AZITHROMYCIN

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Introduction

Azithromycin is a macrolide, belonging to a class of antimicrobials with activity mainly against gram-positive cocci and atypical pathogens.[1] A body of evidence supports its broad activities as an immunomodulator especially among those with chronic inflammatory disease.

Mechanism of Action

The mechanism of action of macrolides as immunomodulators reveals several effects dependent on the target cells. In airway epithelial cells, it inhibits chloride secretion, mucus secretion, adhesion molecules, proinflammatory cytokines and inflammatory mediators. It also enhances tight junctions, cell barriers and defensins. It inhibits neutrophil chemotaxis, adhesion molecules, proinflammatory cytokines, elastase, reactive oxygen species while it promotes apoptosis[2] and regulation of immune cells. These changes underlie many immunomodulatory effects of azithromycin, contributing to resolution of acute infections and reduction of exacerbations in chronic airway diseases.[3]

Clinical Studies

In an open-label study of 36 patients with COVID-19, the use of azithromycin in combination with hydroxychloroquine (6/6) compared to hydroxychloroquine alone (7/14) appeared to be associated with a more rapid decline in viral RNA ($p=0.05$). At day 6 post- inclusion, all of the patients treated with hydroxychloroquine and azithromycin combination were virologically cured.[4] The results this ongoing study should be interpreted with caution due to methodologic concerns and small sample size. (Appendix 7)

At present, there are 109 registered studies in clinicaltrials.gov using Azithromycin alone (1 ongoing trial) or in combination with other immunomodulators for COVID-19.

Adverse Effects

Reactions like QTc prolongation and ventricular arrhythmias, including torsades de pointes have been reported. Patients admitted with COVID-19 are likely to have longer baseline QTc and have higher potential arrhythmic risks especially in the background of a previous cardiac pathology (arrhythmias, heart failure, hypokalemia, hypomagnesemia)[5,6,7] QTc monitoring in this setting is essential to identify those who are at increased risk for torsades de pointes so aggressive countermeasures may be implemented.[6,8]

Hypersensitivity to azithromycin and other macrolides as well as a history of cholestatic jaundice or hepatic dysfunction are contraindications.

Recommended Dose

Adult dose: 500 mg once a day for 5 days or 500 mg once on Day 1 then 250 mg once daily on Day 2- 5

Pediatric dose: 10 mg/kg/day once a day (max of 500 mg/day) for 5 days.[6]

Conclusion

Currently, conflicting data regarding combination therapy from different studies all over the world are starting to come out. Though combination of azithromycin and hydroxychloroquine can decrease viral RNA load the addition of azithromycin may potentially trigger cardiovascular complications. There is one ongoing trial on the use of azithromycin alone in mild to moderate COVID-19.

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