Pharmacokinetic characterization of favipiravir in patients with COVID-19 and patient outcome

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Abstract

Favipiravir is one of the repurposed antiviral medications for the treatment of SARS-CoV-2 infection. Since the dosing regimen is a prominent factor for the success of the antiviral therapy, this prospective observational study aimed to characterize the pharmacokinetic characteristics of favipiravir in COVID-19 patients. Adult patients (n=21) hospitalized for mild to moderate COVID-19 with a positive RT-PCR test, and assigned for favipiravir treatment were included. Favipiravir was administered for 5 days, with a loading dose of 3200 mg and a 1200 mg/day maintenance dose. Serial blood samples were collected on Day-2 and Day-4 of the therapy. Laboratory findings of the patients and in-hospital mortality were assessed. Favipiravir concentrations exhibited high variations and a significant decrease during the treatment of COVID-19. The median favipiravir trough concentration (C0-trough) on Day-2 was 21.26 µg/mL whereas it decreased significantly to 1.61 µg/mL on Day-4, the area under the concentration versus time curve decreased from 345.6 µg.h/mL to 108.6 µg.h/mL, respectively. Gender seems significant to affect favipiravir concentrations. Day-2-C0-trough of female patients was significantly higher than male patients. Of the 5 patients that died, 4 were male with a significant increase in ferritin levels from Day-0 to Day-5 compared to surviving patients. In addition, there was a significant decrease in D-dimer and CRP levels in the surviving patients. Our findings indicate that favipiravir concentrations show significant changes during the treatment of COVID-19. Therapeutic drug monitoring may best guide dose adjustments in patients that do not respond to treatment with favipiravir.

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