/ © 2020 Elsevier España, S.L.U. All rights reserved.

Free-floating right heart thrombus with pulmonary embolism in SARS-CoV-2 patient



Trombo intracardiaco con tromboembolia pulmonar en paciente con SARS-CoV-2

Dear Editor,

Infection with SARS-CoV-2 generates alterations in coagulation factors, mainly elevation of D-dimer values. These coagulation disorders jointly with activation of inflammatory factors trigger thrombotic events such as pulmonary embolism.¹ Although, presence of free floating right heart thrombus is unusual situation in patients with massive pulmonary embolism.

A 56-year-old caucasian male with morbid obesity (BMI 45 kg/m²), with 15-day history of dyspnea, myalgia and dry cough, was admitted to emergency room. First rapid SARS-CoV-2 PCR was negative, but with high clinical suspicion, pharmacological treatment was started. Tachypnea and dry crackles were observed at physical examination. Laboratories studies showed white-cell count $15.80 \times 10^9/L$ (12% lymphocytes), lactate dehydrogenase 425 U/L, C-reactive protein 3.82 mg/dl and D-dimer 32,000 mcg/L. Arterial blood gas PaO₂ 55 mmHg at room air. CT pulmonary angiography (CTPA) could not be performed due to patient's anthropometry. According to high probability of pulmonary embolism (PE), a transthoracic echocardiogram was practiced, revealing multiple thrombus at the right atrium and right ventricle, severe dilatation of the right cavities with signs of overload right ventricle and significant PAH (pulmonary arterial pressure 110 mmHg). Low molecular weight heparin was initiated. Despite negative PCR results, up to three SARS-CoV-2 PCR kept negative results. After a significant weight loss, CTPA could be performed showing filling defects in the main pulmonary artery consistent with pulmonary embolism and ground-glass areas in both upper lobes and left lower lobe. Patient rest instable with severe respiratory failure, subsequently thrombolysis with reteplase was performed with good outcomes. Echocardiogram after procedure showed the absence of intracardiac thrombus and reduced PAH (60 mmHg). Even though having three negative rapid SARS-CoV-2 PCR, 10 days later, serologies showed positive results for IgG (Elisa technique), which confirmed Covid-19 pulmonary affection diagnosis.

SARS-CoV-2 infection generates coagulation disorders with elevated D-dimer values, due to systemic pro-inflammatory cytokine to activate procoagulant factors, which predispose to thromboembolic events like PE.²

Obesity (BMI > 35 kg/m²) is widely reported as a risk factor for thromboembolic disease (especially pulmonary embolism and deep venous thrombosis). Thromboembolic mechanisms generated in morbid obesity include increased platelet activity, procoagulant states, altered fibrinolysis, and endothelial cell activation.³

Dyspnea, as a prevailing symptom of COVID19 pneumonia, makes clinical recognition of PE quite challenging, therefore diagnostics tests are needed for rapid management, and imaging techniques such CT pulmonary angiography are conveniently. In patients with PE, the existence of intracardiac thrombosis in right cardiac cavities is unusual unless atrial fibrillation is set, occurring between 4 and 18% in cases of massive PE. Combination of massive PE an intracardiac thrombosis it's a medical emergency with increased mortality, which requires an urgent treatment. Thrombolysis is usually the best choice due to the double target of the therapy, the PE and the cardiac thrombus.⁴

The diagnostic challenge that arises is that, even with the clinical suspicion of COVID19 infection, with acute respiratory failure and massive PE with intracardiac thrombosis, needing urgent diagnosis and treatment, plus a negative result of a PCR test cannot stop the attitude and management to follow up. The Real-Time reverse-transcriptase polymerase chain reaction (RT-PCR) can present false negatives due to the low viral charge obtained in the sample, requiring the detection of antibodies for the diagnostic. Jin et al. show a sensitivity higher than 90% in IgM and IgG test compared to molecular detection, after 5 days since the realization of serological tests.⁵

In conclusion, although obesity is an independent risk factor for thromboembolic events, other factors must be considered, especially coagulation disorders caused by COVID19 infection. Then, the presence of negative PCR for SARS-CoV-2 healthcare providers should not neglect the disease, so a subsequent serological study may confirm the diagnosis.

