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The Impact of Antiplatelet Therapy on COVID19 Severity and Outcome

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Abstract

The prothrombotic and hypercoagulable state induced by COVID-19 is a unique highly complex process termed COVID-19- associated coagulopathy (CAC). SARS-CoV-2 infection created specific pathophysiological environment under the influence of a plethora of mediators. Coagulation dysregulation in COVID-19 is more strongly involved in the development of thromboembolic complications than platelet mediated imbalances. There are discrepancies in the role of platelet activation in COVID-19. Some studies suggested that the use of an antiplatelet agent might improve the clinical outcome of thrombotic complications in hospitalized COVID-19 infected patients without increasing the risk of bleeding. Potential benefit of antiplatelet therapies in patients with COVID-19 depends on the timing of treatment initiation.

Abbreviations: RECOVERY: The Randomized Evaluation of COVID-19 Therapy; CAC: COVID-19- Associated Coagulopathy; RCT: Randomized Clinical Trial; CRP: C-reactive Protein

Introduction

The prothrombotic and hypercoagulable state induced by COVID-19 is unique well described condition termed COVID-19-associated coagulopathy (CAC). It is associated with worse prognosis. The risk of CAC is higher than that reported with other respiratory viral infections or acute medical illnesses [1]. Major venous thromboembolic events (mostly pulmonary embolism) have been described in 5 to 30% of hospitalized patients while arterial thromboembolic event, particularly myocardial infarction and ischemic stroke occurred in up to 3% of patients. Thromboembolic events and microthrombi are a key feature of moderately and critically ill patients with COVID-19 during the acute and convalescent state. They occurred even in patients with COVID-19 on either prophylactic or therapeutic anticoagulation [1].

COVID-19 infection is thought to be an endothelial disease that causes vascular endothelialitis involving the pulmonary capillary endothelium [2]. Electron microscopy and histological analyses have demonstrated that SARS-CoV-2 infects endothelial cells in multiple organs associated with impaired microcirculation, and apoptosis, leading to inflammation and microthrombosis [2]. SARS-CoV-2 infection, may lead to a state mimicking Virchow's triad, that is, vascular endothelial injury, blood stasis and clotting in concert with systemic inflammation resulting in systemic thrombosis [3]. Microthrombosis has been described in autopsies of COVID-19 patients, and excess megakaryocytes have been observed in the heart, lungs, and kidneys of the affected patients [2]. Pulmonary thrombi in postmortem sections were fibrin(ogen)-rich and platelet-poor, suggesting impaired platelet function. Platelets of severely ill patients with COVID-19 retained their inherent ability to form lamellipodia, which is essential for vascular integrity [4].

The impact of COVID-19 on prothrombotic and procoagulatory platelet function is multifaceted. The underlying molecular mechanisms remain largely obscure [4]. Coagulation dysregulation in COVID-19 is more strongly involved in the development of thromboembolic complications than platelet mediated imbalances. There are discrepancies in the role of platelet activation in COVID-19. Data may be influenced by virus variants, disease stage and sampling technique. Some studies found elevated basal platelet activation in severe COVID-19, enhanced platelet aggregation and prothrombotic capacity,

whereas other studies suggested reduced capacity of platelets to respond to stimulation associated with platelet exhaustion [4].

The role of Antiplatelet Agents in Patients with COVID-19

Although anticoagulants are associated with reduced mortality, the impact of antiplatelet therapy on COVID19 severity and outcome is less clear [4].

- In symptomatic outpatients with COVID-19, aspirin does not reduce major adverse cardiovascular or pulmonary events [2].
- Dual antiplatelet therapy improves hypoxemia [4].
- Aspirin administration reduces the risk for mechanical ventilation, ICU admission and mortality without increasing the bleeding risk in some studies [3].
- No protective effect of aspirin against adverse thrombotic events or mortality in other studies [4].

Results of research studies on antiplatelet therapy in patients with COVID-19

Several small sample size studies demonstrated benefits of variable degree in the severity of ventilation abnormality and patient mortality in patients with COVID-19 who received aspirin. These studies are of limited value due to the small sample size, retrospective cohorts, heterogeneity in outcomes and the antiplatelet agent/s used [3]. The Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial is a large RCT that explore aspirin efficacy in antiplatelet-naive hospitalized patients with moderate COVID-19 infection. It randomized 14 892 patients with COVID-19 (7351 on aspirin and 7541 on usual care). Patients already receiving antiplatelet therapy prior to hospitalization were excluded from the study. They observed small increase in the rate of patients discharged alive within 28 days, duration of hospitalization and bleeding risk (gastrointestinal hemorrhage, cerebral hemorrhage or blood transfusion) among patients who received aspirin [3]. There is also slight reduction in the rate of pulmonary embolism, but not deep vein thrombosis in these patients [2] while the risk of progressing to invasive mechanical ventilation or the 28-day mortality or death is not reduced [3]. The most benefit subgroups are those aged more than 60 years (61-80 years), and patients with comorbidities [2].

