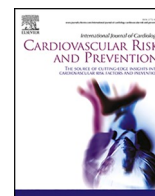Contents lists available at ScienceDirect

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Invited Commentary

Is colchicine the holy grail for treating inflammation and reducing cardiovascular risk?

Colchicine is extracted from the seeds of colchicum autumnale and is used in herbal medicine. Of note, it is a strong plant alkaloid with toxic effects and is lethal in doses of 1 mg/kg body weight, but in therapeutic doses it has anti-inflammatory, antimicrotubular effects (stopping cell division at the metaphase stage), and it reduces uric acid production. It is anti-inflammatory by inhibiting neutrophil chemotaxis and cytokine release. Colchicine is an inhibitor of the NLPR3 inflammasome and has been shown to reduce pro-inflammatory cytokines including interleukin-1β (IL-1β), interleukin-18 (IL-18) and interleukin-6 (IL-6), as well as the inflammatory marker C-reactive protein (CRP) in a variety of experimental models and clinical settings [1–3]. [Fig.1.] The drug is used to treat gout attacks, familial Mediterranean fever, and is the drug of choice for pericarditis. Recent years have brought surprisingly positive data on the use of colchicine as an anti-inflammatory substance in coronary artery disease (CAD) and after myocardial infarction (MI), and recently in the treatment of patients with COVID-19 [3].

1. Colchicine in secondary cardiovascular prevention

In one of the newest meta-analyses, the effect of low doses of colchicine (0.5 mg/24h) on the risk of developing cardiovascular complications (primary endpoint: MI/stroke/cardiovascular death) in patients with CAD was assessed. Five randomized clinical trials involving 11816 patients were included in the meta-analysis. Colchicine was shown to reduce the risk of the primary endpoint by **25%** (RR = 0.75; 95% CI 0.61–0.92, p = 0.005), with **22%** MI (RR = 0.78; 95% CI 0.64–0.94, p = 0.010), **46%** stroke (RR = 0.54; 95% CI 0.34–0.86, p = 0.009) and the need for coronary revascularization reduction by **23%** (RR = 0.77; 95% CI 0.66–0.90, p < 0.001) [4]. Another meta-analysis of four randomized clinical trials (n = 11594 subjects) assessed the effects of adding a low dose of colchicine (0.5 mg/24h) to standard therapy on cardiovascular complications in patients with CAD or MI. Administration of colchicine reduced the risk of: MI by **38%** (HR = 0.62; 95% CI: 0.36–0.88, p < 0.05), ischemic stroke by **62%** (HR = 0.38; 95% CI: 0.13–0.63, p < 0.05) and the need for coronary revascularization by **44%** (HR = 0.56; 95% CI: 0.30–0.82, p < 0.05) [5].

2. Colchicine in the treatment of COVID-19

In a recent meta-analysis, an attempt was made to summarize knowledge about the impact of colchicine administration on the prognosis of patients with COVID-19. Eight studies were included in the meta-analysis involving 5778 patients. A statistically significant **56%** reduction in the risk of severe COVID-19 was demonstrated. Moreover, a statistically significant reduction of **57%** in the risk of death in the course of COVID-19 was found [6]. Fig. 1 shows the mechanism of action of colchicine in the setting of SARS-CoV-2 infection.