Conflicts of interest

Authors declare no conflicts of interest.

References

- Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1 MERS-CoV and lessons from the past. *J Clin Virol*. 2020;127:104362. <http://dx.doi.org/10.1016/j.jcv.2020.104362>.
- Han H, Yang L, Liu R, Liu F, Wu KL, Li J, et al. Prominent changes in blood-coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med*. 2020. <http://dx.doi.org/10.1515/cclm-2020-0188>.
- Faber DR, de Groot PG, Visseren FL. Role of adipose tissue in haemostasis, coagulation and fibrinolysis. *Obes Rev*. 2009;10:554–63. <http://dx.doi.org/10.1111/j.1467-789X.2009.00593.x>.
- Charif F, Mansour MJ, Hamdan R, Najjar C, Nassar P, Issa M, et al. Free-floating right heart thrombus with acute massive pulmonary embolism: a case report and review of the literature. *J Cardiovasc Echogr*. 2018;146–9. <http://dx.doi.org/10.4103/jcecho.jcecho.64.17>.
- Jin Y, Wang M, Zuo Z, Fan C, Ye F, Cai Z, et al. Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019. *Int J Infect Dis*. 2020;94:49–52. <http://dx.doi.org/10.1016/j.ijid.2020.03.065>.

Jordi Juanola Pla^{a,b,*}, Berta Ferreiro Rodriguez^c, Concepció Falga Tirado^d

^a Pulmonology Department, Hospital de Mataró, Consorci Sanitari del Maresme, Mataró, Barcelona, Spain

^b Pulmonology, Consorci Sanitari del Maresme and High school of health science, Tecnocampus-Mataró, Pompeu Fabra University, Barcelona, Spain

^c Cardiology Department, Hospital de Mataró, Consorci Sanitari del Maresme, Mataró, Barcelona, Spain

^d Internal Medicine Department, Hospital de Mataró, Consorci Sanitari del Maresme, Mataró, Barcelona, Spain

* Corresponding author.

E-mail address: jjuanola@cscdm.cat (J.J. Pla).

0025-7753/ © 2020 Elsevier España, S.L.U. All rights reserved.

<https://doi.org/10.1016/j.medcli.2020.06.014>

Use of oral antiseptics for SARS-CoV-2 infection[☆]



Utilización de antisépticos orales para la infección por SARS-CoV-2

Dear Editor,

The health crisis triggered by the SARS-CoV-2 (COVID-19) pandemic and its rapid onset have placed humanity in combat with a pathogen that cannot be won at this moment with any pharmacological treatment that boasts sufficient scientific evidence.¹ While awaiting the results of ongoing clinical trials with different therapeutic options and looking forward to a vaccine that allows population immunity to be achieved, intermediate, fast, safe and verifiable solutions are necessary with limited research effort. A recent study reports that patients affected by COVID-19 have a high viral load in the oropharynx, especially during the first week after the onset of symptoms, which would partly explain its high transmission rate, its contagiousness and its rapid geographical spread.²

It is also known that different antiseptics (povidone iodine) have virucidal action on skin and mucosa, and are well tolerated for short-term treatments.³ In 2015, a study reported that the *in vitro* application of antiseptic products with povidone iodine achieved a decrease in the titres of the MVA (Modified Vaccinia Ankara) and MERS-CoV (Middle East Respiratory Syndrome) viruses, corresponding to a viral inactivation greater than 99% after 30 and 15 s of applying the mouthwash product (1% concentration) in MVA and MERS-CoV, respectively.⁴ These investigations were later expanded and with similar results both in the case of bacteria (*Klebsiella pneumoniae* Y *Streptococcus pneumoniae*) and with other viruses (SARS-CoV, influenza A-H1N1 and rotavirus). These findings are summarised in another publication in August 2019, prior to the epidemic situation.⁵

