Pharmacogenetics of Pain

Web Seminar: Pharmacogenetics in the Practice of Medicine

Order Pharmacogenetic Testing

Many common pain medications require activation by CYP2D6 to become effective. Approximately half of patients have genes that alter the function of 2D6. Testing for these gene alterations allows for alteration of dosage regimens to compensate for altered metabolism and optimize the safety and efficacy of the opioid family of analgesics. Physicians who adopt pharmacogenetic testing into their practice don't know how they were ever able to get along without it.

Would you like information sent? Simply complete the request form.

How to Order? Click here

POTENTIAL FOR DRUG DRUG INTERACTIONS (DDIS).

CYP2D6 metabolizes virtually all of the anti depressants, many of which are also strong inhibitors of the enzyme. Adverse events driven by interactions between opioid analgesics and anti depressants can be greatly increased in patients with gene based decreased CYP2D6 functioning.

POTENTIAL TESTING APPLICATIONS AND BENEFITS

Resource tool to help physicians resolve medical conditions resulting from adverse drug reactions.

- Supports evidence based decision making.
- Determine the need for higher doses or more expensive drugs.
- Optimize drug therapy at an earlier stage in treatment, by narrowing the therapeutic options for the patient.
- Help patient understand difficulties.

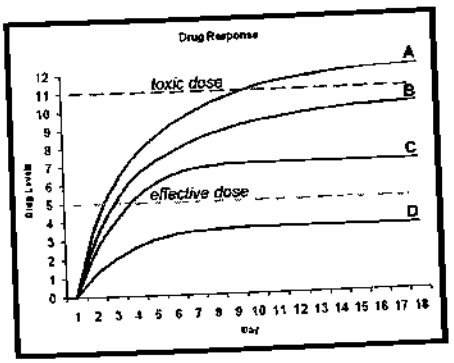
Screening tests to to help physicians anticipate and prevent future difficulties as more and different drugs are taken.

- Family members of patients who have had an adverse drug reaction.
- Patients who have had therapeutic failures and need to receive a problem drug again.
- Patients who want to be prepared for emergent situations.

ACTIVATION OF COMMON ANALGESICS BY CYP 2D6

Inactive Prodrug	metabolized Form	Increase in receptor binding potency
Codeine	Morphine	300 - 7000
Oxycontin	Oxymorphone	14 - 64
Hydrocodone	Hydromorphone	7-33
Dihydrocodeine	Dihydromorphine	67

PHARMACOGENETIC EFFECT OF



A. PM poor metabolizer, absent or greatly reduced ability to clear or activate drugs.
B. IM intermediate metabolizer. Heterozygotes for normal and reduced activity genes.
C. EM Normal Metabolizer. The norm.
D. UM Ultra Metabolizer. Greatly increased activity accelerating clearance or activation

POPULATION FREQUENCY OF CYTOCHROME P450 (CYP) GENOTYPES

Gene	PM	IM	EM	UM
CYP2D6	10%	35%	48%	7%
CYP2C9	4%	38%	58%	N/A
CYP2C19	3-21%	N/A	79-97%	N/A

Currently Available Tests

Individualized Patient Reports based on patient drug, herbal and diet regimens

Ordering Tests

CURRENTLY AVAILABLE TESTS

CYP2D6 (cytochrome P450 2D6) is the best studied of the DMEs and acts on one-fourth of all prescription drugs, including the selective serotonin reuptake inhibitors (SSRI), tricylic antidepressants (TCA), betablockers such as Inderal and the Type 1A antiarrhythmics. Approximately 10% of the population has a slow acting form of this enzyme and 7% a super-fast acting form. Thirty-five percent are carriers of a non-functional 2D6 allele, especially elevating the risk of ADRs when these individuals are taking multiple drugs. Drugs that CYP2D6 metabolizes include Prozac, Zoloft, Paxil, Effexor, hydrocodone , amitriptyline, Claritin, cyclobenzaprine, Haldol, metoprolol, Rythmol, Tagamet, tamoxifen, and the over-the-counter diphenylhydramine drugs, Allegra, Dytuss, and Tusstat. CYP2D6 is responsible for activating the pro-drug codeine into its active form and the drug is therefore inactive in CYP2D6 slow metabolizers.

