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LETTER TO THE EDITOR

Use of aspirin for primary prevention in patients with diabetes during the COVID-19 pandemic

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We read with interest the recently published cohort study by Tan and colleagues [1] which examined the appropriateness of aspirin prescribing among 400 patients with type 2 diabetes attending the Irish ambulatory clinics. It was reported that 49.0% ($n=196$) of the cohort were prescribed aspirin, of whom 10.2% ($n=20$) were receiving it for primary prevention of cardiovascular disease despite with < 10% of 10-year cardiovascular risk. The authors specifically discouraged aspirin prescription in patients with type 2 diabetes who have < 10% of 10-year cardiovascular risk. Indeed, the recommendation of the authors coincided with the recommendation in the 2019 European Society of Cardiology (ESC)'s guidelines on diabetes, pre-diabetes, and cardiovascular diseases, which also discouraged the prescription of aspirin in patients with diabetes at low-to-moderate cardiovascular risk [2].

Nevertheless, the pleiotropic effects of aspirin have been well recognized in the literature; aspirin has been reported to possess anti-inflammatory, analgesic, antipyretic, antithrombotic effects, as well as antiviral properties against RNA viruses [3]. Indeed, during the coronavirus disease 2019 (COVID-19) pandemic, aspirin has been proposed as a treatment for COVID-19 based on its antithrombotic properties [4]. Therefore, we believe the recommendations on the use of aspirin in patients with diabetes should be revised in the current context where COVID-19 is still a serious global health threat despite the availability of COVID-19 vaccines. As reported in a meta-analysis [5] of observational studies, the pre-diagnosis use of aspirin in patients with COVID-19 is associated with a significantly reduced risk of fatal course of COVID-19, relative to non-use of aspirin (pooled odds ratio = 0.50, 95% confidence interval 0.32–0.77 and pooled hazard ratio = 0.50, 95% confidence interval 0.36–0.69). In addition, a recently published observational cohort study [6] (not included in the meta-analysis) also reported significantly lower in-hospital mortality (hazard ratio = 0.81, 95% confidence interval 0.76–0.87), with pre-hospitalization use of antiplatelets (83.9% were aspirin users) compared with non-use of antiplatelet therapy.

While we acknowledged the negative findings in the RECOVERY trial [7] in which the use of aspirin was not associated with reduction in 28-day mortality in patients with COVID-19 (rate ratio = 0·96, 95% confidence interval 0·89–1·04), it should be noted that diabetic patients constituted only 22% of the trial participants. Increased platelet activation has been described previously in patients with diabetes (regardless of diabetes control), which may be due to hyperglycemia, low-degree inflammation, and increased oxidation [8]. In addition, thrombin generation in platelets appears to be enhanced in patients with diabetes [9]. Thus, the development of COVID-19 in patients with diabetes may enhance the pre-existing platelet dysfunction, since COVID-19 itself, and many of its complications, have been associated with platelet activation, mainly due to uncontrolled overproduction of inflammatory cytokines [10].

Therefore, in contrary with the current recommendation [2] and the findings by the authors [1], we opined that during the COVID-19 pandemic, the use of aspirin should be encouraged in patients with diabetes, even for those who are at low-to-moderate cardiovascular risk, to reduce the risk of COVID-19-related complications (including death). Thus far, the beneficial effects of aspirin in patients with COVID-19 had been associated with its pre-diagnosis use [5, 6]; the prescription of aspirin after the development of COVID-19 may not be adequate to counteract the enhanced platelet dysfunction as reported in the RECOVERY trial

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[7]. Nonetheless, future trials with aspirin in patients with COVID-19 should aim to recruit those with concurrent diabetes to better ascertain its effects in this population.

Declarations

Conflict of interest The authors declare no competing interests.

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