

The Thrombo Protective Role of Aspirin against the Complications Associated with the Unceasing Outbreak of the Novel Coronavirus (SARS-CoV-2)

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Abstract: This paper presents an overview on the thrombo protective role of aspirin against the complications associated with the unceasing outbreak of the novel coronavirus (SARS-CoV-2)

Keywords: Aspirin, Coronavirus, Thrombo protective.

1. Introduction

The recent unceasing outbreak of the 2019 novel coronavirus (SARS-CoV-2), which is still at its peak even in 2021, has posed remarkable and pronounced threats to international health and the economy. In late December 2019, a cluster of patients were admitted to hospitals with an initial diagnosis of pneumonia of an unknown etiology. These patients were epidemiologically linked to the seafood and wet animal wholesale market in Wuhan, Hubei Province, China [1]. The effect of the deadly disease in terms of both mortality and morbidity has become significant in the highly industrialized environment since the outbreak. Because of the global economy's stagnation and clogging, the workings of public global health sectors have been greatly cleaved and buckled. Although pneumonia and acute respiratory distress syndrome (ARDS) are hallmarks of the disease, thrombotic complications have been reported in 25%–42% of patients and are associated with increased mortality [2]–[8]. Evidence of hypercoagulability has been observed on viscoelastic coagulation testing and SARS-CoV-2 infected patients frequently have elevated D-dimer and fibrinogen concentration [2]–[8]. Deep vein thrombosis (DVT) and arterial thrombosis are relatively common, and on autopsy, megakaryocytes and platelet-rich thrombi have been observed in the heart, lung, and kidneys of SARS-CoV-2 infected patients [2]–[8].

2. Clinical Presentation

There is compelling evidence suggesting that SARS-CoV-2 infection may be asymptomatic, pauci-symptomatic, or symptomatic [9]. The most common clinical presentation of SARS-CoV-2 infection includes fever, fatigue, and dry cough;

some patients present with nasal congestion, runny nose, myalgia, and chills [1]. Headache, confusion, chest tightness, pleuritic chest discomfort, rhinorrhea, sore throat, hemoptysis, vomiting, abdominal discomfort, constipation, and diarrhea have been reported but are less common [1]. Some patients with SARS-CoV-2 have experienced gastrointestinal symptoms, such as diarrhea and nausea, prior to developing fever and lower respiratory tract signs and symptoms. In one case report, the patient complained of psychiatric symptoms, such as depression, insomnia, and suicidal thoughts after isolation, due to stress regarding people's reactions from the media reports about the SARS-CoV-2 patients [1].

3. Protective role of Aspirin

Aspirin irreversibly inhibits COX-1 by acetylating serine-529, thereby hindering the production of TXA₂, a promoter of platelet aggregation, and prostaglandin I₂, a potent inhibitor of platelet aggregation and a highly potent vasodilator, in platelets and vascular endothelial cells, respectively. In absence of protein synthesis in platelets, TXA₂ inhibition persists for the lifetime of the platelet compared with vascular endothelial cells, which recover COX-1 activity shortly after exposure to aspirin. Aspirin is also likely permanently blocks prostanoid biosynthesis, particularly the prostanoid precursors PGG₂ and PGH₂, thereby curbing a variety of pro-inflammatory responses. Additionally, Aspirin leads to the suppression of the prototypical pro inflammatory signaling pathway NF-κB. The American Heart Association recommends the daily use of aspirin (71–326 mg) indefinitely in all patients with known CVD for secondary prevention, unless contraindicated [10]. In 2009, the U.S. Preventive Services Task Force (USPSTF), based on the results presented in different trials, concluded that aspirin is in fact effective for primary CVD prevention, indicating that aspirin for primary prevention should be recommended when benefits outweigh risks [11].

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The Second Copenhagen Atrial Fibrillation, Aspirin, and Anticoagulant Therapy (AFASAK 2) study showed a nonsignificant decrease in risk of stroke with 75 mg aspirin, while the Stroke Prevention in Atrial Fibrillation (SPAF) study found a significant decrease of 44% associated with 325 mg aspirin [12], [13].

The efficacy of low doses of aspirin (75–100 mg daily HS) as an antiplatelet agent has been documented in several randomized controlled trials, with evidence of non-superiority for higher doses as compared to lower doses in terms of antithrombotic efficacy [14]. Based on this evidence and on the results of additional randomized clinical trials, low doses of aspirin are currently used for inhibiting platelet aggregation and preventing ischemic arterial events (e.g., myocardial infarction, stroke) in patients at higher thrombotic risk [15] and also, most importantly, in coronavirus associated pneumonia.

The pooled results of the Warfarin and Aspirin (WARFASA) and the Aspirin to Prevent Recurrent Venous Thromboembolism (ASPIRE) trials showed that in patients with a first unprovoked venous thromboembolism, after warfarin was discontinued, aspirin reduced the risk of thrombotic event recurrence by 32% [16]. Interestingly though, aspirin is considered a linchpin keystone in the prevention and treatment of thrombo-ischemic complicating events, this antiplatelet drug appears to be less effective in individuals with poorly controlled diabetes [17].