CYP2C9 (cytochrome P450 2C9) is the primary route of metabolism for Coumadin (warfarin) and Dilantin (phenytoin). Approximately 10% of the population are carriers of at least one allele for the slow-metabolizing form of CYP2C9 and may be treatable with 50% of the dose at which normal metabolizers are treated. Other drugs metabolized by CYP2C9 include Amaryl, isoniazid, sulfa, ibuprofen, amitriptyline, Hyzaar, THC (tetrahydrocannabinol), naproxen, and Viagra.

CYP2C19 (cytochrome P450 2C19) is associated with the metabolism of carisoprodol, diazepam, Dilantin, Prernarin, and Prevacid.

CYP1A2 (cytochrome P450 1A2) is associated with the metabolism of amitriptyline, olanzapine, haloperidol, duloxetine, propranolol, theophylline, caffeine, diazepam, chlordiazepoxide, estrogens, lamoxifen, and cyclobenzaprine.

NAT2 (N-acetyltransferase 2) is a second-step DME that acts on isoniazid, procainamide, and Azulfidine. The frequency of the NAT2 "slow acetylator" in various worldwide populations ranges from 10% to more than 90%.

INDIVIDUALIZED PATIENT REPORTS BASED ON PATIENT DRUG, HERBAL AND DIET REGIMENS

DNA test reports can include patient specific information on potential drug-drug interactions (DDIs) mediated by the tested polymorphic drug metabolizing enzymes, taking into account patient diet, over the counter medicines, herbal preparations drugs of abuse and other factors. Testing patients for drug metabolizing enzyme genotypes can provide physicians with immediate insight into common individual differences in their patients' drug processing ability and helps the physician more quickly improve the efficacy and safety of the prescribed treatments. This information will be especially valuable when potential drug-drug interactions (DDIs) are a possibility.

ORDERING TESTS

Now you can add another dimension to providing safer and more efficacious care to your patients by ordering DNA Drug Sensitivity Testing™ for them. Call (800) 523-3080 for more information or to obtain collection kits, or visit how to order for test requisition forms and sample requirements.

REFERENCES

http://www.medscape.com/viewarticle/508543_2

Oesterheld, Jessica, M.D. GeneMedRx Drug Metabolism Tables

Foster A, Mobley E, and Wang Z. Complicated pain management in a CYP450 2D6 poor metabolizer, *Pain*

Pract. 2007 Dec;7(4):352-6.

Gan SH, Ismail R, Wan Adnan WA, Zulmi W. Impact of CYP2D6 genetic polymorphism on tramadol pharmacokinetics and pharmacodynamics, *Mol Diagn Ther. 2007;11(3):171-81.*

Kirchheiner J, Keulen JT, Bauer S, Roots I, Brockmöller J. Effects of the CYP2D6 gene duplication on the pharmacokinetics and pharmacodynamics of tramadol, J Clin Psychopharmacol. *2008 Feb;28(1):78-83.*

Stamer UM, Stüber F, Muders T, Musshoff F. Respiratory depression with tramadol in a patient with renal impairment and CYP2D6 gene duplication, *Anesth Analg. 2008 Sep;107(3):926-9.*

Coller JK, Christrup LL, Somogyi AA. Role of active metabolites in the use of opioids, Eur J Clin Pharmacol. 2008 Oct 29.

http://www.medscape.com/viewarticle/552096

Cozza KL, Armstrong SC, Oesterheld JR (2003) Drug Interaction principles for Medical Practice. *American Psychiatric Publishing Inc*

Zhou SF. Polymorphism of human cytochrome P450 2D6 and its clinical significance: Part I. *Clin Pharmacokinet.* 2009;48(11):689-723

Zanger UM, Raimundo S, Eichelbaum M. Cytochrome P450 2D6: overview and update on pharmacology, genetics, biochemistry. Naunyn Schmiedebergs *Arch Pharmacol.* 2004 Jan;369(1):23-37

By Howard Coleman, B.S. Last Reviewed 8/20/10

3000 First Ave., Suite One, Seattle, WA 98121

800 523-3080