3. Summary and important questions for the future

- Should colchicine be incorporated into guidelines on CAD and MI secondary prevention?
- What is the role of colchicine in COVID-19 era?
- Are there any more prospective, randomized, double-blinded, placebo controlled clinical trials needed to answer those questions or are we ready to implant this knowledge now?
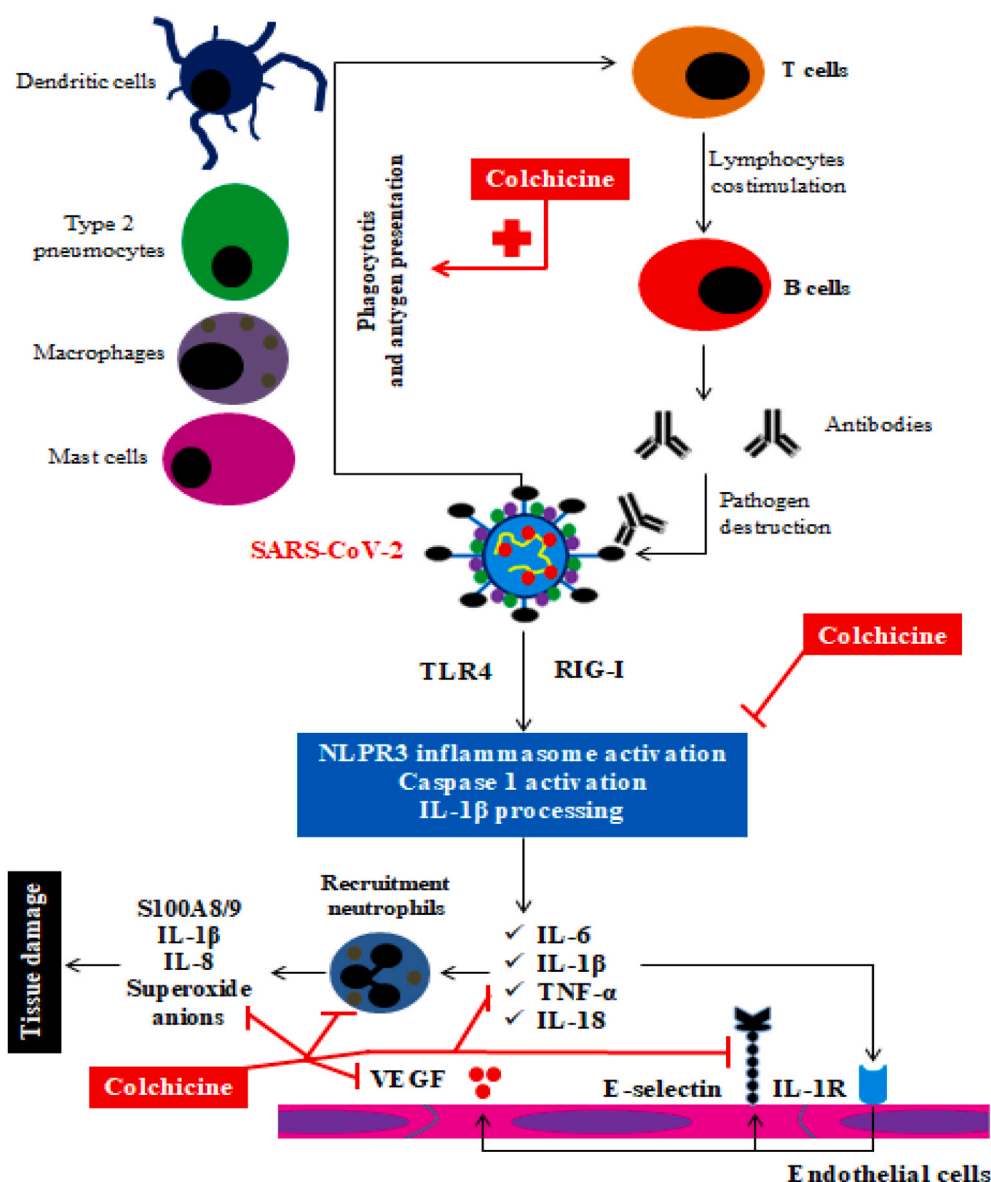
Fig. 1. Mechanism of action of colchicine in SARS-CoV-2 infection [3]. TLR4 - toll-like receptor 4; RIG-I - retinoic acid-inducible gene I; NALP3 - NLR family, pyrin domain containing 3; IL-1β – interleukin 1β; IL-6 – interleukin 6; TNF-α – tumor necrosis factor α; IL-18 – interleukin 18; IL-1R - interleukin-1 receptor; VEGF - vascular endothelial growth factor.

Declaration of competing interest

None declared.

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