CORRESPONDENCE

Role of aspirin in patients with septic shock: a complex and intriguing relationship

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Dear Editor,

Kiers et al. [1] raise an important issue related to the results of our recent report in which we demonstrated that patients with community-onset pneumonia on treatment with macrolides plus low-dose aspirin have improved survival compared to untreated ones [2].

Aspirin is a drug which irreversibly acetylates COX-1, so preventing formation of eicosanoids such as thromboxane (Tx) A₂, which aggregates platelets and prostaglandins. Improved survival rate could be dependent upon lowered formation of TxA₂ and cardiovascular events, but Kiers et al. propose another more intriguing possibility. They argue, in fact, that as prostaglandins attenuate pro-inflammatory cytokine production at the transcriptional level aspirin, which inhibits prostaglandin biosynthesis, they may counteract lung infection via an enhanced pro-inflammatory cytokine response to invading pathogens; this pro-inflammatory activity could result in more effective clearance of bacteria. The intriguing and provocative hypothesis of Kiers and colleagues may have another biologic plausibility, which has been demonstrated in a study performed in diabetic patients on chronic treatment with low-dose aspirin [3]. This study revealed that type II diabetic patients display an enhanced production of platelet F₂-isoprostanes, which are chemically stable eicosanoids with pro-aggregating activity. Of note, F₂-isoprostanes stem from arachidonic acid interaction with superoxide anion, which is a reactive oxidant species (ROS) formed by activation of Nox2, the enzyme of the innate immune system which is crucial for bacteria killing [3]. The authors speculated that, as a consequence of COX1 inhibition by aspirin, arachidonic acid is shifted towards Nox-2-derived ROS activation

with ensuing enhanced production of isoprostanes [2]. Interestingly, an enhanced formation of isoprostanes has been detected in patients with coronary heart disease on chronic treatment with aspirin [4]. Based on this observation, it is possible that the improved survival by aspirin may be dependent on a paradoxical increase of inflammation, which is related not only to prostaglandin down-regulation but also to a pro-oxidant activity derived from Nox2 activation. However, generalizability of this hypothesis needs further investigation.

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Compliance with ethical standards

Conflicts of interest

The authors state that there are no conflicts of interest pertaining to this manuscript.

Accepted: 26 February 2016

Published online: 31 March 2016

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