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Letter to the Editor

Convalescent plasma for covid19 – How long should a donor be excluded from donation?

Convalescent plasma (CP) has been used to treat emerging diseases in the past, and despite its empirical use, the results were positive and now has been tested for COVID19 [1,2]. The FDA (Food and Drug Administration, USA) the EC (European Commission, Belgium) and other regulatory agencies have authorized the use of CP from patients with resolved COVID19 with different regulations [3,4]. Clinical and laboratory criteria are basically defined by the evidence of SARS-CoV-2 documented by clinical and/or laboratory evidence, and 14–28 days of resolution of symptoms prior to donation. Negative results for SARS-CoV-2 molecular diagnostic test, are sometimes requested [3,4]. There are different criteria, and even though SARS-COV-2 is not considered transmissible by blood [5], the safest screening profile is still a matter of debate.

We evaluated a prospective cohort of convalescent COVID19 patients in order to find potential donors. Eligibility required a positive previous diagnostic test by naso-oropharingeal swab (NOS) RT-PCR and resolution of symptoms for at least 14 days. The candidate was then tested for SARS-COV-2 by RT-PCR on both blood drawn and NOS. RT-PCR test was based on Corman Victor M et al. as previously described [6] (an internal control was applied for all samples and all assay runs were performed with positive and negative controls. Five copies/reaction of sensitivity and 100 % of specificity was determined for RT-PCR). The immunoglobulin IgG nucleoprotein-based SARS-CoV-2 enzyme-linked immunosorbent assays (ELISAs) method was adapted from Oliveira et al. [7]. The optical density at 450 nm was measured (BMG Labtech, Ortenberg, Germany). Results were performed in optical density (OD) and cut-off value set as 0.3. An analysis of the post-asymptomatic period and the molecular test results was carried out. Candidates had to follow the regular Brazilian regulations for blood donation. An informed consent was obtained from all candidates and the study was approved by the Brazilian Ethics Commission. Qualitative characteristics were described using absolute and relative frequencies and quantitative characteristics were described using means and standard deviation, median, minimum and maximum. Time after the end of symptoms was described according to the result of NOS and blood RT-PCR and compared between categories using analysis of variance (ANOVA). The test was performed with a 5% significance level.

Between April 8th and May 25th 2020, 119 plasma donor candidates were evaluated at Hospital Israelita Albert Einstein's Blood Bank (Sao Paulo, Brazil). All have had mild to moderate disease, but none had to be treated as an in-hospital patient. Seventy-seven (64.7 %) were males and 42 (35.3 %) were females. The median age was 35 yo (min 21; max 58; mean ± SD 36 ± 7.5), and the COVID19 symptomatology lasted from 0 to 33 days (median 12; mean ± SD 11.6 ± 5.2). The time period between the end of the symptoms and the blood bank pre-donation screening and sample collection varied from 12 to 37 days (median 23.0; mean ± SD 3.4 ± 4.7). The immunoglobulin IgG for SARS-CoV-2 ELISA results varied from 0.1–4 (median 2.5; mean ± SD 2.3 ± 1.3). Seven individuals (5.8 %) still had NOS and serum positive tests, 68 (57.2 %) had both tests negative, 34 (28.6 %) had only the NOS test positive and 10 (8.4 %) had only the serum test positive. The CT (cycle threshold) from the serum tests positive were also analyzed and showed results varying from 35.2 and 40.1 (median 37.2; mean ± SD 37.5 ± 1.8), RT-PCR was performed until the 45th cycle was concluded. Donors candidates with any kind of positive results were excluded for plasma donation. No statistical difference was found between the positive results and the time period without symptoms (Table 1). There was one positive NOS donor on the 34th day and one positive serum donor on the 32nd day after the end of symptoms. The Fig. 1 shows the correlation between the days without symptoms and the test results. Not all regulatory agencies request a negative test in order to allow the donation when it occurs between 14–30 days post-symptoms [3,4]. The incidence of serum samples positivity among symptomatic patients is reported to be around 1% [5]. In our analysis, we found an 14.3 % positivity in serum samples (17 donors) and 34.5 % positivity in NOS (41 individuals), and the latest detected day of each one was respectively on the 32nd and 34th day without symptoms. It is not known from which source the sample test would be more suitable regarding the prevention of an unexpected blood transfusion transmission: serum or NOS.

