## Dexamethasone/remdesivir/warfarin interaction

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### Elevation of international normalised ratio and off-label use: 2 case reports

In a case series, 2 male patients (a 71-year old man and a 62-year-old man) were described, who developed elevation of the international normalised ratio (INR) following the concomitant administration of dexamethasone, remdesivir and warfarin [*not all routes stated*]. Additionally, they received off-label treatment with dexamethasone for COVID-19 pneumonia.

Case 1: A 71-year-old man, weighing 98kg, was on warfarin due to a history of pulmonary embolisms. His most recent appointment with the pharmacist for warfarin management in the outpatient setting was 10 days before the admission, and at that time, his INR was 2.6. He was prescribed to continue his warfarin dose of 7.5mg daily except 5 mg on Tuesdays and Fridays to maintain INR within his goal range of 2 to 3. On presentation, he underwent several laboratory tests, and was diagnosed with COVID-19 pneumonia. He had no history of missed dosages, no changes in diet or vitamin K intake, no recent signs/symptoms of bleeding or thromboembolism and no history of alcohol or nicotine use. He was maintained on a regular diet during the admission, and his inpatient medications included paracetamol [Acetaminophen], ipratropium-bromide/salbutamol [albuterol/ipratropium], aspirin [Aspirin EC], atorvastatin, budesonide/formoterol, benzonatate, colecalciferol [cholecalciferol], dextrose, dioctyl sulfosuccinic acid [docusate], dorzolamide, glucagon, glucose, heparin, insulin aspart, metoprolol tartrate, sodium chloride [Normal saline], pantoprazole [Pantoprazole EC], senna-alexandrina [senna] and tamsulosin. He was admitted to a general medicine ward for days 1 and 2 with no significant observed events. On day 3, he developed a fever and increased oxygen requirements required a closer monitoring, for which, he was transferred to the medical intensive care unit. On day 3, he received off-label treatment with oral dexamethasone 6mg daily. On day 4, he was initiated on one time IV remdesivir 200mg. On day 5, an INR was drawn with morning labs and resulted at 5.5, and warfarin was stopped. The IV remdesivir was continued on day 5 at a maintenance dose of 100mg daily for the remainder of remdesivir therapy. From day 6 to day 8 of admission, no significant events were observed, and dexamethasone and remdesivir maintenance doses were continued and warfarin remained on hold as INR remained supratherapeutic. On day 9, he had completed his course of remdesivir and had a transfer back to the general medicine ward. On the same day, INR had returned to 2.4, and warfarin was restarted at a dose of 5mg daily. On day 10, INR remained at 2.1 and as he was clinically stable, discharge was planned. On day 11, INR again elevated to 3.9 and warfarin was again stopped. On day 12, INR had fallen to a subtherapeutic level of 1.8; however, he was discharged home on a warfarin dose of 6mg daily. He received his last dose of dexamethasone on day 12, and he remained COVID-19 positive upon discharge.

Case 2: A 62-year-old man, weighing 127kg, was on warfarin due to aortic mechanical heart valve replacement secondary to aortic aneurysm. His most recent appointment with the pharmacist for warfarin management in the outpatient setting was 44 days before the admission. At that time, his INR was 2.6, and he was instructed to continue his warfarin dose of 11.25mg daily to maintain INR within his goal range of 2.5 to 3.5. On presentation, he underwent several laboratory tests, and was diagnosed with COVID-19 pneumonia. He had no history of missed dosages, no changes in diet or vitamin K intake, no recent signs/symptoms of bleeding or thromboembolism and no history of alcohol or nicotine use. He was maintained on a low sodium diet during the admission, and his inpatient medications included paracetamol [Acetaminophen], salbutamol [albuterol], benzonatate, carvedilol, dextrose, glucagon, glucose, lidocaine and loperamide. He was admitted to a general medicine ward from the emergency department on day 1. His home warfarin regimen of 11.25mg daily was resumed. On day 2, warfarin was stopped due to a supratherapeutic INR result of 4.0. Later that day, he was initiated on one dose of IV remdesivir 200mg due to an oxygen saturation of 92% on room air. On day 3, warfarin was resumed at 11.25mg daily as the INR was 2.3. The IV remdesivir was continued at maintenance dose of 100mg daily for the duration of treatment. On day 4, he was initiated on oral dexamethasone 6mg daily, and no other significant events were noted on day 4 or day 5 (INR at 3.4). Warfarin 11.25mg daily, oral dexamethasone 6mg daily, and IV remdesivir 100mg daily were continued. On day 6, his INR was elevated to 6.2, and thus warfarin was stopped. However, on day 6, he completed the 5 day course of remdesivir. On day 7, the INR remained at supratherapeutic at 6 with warfarin remaining on hold. On day 7, treatment course of dexamethasone was stopped after 4 days of therapy. He was otherwise stable, and was discharged on day 7 with a INR of 6. He was instructed to hold warfarin until follow-up with his outpatient pharmacist 2 days later. He remained COVID-19 positive upon discharge.

Landayan RP, et al. Probable Interaction Between Warfarin and the Combination of Remdesivir With Dexamethasone for Coronavirus Disease 2019 (COVID-19) Treatment: A 2 case Report. Journal of Pharmacy Practice : no pagination, 15 Apr 2021. Available from: URL: http://doi.org/10.1177/08971900211008623 803561774