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P51. THE POTENTIAL ROLE OF CYP2D6 PHARMACOGENETICS ON CODEINE TOXICITY

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Codeine, known as 3-methylmorphine, is currently the most widely used opiate in the world. Furthermore, codeine is one of the most commonly used drugs overall according to WHO reports. Codeine is widely administered for the treatment of postoperative pain, especially in paediatric patients.

Pharmaceutical drugs have been commonly implicated in drug-related deaths. It can be due to the relationship between genetic polymorphisms and drug interactions on codeine and morphine concentrations in codeine-related deaths.

Codeine is mainly metabolized in the liver. Morphine, the product of codeine O-demethylation by the highly polymorphic enzyme cytochrome P450 2D6 (CYP2D6), is the metabolite primarily responsible for the analgesic effect of codeine. The amount of morphine formed from codeine is highly variable, ranging from 0 to up to 75% of total codeine metabolism. Genetic polymorphisms are extremely responsible for the inter-individual variation in enzyme expression and activity. In contrast to other CYPs, CYP2D6 is not inducible, consequently, there is a large inter-individual variation in the enzyme activity of CYP2D6. Phenotyping for CYP2D6 have four types of metabolizers – Ultra Rapid Metabolizers (UMs: CYP2D6XN); Extensive Metabolizers (EMs: CYP2D6 *2, *33, *35); Intermediate Metabolizers (IMs: CYP2D6*9, *10, *17, *36 and *41); Poor Metabolizers (PMs: CYP2D6 *3, *4, *5 and *6). The differences in drug metabolism could lead to severe toxicity or therapeutic failure by altering the relationship between the dose and the blood concentration of the pharmacologically active parent drug or metabolite. As a result, pharmacogenetic analysis may reveal new insight to the interpretation of codeine toxicity.

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