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Letter to the Editor

Blood pressure increase after Pfizer/BioNTech SARS-CoV-2 vaccine

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To the Editor.

Although various strategies modify the transition from infection to life-threatening forms of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), vaccines remain highly effective measures to curb the pandemic [1]. SARS-CoV-2 vaccines approved by the European Medical Agency (EMA) elicit an immune neutralizing response [2] and demonstrated an excellent safety/efficacy profile in Phase III vaccine trials [1, 3].

However, some concerns have been raised regarding the safety of SARS-CoV-2 vaccines, largely based on reports of serious thromboembolic events after vaccination [1]. There are also anecdotal data of systemic reactions to vaccination including hypertension [4] and tachycardia [5].

We designed a prospective survey among health workers in our Institution. The online survey included 70 questions focusing on comorbidities, type of adverse reaction (including fever, nausea, headache, myalgia, diarrhea, pain at the injection site, and loss of taste or smell), rise in BP (defined by an average rise in home systolic or diastolic BP by at least 10 mmHg from the 5 days before to the 5 days after vaccination), and occurrence of symptomatic tachycardia (defined by resting heart rate [HR] >100 bpm). Subjects were instructed to measure home BP before breakfast and before dinner according to current Guidelines [6]. The survey took place from May 12 to May 27, 2021.

A total of 113 respondents completed the survey. Two doses of Pfizer/BioNTech vaccine (0.3 mL containing 30 micrograms of SARS-CoV-2 single-stranded, 5'-capped messenger RNA) were administered at distance of 21 days in the deltoid muscle of the upper arm.

Prevalence of women and current smokers was 73% and 15%, respectively. Mean age was 43±11 years. Prevalence of hypertension, diabetes mellitus, dyslipidemia, and asthma was 18%, 1%, 19%, and 10%, respectively. A previous myocardial infarction was recorded in 1 subject and 13 subjects had a previous documented exposure to SARS-CoV-2.

Adverse reactions occurred in 87% of subjects after the first dose and 83% after the second dose of vaccine. Most reactions were mild and none of the subjects discontinued normal daily activities. There was transitory loss of taste and smell in 1 subject. Body temperature >38.0 °C, tachycardia, or a rise in BP occurred in 13% and 27% of subjects after the first and second dose, respectively.

The subjects with documented infection by SARS-COV-2 over the previous year showed a higher frequency of systemic reactions to vaccine when compared with those without history of documented infection (38% vs 10%, $p = 0.004$).

Overall, 6 subjects (5.3%) showed an average rise in systolic or diastolic BP at home by ≥ 10 mmHg during the first 5 days after the first dose of vaccine when compared with the five days before the vaccine. Table 1 shows the main characteristics of these subjects. The BP rise required an intensification of BP-lowering treatment in 4 subjects. Two of the subjects with a BP rise after the first dose experienced a BP rise also after the second dose. Of note, history of COVID-19 was associated with a higher incidence of rise in BP when compared with subjects without previous exposure to SARS-CoV-2 (23% vs 3%, $p = 0.002$).

Symptomatic tachycardia was noted in 7 and 3 respondents after the first and second dose of vaccine, respectively (HR ranged from 101 to 130 bpm). There were no cardiovascular events (including thrombotic events) or severe or immediate allergic reactions during a follow-up of 103 days after the first dose of vaccine. One of the subjects developed a SARS-CoV-2 infection, which did not require hospitalization.

These findings extend those by Meylan et al. [4] who described 9 patients with stage III hypertension after the Pfizer/BioNTech vaccine. In the present study we had the opportunity to investigate self-measured home BP before and after vaccination. Notably, a rise in the average home BP by at least 10 mmHg from before to after vaccination occurred also in subjects with apparently normal home BP.

Although the potential link between the Pfizer/BioNTech vaccine and the rise in BP and HR remains elusive, some mechanisms might play a role. Pfizer/BioNTech vaccine contains messenger RNA which encodes the Spike protein of SARS-CoV-2. Once synthetized in the cells reached by the vaccine, the Spike proteins first assemble in the cytoplasma and then migrate to the cell surface to protrude with a native-like conformation [1]. These Spike proteins are recognized by the immune system [1]. Furthermore, the Spike proteins assembled in the cells which are eventually destroyed by the immune response circulate in the blood as

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Table 1
Main features of subjects who reported an increase in blood pressure after vaccination.