Even considering the low probability of transfusion transmitted SARS-COV-2, and the very few cases analyzed, we suggest that blood centers do not collect CP before the 30th day without symptoms of the donor and if it is done, to have at least the serum tested based on

Table 1
SARS-CoV-2 detection results tests (RT-PCR) time period without symptoms (days).

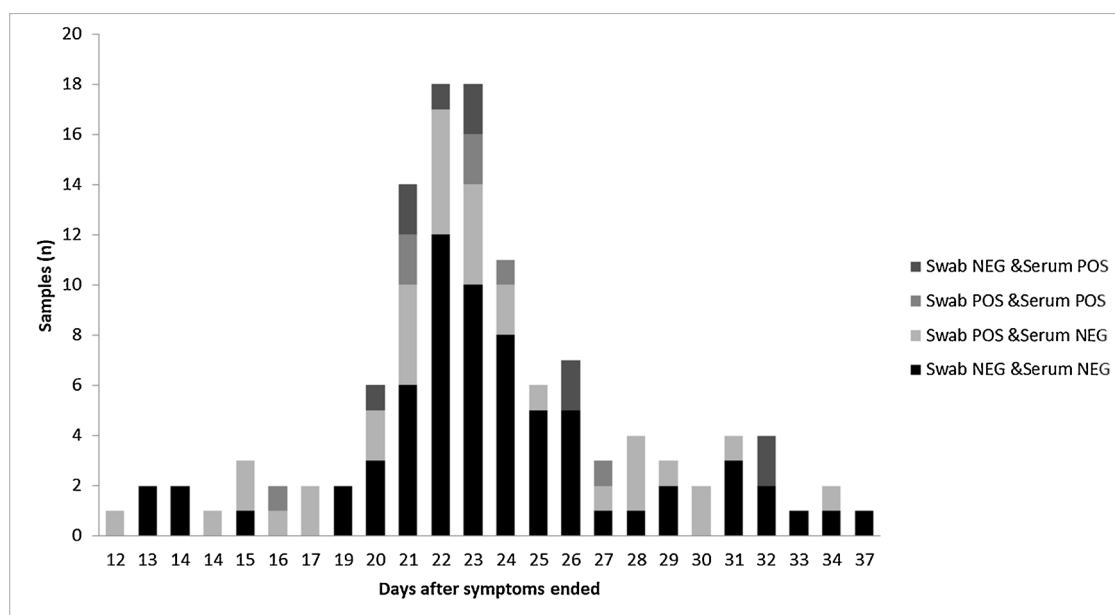| Naso-Oropharingeal/Serum RT-PCR	mean ± SD	median (min.; max.)	p
Negative/Negative	23.7 ± 4.7	23 (13; 37)	0.542
Positive/Negative	22.7 ± 5.3	22 (12; 34)	
Negative/Positive	24.60 ± 4.4	23 (20; 32)	
Positive/Positive	22.1 ± 3.4	23 (16; 27)	
ANOVA			

Fig. 1. Correlation between the days without symptoms and the test results.

molecular methods. The precautionary principle might be applied to this situation. As the pandemic goes on, it may be easier to find later and safer convalescent donors.

Declaration of Competing Interest

The authors declare no conflicts of interest

References

[1] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.

[2] Bloch E, et al. Deployment of convalescent plasma for the prevention and treatment of COVID-19. J Clin Invest 2020. In-Press Preview.

[3] FDA – Food and Drug Administration. Investigational COVID-19 Convalescent Plasma, Guidance for Industry. Available www.URL: https://www.fda.gov/media/136798/download, accessed April 20th, 2020.

[4] European Commission - An EU Program of COVID-19 Convalescent Plasma Collection and Transfusion. 2020 Available www.URL: https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/guidance_plasma_covid19_en.pdf, accessed April 20th.

[5] Chang L, Yan Y, Wang L. Coronavirus Disease 2019: Coronaviruses and Blood Safety. Transfus. Med. Rev. 2020. https://doi.org/10.1016/j.tmrv.2020.02.003.

[6] Corman Victor M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill 2020;25(3). https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045. pii = 2000045.

[7] Oliveira DBL, Almeida FJ, Durigon EL, et al. Prolonged shedding of zika virus associated with congenital infection. N Engl J Med 2016. https://doi.org/10.1056/NEJMc1607583.

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