

Increased Cytochrome P450-2D6 activity in people with codeine use disorders.

DAGLISH MRC^{1,2,3}, HAYLLAR JS², REILLY S², MOSTAFA S^{4,5}, EDWARDS CJ², O'GORMAN TM²

¹Hospital Alcohol & Drug Service, Royal Brisbane & Women's Hospital, Metro North Health, Brisbane, Australia; ²Mental Health, Alcohol & Drug Services, The Prince Charles Hospital, Metro North Health, Brisbane, Australia; ³Faculty of Medicine, The University of Queensland, Brisbane, Australia; ⁴MyDNA Life, Australia Limited, South Yarra, VIC, Australia, ⁵Centre for Medicine Use and Safety, Monash University, Parkville, VIC, Australia

Presenter's email: <mark.daglish@health.qld.gov.au>

Introduction: Prior to rescheduling, over-the-counter compound-analgesics containing codeine (CACC) were a common source of codeine use disorder (CUD) for people seeking opioid replacement therapy (ORT). Codeine is a pro-drug, metabolised by cytochrome P450-2D6 to morphine. CYP2D6 has a wide range of genotype allele variants and activity levels. We hypothesised that more people with CUD would be normal or ultrarapid and fewer poor metabolisers than in the general population. Following our previous work demonstrating no relationship between pre-treatment CACC and ORT buprenorphine doses we hypothesised that CYP2D6 activity would partially account for this disconnection.

Method: 106 participants with CUD had CYP2D6 genotyping and were compared to a published population sample of 5,408 people. Demographics, pre-treatment CACC and ORT doses were recorded. Local Institutional Ethics Committee approval was gained.

Results: Mean age of people with CUD at treatment entry was 35 years, with mean 6.1 years duration of CUD. Mean codeine dose was 660mg/day (range 40mg – 2700mg). There was a significant upward shift in CYP2D6 phenotype activity in the CUD group (one-sided Mann-Whitney U=347001, p<0.0001). 96% commenced on buprenorphine and stabilised on 16mg/day (sublingual), continued for mean 4.5 years, with mean peak dose 20mg/day. 21 (20%) of people transitioned to buprenorphine long-acting injections. Pre-treatment CACC dose poorly predicted buprenorphine doses however there was a significant interaction with CYP2D6 phenotype. CACC doses only predicted buprenorphine doses in the normal and ultrarapid metaboliser groups.

Discussions and Conclusions: Our primary hypothesis was confirmed. CYP2D6 poor or intermediate metaboliser status may protect against CUD.

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