Aktivitas Antivirus dan Anti-inflamasi Repurposing Obat Favipiravir dan Kina Sulfat terhadap Virus Dengue Serotipe 1 secara In Vitro = Antiviral and Anti-Inflammatory Activities Repurposing Drugs Favipiravir and Quinine Sulfate against Dengue Virus Serotype 1 In Vitro

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Abstrak

Infeksi virus dengue (DENV) masih menjadi masalah kesehatan global di dunia termasuk Indonesia. Menurut data CDC, diseluruh dunia terdapat sekitar 400 juta kasus DENV dengan 40.000 jiwa setiap tahunnya. Keparahan infeksi DENV berkaitan dengan jumlah viral load yang tinggi dan badai sitokin yang disebabkan oleh inflamasi berlebih. Sampai saat ini tidak ada antivirus spesifik digunakan untuk DENV, sementara itu penggunaan obat anti inflamasi untuk DENV terbatas hanya untuk pasien dengan gejala klinis berat. Favipiravir dan Kina Sulfat telah dilaporkan sebagai drug repurposing yang dapat menghambat replikasi DENV, namun apakah kedua obat ini memiliki aktivitas anti-inflamasi yang disebabkan oleh infeksi DENV belum dikaji lebih lanjut. Aktivitas antivirus favipiravir dan kina sulfat dianalisis melalui nilai IC50 dan CC50 terhadap DENV serotipe-1 (DENV-1) pada sel Vero. Ekspresi relatif sitokin TNF-a, IL-6, IL-10 dan faktor transkripsi NFkB dianalisis dari PBMC donor sehat yang diinfeksikan DENV-1 dengan pemberian Favipiravir atau Kina Sulfat. Hasil penelitian menunjukkan IC50 dan CC50 untuk Favipiravir sebesar 2,72 ug/mL dan 156,78 ug/mL dengan nilai SI 58, sementara IC50 dan CC50 Kina Sulfat sebesar 14,97 ug/mL dan 85,2 ug/mL dengan nilai SI 5,69. Favipiravir dan Kina Sulfat mampu menurunkan ekspresi IL-6 dan IL-10, namun menginduksi ekspresi TNF-a dan faktor transkripsi NFkB pada dua skema uji infeksi DENV-1 dengan atau tanpa antibodi. Dari penelitian ini dapat disimpulkan bahwa Favipirafir memiliki aktivitas antivirus dengue yang lebih baik dibandingkan Kina Sulfat sementara peranan Favipiravir dan Kina Sulfat sebagai anti-inflamasi infeksi DENV masih memerlukan studi lebih lanjut.
.....Dengue virus (DENV) infection is still a global health problem in the world, including Indonesia. According to CDC data, worldwide there are around 400 million DENV cases with 40,000 deaths each year. The severity of DENV infection is related to the high viral load and cytokine storm caused by excessive inflammation. Until now there is no specific antiviral used for DENV, meanwhile the use of anti-inflammatory drugs for DENV is limited to patients with severe clinical symptoms. Favipiravir and Quinine Sulfate have been reported as repurposing drugs that can inhibit DENV replication, but whether these two drugs have anti-inflammatory activity caused by DENV infection has not been studied further. The antiviral activity of Favipiravir and Quinine Sulfate was analyzed through IC50 and CC50 values against DENV serotype-1 (DENV-1) on Vero cells. The relative expression of cytokines TNF-a, IL-6, IL-10 and the transcription factor NFkB was analyzed from PBMCs of healthy donors infected with DENV-1 with the addition of Favipiravir or Quinine Sulfate. The results showed that the IC50 and CC50 for Favipiravir were 2,72 ug/mL and 156,78 ug/mL with an SI value of 58, while the IC50 and CC50 of Quinine Sulfate were 14,97 ug/mL and 85,2 ug/mL with an SI value 5,69. Favipiravir and Quinine Sulfate were able to reduce the expression of IL-6 and IL-10, but induced the expression of TNF-a and the transcription factor NFkB in two DENV-1 infection test schemes with or without ADE. From this study it can be concluded that Favipiravir

has better dengue antiviral activity than Quinine Sulfate, while the role of Favipiravir and Quinine Sulfate as an anti-inflammatory for DENV infections still requires further study. From this study, it can be concluded that Favipiravir has better dengue antiviral activity than Quinine Sulfate while the role of Favipiravir and Quinine Sulfate as anti-inflammatory of DENV infection still requires further study.