Paper:
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Abstract: 300 words

Title: How are pain treatment response rates in primary care influenced by co-prescription of CYP2D6 inhibitors?

Authors: Rhys Pockett, Caroline O'Leary, Pippa Anderson, Ahmed Nasser, Thomas Winfield, David Ansell

Objectives: To determine the rates of co-prescription of CYP2D6-inhibiting medications with pain medication and the impact on response rates to pain medications, in the UK primary care setting.

Methods: Codeine and tramadol are prodrugs requiring activation by the CYP2D6 enzyme. These drugs may have limited effectiveness when co-prescribed with other medications known to inhibit the CYP2D6 pathway. This contrasts with CYP2D6-independent analgesia, e.g. buprenorphine, which do not require CYP2D6 activation.

We identified the co-prescription of three study pain medications; buprenorphine, codeine and tramadol with CYP2D6-inhibiting drugs including amitriptyline and fluoxetine. Patients aged ≥18 years with chronic non-malignant pain and prescribed buprenorphine, codeine or tramadol between 01/01/2009 and 31/01/2013 were identified in The Health Improvement Network (THIN) database. Patients were excluded if they had history of; chronic kidney disease stage 4/5, cancer, neuropathic pain, sciatica/radiculopathy, diabetes, back pain or a prior prescription for a study drug. Patients were classified as responders if they were either "cured" (discontinued treatment) or stable (remained on treatment), or a non-responder if they were referred to a pain clinic or switched to a CYP2D6-independent analgesic. Multivariate logistic regression was used to identify the predictors of response and estimate the influence of CYP2D6-inhibitors.

Results: The cohort consisted of 43,632 patients: 90.8% were responders, and CYP2D6-inhibiting drugs were prescribed to 33.8% of the cohort. Almost three times as many patients failed to respond in those prescribed a CYP2D6-inhibitor (16% vs. 6%). Controlling for medication, demographics and co-morbidities the logistic regression indicated the odds of responding for those with a CYP2D6-inhibiting co-prescription were 39% lower than those without a co-prescription for a CYP2D6 inhibiting drug (OR= 0.61, 95% CI 0.57 to 0.66).

Conclusion: Chronic non-malignant pain patients with a co-prescription for a CYP2D6-inhibiting medication were significantly less likely to respond to analgesia treatment and therefore received suboptimal pain management.