

The GeriJournal



Volume 17, Number 7
July 2022

A publication of GeriatRx Pharmacy

Methotrexate & Vaccines

Sadly, it seems that COVID boosters will be with us for a while. Experience is teaching us about the impact some drugs have on vaccine response. Immunosuppressive drugs are of particular interest. Holding these drugs could improve vaccine success, but the cost may be a worsening of the condition being treated.

Methotrexate use is common in the elderly. It is given primarily for arthritis, though it is also used to treat a variety of cancers and other conditions. Rheumatoid arthritis (RA) is an inflammatory disorder. Since methotrexate reduces immune responsiveness, it blunts inflammation, limiting joint pain and damage in RA. A few studies have examined the response to COVID vaccine in conjunction with holding methotrexate for two weeks, vs. giving methotrexate without interruption.

The most recent notable study was conducted in England. The *VROOM* trial was published in *Lancet* last month and evaluated 254 patients (mean age 59-years; two doses of

COVID vaccine on board) with RA and some other auto-immune, inflammatory conditions.

After all participants received a third dose of COVID vaccine, half of the cohort continued their weekly methotrexate as usual. The other half received no methotrexate for two weeks. Antibody titers were more than twice as high (2.19 times greater) in the group that held methotrexate. That group had no disease flareups, although there is no assurance this would be the case in all circumstances. Prior research with Influenza vaccine has shown similar results and that holding methotrexate for four weeks provides no further benefit. In most cases, residents taking methotrexate should have the drug held for two weeks after receiving any vaccination.

Easy on the Crestor

Rosuvastatin (Crestor®) is our most potent statin. Roughly half the dose of Crestor® achieves the same cholesterol lowering effect relative to the next most potent statin, atorvastatin (Lipitor®).

Due to its high potency, we must be careful when using this valuable medication. At high doses and in vulnerable populations its use is linked to serious adverse effects, especially kidney damage and muscle breakdown (these breakdown products can

exacerbate the renal damage). The FDA has a warning to limit Crestor® dosage to 10mg per day in the presence of Stage 4 (eGFR < 30ml/min) chronic kidney disease (CKD). Asian populations are particularly susceptible to these renal effects, and they should be dosed very cautiously.

Over one million new users of Lipitor® and Crestor® were analyzed in the July issue of *J Am Soc Nephrology*. Crestor® users with Stage 4 or 5 CKD had twice as much hematuria and nine times as much proteinuria as new Lipitor® users. Although this is an observational study, it seems clear we should use caution, especially with Crestor® doses of 20 and 40mg.

Statin Combo for Safety

As mentioned above, high dose statins, especially rosuvastatin, can be dangerous. One strategy to mitigate this risk is to use a combination of ezetimibe (Ezetrol®) with a lower dose of the statin drug. *RACING*, a study just published in *Lancet*, showed ezetimibe 10mg daily + Crestor® 10mg daily yielded lower LDL cholesterol levels than Crestor® 20mg daily alone. CV benefits were similar between the groups, with much better tolerance (roughly half the number of withdrawals – primarily due to myalgia) in the combo group. Ezetimibe plus a statin looks like a good option for safety and drug tolerance.

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