It would be feasible to hypothesise that treatment with mouthwashes/gargling with antiseptics (povidone iodine or others) could contribute to reducing the viral load of COVID-19 in sick patients, as well as reducing contagiousness through respiratory droplets towards other persons and the environment.⁴ This hypothesis could be tested quite simply and quickly by applying the scientific method with a study designed with paired data (*cross-over* or *within patient*), which would require a smaller number of patients. The viral load would be assessed before and after (at different times) the application of the oral antiseptic. Relevant questions to be resolved would be: an estimation of the minimum concentration necessary for the product to obtain positive results while minimising adverse effects; and determining the time during which the viral load in the oropharynx is low enough to have a protective effect for the

patient, for others and for the environment. Likewise, it would be of interest to assess whether the decrease in the viral load in the oropharynx could have a clinically relevant effect in patients.

It should be noted that the studies cited above^{4,5} were sponsored by a specific manufacturer of povidone iodine, therefore future studies should ensure the independence of the research groups to avoid conflicts of interest. The proposition of other possible prophylactic/therapeutic options would also be of importance, especially as an alternative to those subjects with COVID-19 infection in which povidone iodine presents some contraindication or precaution (pregnant women, children, goiter or hyperthyroidism), as stated in the product's technical data sheet: https://cima.aemps.es/cima/dochtml/ft/36339/FT_36339.html.

If positive results are obtained, this therapeutic option could be a practical and safe solution, pending more effective therapies or an adequate vaccine. It could be indicated for relatively short periods (1–2 weeks), coinciding with the greatest contagious wave. The application by the patient (in home isolation or during a hospital stay) would be simple to learn and to carry out. Additionally, antiseptics are easily accessible and are low cost, so this alternative could be feasible for countries with low economic resources.

This proposal has been sent to Spain's Ministry of Health on behalf of the Drug Use Working Group of the Spanish Society of Family and Community Medicine (semFYC). Family practitioners are on the front line caring for patients with COVID-19 and trying to manage the elevated level of uncertainty in general and especially regarding the use of current drugs, that are all 'off-label' and lack the 'backing' of scientific evidence.¹ Possible solutions such as the one proposed, if its effectiveness is confirmed, even though modest, would contribute to improving the management of SARS-CoV-2 infection in both primary care and hospitals. In the current situation of health crisis, any step forward is a great step forward.

References

- Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. *JAMA*. 2020. <http://dx.doi.org/10.1001/jama.2020.6019>.
- Kai-Wang To K, Tak-Yin Tsang O, Leung W-S, Raymond Tam A, Wu T-C, Christopher Lung D, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020. [http://dx.doi.org/10.1016/S1473-3099\(20\)30196-1](http://dx.doi.org/10.1016/S1473-3099(20)30196-1).
- Reynolds JEF, Martindale: *The Extra Pharmacopoeia*. 1st ed Española. Barcelona: Pharma Editores, S.L.; 2003.
- Eggers M, Eickmann M, Zorn J. Rapid and effective virucidal activity of povidone-iodine products against Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Modified Vaccinia Virus Ankara (MVA). *Infect Dis Ther*. 2015;4:491–501. <http://dx.doi.org/10.1007/s40121-015-0091-9>.
- Eggers M. Infectious disease management and control with povidone Iodine. *Infect Dis Ther*. 2019;8:581–3. <http://dx.doi.org/10.1007/s40121-019-00260-x>.

[☆] Please cite this article as: Palop Larrea V, Hernández Rodríguez MÁ. Utilización de antisépticos orales para la infección por SARS-CoV-2. *Med Clin (Barc)*. 2020;155:416–417.