The HOPE-COVID-19 registry evaluated 730 patients with COVID-19 who received at least one antiplatelet agent. Concomitant anticoagulation was administered in 66% of the patients. The multivariate analysis revealed a lower mortality risk in patients receiving antiplatelet agents—principally aspirin. No difference in the use of invasive ventilation or in-hospital mortality or bleeding was identified between patients on antiplatelet drugs or not [3]. A research conducted in the School of Medicine at the University of Maryland on four hundred and twelve (412) patients showed that low dosage of aspirin (75-81 mg/day) was associated with decreased mechanical ventilation, ICU admission, reduced lung injury, and in-hospital mortality in hospitalized patients with COVID-19. However, this trial was not a randomized, double-blind, placebo-controlled study [5].

The beneficial mechanisms of antithrombotic low-dose aspirin treatment

The beneficial effects of low-dose aspirin treatment in prevention of both arterial and venous thrombotic events in severe COVID-19 is explained by several mechanisms: its inhibitory effect on cyclooxygenase (COX) which decreases IL-6 and C-reactive protein (CRP) production, inhibition of thromboxane (TX)-dependent platelet activation, prohibiting virus replication by suppressing prostaglandin E2 (PGE2) in macrophages and up-regulating the production of type I interferon [5], reduced formation of neutrophil extracellular traps [6] and acetylation of fibrinogen and acceleration of fibrinolysis [7]. These protective effects may be augmented in COVID19, where the procoagulant tendency is high, and endothelial cell dysfunction is common [5]. Aspirin's lung-protective effects in COVID-19 are thought to be related to reduced platelet-neutrophil aggregates in the lungs, anti-inflammatory properties, and increased lipoxin formation, which restores pulmonary endothelial cell function [5]. Aspirin could also reduce the incidence of cytokine storm in patients with COVID-19, through decrease of interleukin-6 (IL-6), CRP, and macrophage colony-stimulating factor production [5].

Timing of aspirin initiation in hospitalized patients with COVID-19

Potential benefit of aspirin antithrombotic therapies in patients with COVID-19 depends on the timing of treatment initiation, especially if thrombi have already developed at the time of admission [1]. The 28-day in-hospital mortality and pulmonary embolism incidence were lower in patients who received early aspirin during the first day of hospitalization compared with those who did not receive early aspirin [2]. No evidence of heterogeneity in response based on symptoms duration, baseline disease severity, or background thrombotic prophylaxis regimen [1]. Early aspirin use was not associated with higher rates of hemorrhagic complications [2].

Other antiplatelet agents in patients with COVID-19

a. P2Y12 inhibitor: Ticagrelor was the preferred P2Y12 inhibitor, but clopidogrel and prasugrel were also tried. P2Y12 inhibition in moderately ill patients with COVID-19 is of no more benefit to therapeutic doses of heparin. There is 3-fold increased risk of major bleeding without any reduction in thrombotic events in the P2Y12 trial [8].

b. Glycoprotein IIb/IIIa inhibitors (such as abciximab, eptifibatide, or tirofiban) could be more effective because they interfere with platelet aggregation via the fibrinogen bridge [8].

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c. P-selectin inhibitor (such as crizanlizumab or Glenzocimab) is tested in clinical trials. P-selectin inhibition is more effective against microvascular thrombosis because it targets the activated platelet and endothelium [8].

d. Glycoprotein VI inhibition may be promising because of its postulated antithrombotic potency, while hemostasis is largely unaffected [8].

Conclusion

Antiplatelet therapy during hospitalization for COVID-19 could be associated with lower mortality risk without increased risk of bleeding. Aspirin is a cheap, universally available and well-tolerated medication. Its use in hospitalized patients with moderate COVID-19 infected patients should be encouraged unless contraindicated. More randomized trials are still needed to confirm these initial data.

References

1. RECOVERY Collaborative Group (2022) Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomized, controlled, open-label, platform trial. Lancet 399(10320): 143–151.
2. Chow JH, Khanna AK, Kethireddy S, Yamane D, Levine A, et al. (2021) Aspirin use is associated with decreased mechanical ventilation, intensive care unit admission, and in-hospital mortality in hospitalized patients with coronavirus disease 2019. Anesth Analg 132(4): 930–941.
3. Voruganti D, Bassareo PP, Calcaterra G, Mehta JL (2022) Does aspirin save lives in patients with COVID-19? BMJ Heart 108 (2): 88-89.
4. Schrottmaier WC, Pirabe A, Pereyra D, Heber S, Hackl H, et al. (2022) Platelets and antiplatelet medication in COVID-19-related thrombotic complications. Frontiers in Cardiovascular Medicine 8: 1-15.
5. Chow JH, Rahnavard A, Gomberg-Maitland M, Chatterjee R, Patodi P, et al. (2022) Association of early aspirin use with in-hospital mortality in patients with moderate COVID-19. JAMA Network Open 5(3): e223890.
6. Law S, Leung AW, Xu C (2021) The arguments of aspirin for COVID-19 complications. Microbes and Infectious Diseases 2(1): 7-8.
7. Liuzzo G, Patrono C (2022) Can low-dose aspirin help the RECOVERY of patients hospitalized with COVID-19?. European Heart Journal 43(8): 714–715.
8. Spaetgens B, Nagy M, Cate Ht (2022) Antiplatelet therapy in patients with COVID-19—more is less? JAMA 327(3): 223-224.

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