Case	Sex	Age (years)	BMI (Kg/m^2)	Hystory of hypertension	BP-lowering drugs	Co-morbidities	Time of rise in BP	Home BP before vaccination (mmHg)	Home BP after vaccination (mmHg)	Intensification of anti-hypertensive treatment	Other adverse reactions
1	M	48	22.7	No	None	Dyslipidemia	After first and second dose	100/60	115/75 (after the first dose) 120/78 (after the second dose)	No	Fever, loss of taste or smell, headache, myalgia, diarrhea
2	F	35	20.4	Yes	CCB	Diabetes	After first and second dose	125/70	144/92 (after the first dose) 150/94 (after the second dose)	Yes	Headache, myalgia
3	M	44	27.6	Yes	BB + ACE-I	Ischemic Heart Disease	After first dose	115/70	154/102 (after the first dose)	Yes	Fever, headache, myalgia, diarrhea
4	F	52	22.4	Yes	BB + ACE-I	None	After first dose	120/65	130/85 (after the first dose)	No	None
5	F	48	24.5	Yes	CCB + Diur	Dyslipidemia	After first dose	125/75	195/105 (after the first dose)	Yes	Fever, headache
6	F	51	24.9	Yes	BB	None	After first dose	135/65	185/115 (after the first dose)	Yes	Fever, headache

Legend: M = male; F = female; BMI = body mass index; BP = blood pressure CCB = calcium-channel blocker; BB = beta-blocker; ACE-I = ACE-inhibitor; Diur = diuretic.

free-floating Spike proteins [1,7]. These proteins might exert a massive interaction with the angiotensin converting enzyme 2 (ACE2) receptors leading to internalization and degradation of these receptors [1]. The loss of ACE2 receptor activity may lead to a marked and rapid drop in the generation of antiotensin$_{1\text{-}7}$ resulting from inactivation of angiotensin II [8]. The resulting imbalance between angiotensin II (overactivity) and angiotensin$_{1\text{-}7}$ (deficiency) might play a role in the genesis of hypertension and tachycardia [8,9]. However, the short latency between vaccination and BP rise does not exclude the possibility that individual emotional factors may contribute to trigger the reaction.

Interestingly, we also documented an increased rate of systemic adverse reactions (including a significant rise in BP) among subjects with history of documented SARS-CoV-2 infection when compared to those without previous exposure to the virus. Such finding confirms previous results from a clinical study by Kramer and co-workers [10]. Specifically, these Authors analyzed the frequency of systemic reactions including fatigue, headache, chills, muscle pain, fever, and joint pain after the first dose of vaccine in 148 seronegative and 82 seropositive participants. The vaccine recipients with preexisting immunity had a higher frequency and severity of systemic reactions than those without immunity [10]. Taken together, such results seem to support the hypothesis that the vaccination of subjects with preexisting immunity to SARS-Cov-2 might enhance some adverse reactions.

In conclusion, our study suggests that BP should be systematically measured at home in the week before and after SARS-CoV-2 vaccination, particularly in hypertensive subjects. Further studies are needed to clarify the frequency and the potential mechanisms of hypertension after vaccination.

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All Authors have no disclosure related to this paper.

Declaration of Competing Interest

The Authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Angeli F, Spanevello A, Reboldi G, Visca D, Verdecchia P. SARS-CoV-2 vaccines: lights and shadows. Eur J Intern Med 2021. https://doi.org/10.1016/j.ejim.2021.04.019.
[2] Teijaro JR, Farber DL. COVID-19 vaccines: modes of immune activation and future challenges. Nat Rev Immunol 2021;21:195–7. https://doi.org/10.1038/s41577-021-00526-x.
[3] Connors M, Graham BS, Lane HC, Fauci AS. SARS-CoV-2 vaccines: much accomplished, much to learn. Ann Intern Med 2021;174:687–90. https://doi.org/10.7326/M21-0111.
[4] Meylan S, Livio F, Foerster M, Genoud PJ, Marguet F, Wuerzner G, Center CCV. Stage III Hypertension in patients after mRNA-based SARS-CoV-2 vaccination. Hypertension, 2021;77:e56–7. https://doi.org/10.1161/HYPERTENSIONAHA.121.17316.
[5] Quer G, Gadaleta M, Radin JM, Andersen KG, Baca-Motes K, Ramos E, Topol EJ, Steinhubl SR. The physiologic response to COVID-19 vaccination. medRxiv 2021. https://doi.org/10.1101/2021.05.03.21256482.
[6] Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, et al. International society of hypertension global hypertension practice guidelines. Hypertension, 2020;75:1334–57. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026.
[7] Ogata AF, Cheng CA, Desjardins M, Senussi Y, Sherman AC, Powell M, Novack L, Von S, Li X, Baden LR, et al. Circulating SARS-CoV-2 vaccine antigen detected in the plasma of mRNA-1273 vaccine recipients. Clin Infect Dis 2021. https://doi.org/10.1093/cid/ciab465.
[8] Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. Eur J Intern Med 2020;76:14–20. https://doi.org/10.1016/j.ejim.2020.04.037.
[9] Verdecchia P, Cavallini C, Spanevello A, Angeli F. COVID-19: ACE2centric infective disease? Hypertension 2020;76:294–9. https://doi.org/10.1161/HYPERTENSIONAHA.120.15353.
[10] Krammer F, Srivastava K, Alshammary H, Amoako AA, Awawda MH, Beach KF, Bermudez-Gonzalez MC, Bielak DA, Carreno JM, Chernet RL, et al. Antibody responses in seropositive persons after a single dose of SARS-CoV-2 mRNA vaccine. N Engl J Med 2021;384:1372–4. https://doi.org/10.1056/NEJMc2101667.

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