Favipiravir Induced Nephrotoxicity in two Patients of COVID-19

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idney is reported second major organ affected after lungs in severe coronavirus disease 2019 (COVID-19) and is associated with poor outcome.1 The pathophysiology of acute kidney injury (AKI) in COVID-19 is unclear and may be multi-factorial; virus-host complex immune interactions, hemodynamic alterations, effect of therapies like invasive mechanical ventilation on renal blood flow and/or nephrotoxic drugs.2 We report two cases of AKI with favipiravir induced nephrotoxicity.

Patient 1: 38-year male, confirmed reverse transcriptase polymerase chain reaction positive (RT-PCR) present for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and moderate pneumonia was given hydroxy-chloroquine (HCQ) 400 mg BID followed by 200 mg BID for 10 days and favipiravir at 1600 mg BID followed by 600 mg BID for 5 days. There was progressive rise in creatinine with good urine output from day three of starting favipiravir. The favipiravir was stopped, creatinine showed a progressive decreasing trend in 48 hours and reached baseline in five days (Figure).

Patient 2: 51-year male RT-PCR positive, severe COVID-19 was started on HCQ and favipiravir at same dose as in patient one along with methylprednisolone 40 mg BID for days and enoxaparin 40 mg subcutaneous once daily. His serum creatinine started increasing 48 hours after favipiravir with non-oliguria. The respiratory failure showed improvement in four days. The patients favipiravir was stopped and renal functions improved over three days (Figure 1). The AKI in both patients was non-oliguric, urine analysis unremarkable and ultrasound showed no features of obstructive uropathy and renal vasculature thrombosis. The AKI improved within 24-48 hours of favipiravir discontinuation proving temporal association of drug induced nephrotoxicity. Both our patients had resolving respiratory failure and inflammatory markers which cannot explain direct SARS-CoV-2 related AKI. The patients had normal renal functions at baseline, did not have any hemodynamic alterations and superadded bacterial or fungal sepsis. We could not do renal biopsy in our patients as renal functions started recovering after favipiravir discontinuation. There are no reports of nephrotoxicity with favipiravir and drug insert advises for general caution about monitoring of AKI.3 The nephrotoxicity is known with other anti-viral agents and involve either direct renal tubular toxicity (e.g. cidofovir) or crystal nephropathy (e.g. acyclovir). In conclusion, we believe as many repurposed drugs are being used for COVID-19 on experimental and compassionate basis without well conducted research, the clinicians need to be very careful of any new adverse event. The AKI like in any other patient needs comprehensive review for all possible etiology before linking it to COVID-19.

References


Fig. 1: Trend of serum creatinine and its relation to Favipiravir. Hollow arrow: Start of favipiravir. Solid arrow: stop of favipiravir