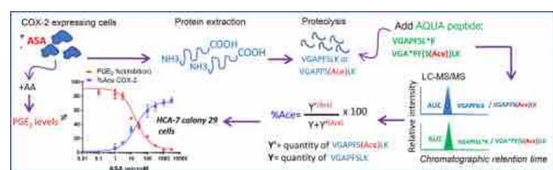


Fig. 1. Image Courtesy

4. Conclusion

Aspirin may be useful against the aspecific symptoms of novel coronavirus (2019-nCoV) infection, due to its analgesic and antipyretic effect. It may likely exert anti-inflammatory, antithrombotic, and antiviral effects which altogether may be useful to inhibit the wide and unspecific pathophysiological processes leading to the most severe, devastating and complex clinical manifestations of novel coronavirus (SARS-CoV-2) and even minimize the chance of ICU admission and incidence of mechanical ventilation. Hence, aspirin might reasonably be considered as an evidence-based operative therapeutic candidate amongst the horizon of treatment protocols of novel coronavirus. The dose of aspirin administration and duration of treatment in the all subgroups of novel coronavirus infected patient's needs to be clinically evaluated first and then established.

References

- [1] Patel R S, Patel N, Baksh M, et al. Clinical Perspective on 2019 Novel Coronavirus Pneumonia: A Systematic Review of Published Case Reports. *Cureus*, vol. 12, no. 6, 2020.
- [2] Klok FA, Kruij MJHA, van der Meer NJM, et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis. *Thromb Res*. vol. 191. pp. 148–150, 2020.
- [3] Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost*, vol. 18, pp. 1421–1424, 2020.
- [4] Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost*, vol. 18, pp. 1995–2002, 2020.
- [5] Spiezia L, Boscolo A, Poletto F, et al. COVID-19-related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure. *Thromb Haemost*, vol. 120, pp. 998–1000, 2020.
- [6] Wright FL, Vogler TO, Moore EE, et al. Fibrinolysis shutdown correlation with thromboembolic events in severe COVID-19 infection. *J Am Coll Surg*, vol. 231, pp. 193–203.e1, 2020.
- [7] Ranucci M, Ballotta A, Di Dedda U, et al. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. *J Thromb Haemost*, vol. 18, pp. 1747–1751, 2020.
- [8] Rapkiewicz AV, Mai X, Carsons SE, et al. Megakaryocytes and platelet-fibrin thrombi characterize multi-organ thrombosis at autopsy in COVID-19: a case series. *E Clinical Medicine*, vol. 24, pp. 100–434, 2020.
- [9] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X., Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, GAO Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, vol. 395, pp. 497–506, 2020.
- [10] S. C. Smith Jr., J. Allen, S. N. Blair et al., “AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update. Endorsed by the national heart, lung, and blood institute,” *Journal of the American College of Cardiology*, vol. 47, no. 10, pp. 2130–2139, 2006.
- [11] N. Calonge, D. B. Petitti, T. G. DeWitt et al., “Aspirin for the prevention of cardiovascular disease: U.S. preventive services task force recommendation statement,” *Annals of Internal Medicine*, vol. 150, no. 6, pp. 396–404, 2009.
- [12] Z. M. Chen, “CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke,” *The Lancet*, vol. 349, no. 9066, pp. 1641–1649, 1997.
- [13] P. A. G. Sandercock, “The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19 435 patients with acute ischaemic stroke,” *The Lancet*, vol. 349, no. 9065, pp. 1569–1581, 1997.
- [14] Patrono C, Baigent C, and Hirsh J, Roth G. Antiplatelet drugs: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition) Chest, vol. 133, pp. 199S–233S, 2008.
- [15] Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svtil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Valgimigli M, Achenbach S, Bax JJ, ESC Scientific Document Group 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J*. vol. 41, pp. 407–477, 2020.
- [16] Simes J, Becattini C, Agnelli G, Eikelboom JW, Kirby AC, Mister R, Prandoni P, Brighton TA, INSPIRE Study Investigators (International Collaboration of Aspirin Trials for Recurrent Venous Thromboembolism) Aspirin for the prevention of recurrent venous thromboembolism: the INSPIRE collaboration. *Circulation*, vol. 130, pp. 1062–1071, 2014.
- [17] Stefania Tacconelli, Annalisa Contursi, Lorenza Falcone, Matteo Mucci, Ilaria D'Agostino, Rosa Fullone, Angela Sacco, Mirco Zucchelli, Annalisa Bruno, Patrizia Ballerini, Melania Dovizio, Paola Patrignani “Characterization of cyclooxygenase-2 acetylation and prostanoid inhibition by aspirin in cellular systems.” *Biochemical Pharmacology*, vol. 178, 2020.