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Drug Interactions May Increase Side Effects of Chemotherapy in Elderly Patients

Summary contains updated data not in the abstract

Elderly patients frequently take medications for multiple conditions, such as high blood pressure and diabetes. Researchers have found that these drugs may interact with anti-cancer drugs and can affect how well patients tolerate cancer treatments. The investigators analyzed 284 patients age 70 and older who were receiving chemotherapy for cancer and found that patients were more likely to experience severe hematological side effects from chemotherapy (such as low blood cell counts) if they took drugs that interfered with protein binding, examples of these types of drugs include amlodipine (Norvasc), omeprazole (Prilosec), or celecoxib (Celebrex). Patients were more likely to experience moderate to severe non-hematological toxicity (such as fatigue or diarrhea) if they took drugs that inhibited cytochrome p450 (a family of enzymes involved in drug metabolism); examples of these include ketoconazole (Nizoral) and amiodarone (Pacerone, Cordarone), among others.

Other factors, such as tumor stage, kidney functioning, and body mass index, also influenced the interactions between anti-cancer drugs and other medications. Limited data exist on cancer treatment for older people; this study provides physicians with important information to guide cancer treatment and monitor patients.

Abstract #9505

The impact of polypharmacy on toxicity from chemotherapy in elderly patients: Focus on cytochrome P-450 inhibition and protein binding effects

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Background: Drug-drug and disease-drug interactions are significant clinical issues in the elderly. Of the elderly taking 3+ chronic medications, 33% are rehospitalized within 6 months of discharge from a hospital. Drug interactions can also be relevant to toxicity from chemotherapy, such as ketoconazole and irinotecan, via p450 inhibition, or oxaliplatin and warfarin, possibly via competition for protein binding.

Methods: To assess the impact of polypharmacy on toxicity from chemotherapy, we analyzed a cohort of 290 patients 70+ receiving chemotherapy at Moffitt Cancer Center. In previous analyses using unweighted inhibition/induction of p450 interactions we found results approaching significance, and albumin level predicting non-hematologic toxicity. We refined our analysis by using weighted effects according to the strength of p450 inhibition/induction. We also assessed the impact of competition by highly protein-bound drugs (>50%). Stepwise logistic regression was used to assess predictors of G4 hematologic (G4H) or G3-4 non-hematologic (G3-4NH) toxicity. CART software was used to assess heterogeneity of effects.

Results: In unconstrained models, higher likelihood of G4H was predicted by high competitive protein binding ($p=.003$), bone marrow invasion ($p=0.027$), tumor stage ($p=0.005$), mean bilirubin ($p=0.025$), and mean red blood cells during chemotherapy ($p=0.012$). In unconstrained models, higher likelihood of G3-4H was predicted by higher BMI ($p=0.048$), tumor stage ($p=0.029$), lower mean albumin during chemotherapy ($p=0.005$), and higher AST before chemotherapy initiation ($p=0.018$). When entry order was preset with MAX2, p450 interaction, and competitive protein binding being entered first, MAX2 score ($p=.016$) and competitive protein binding ($p=.009$) predicted higher likelihood of G4H, but no predictor significantly influenced G3-4NH. The CART analyses indicate a dominant effect of MAX2 for G4H, and of mean albumin for G3-4NH, with no major heterogeneity.

Conclusions: Our results suggest that drug distribution factors play important roles in chemotherapy toxicity in elders. The role of protein binding in the pharmacokinetics/dynamics of chemotherapy drugs should be further explored.

Disclosures for research team: Nothing to disclose.