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Can genetic tests predict the safety or effectiveness of prescribed medicines?

When the Human Genome Project completed their mapping of all human genes in 2003, this newly revealed information generated a lot of excitement on the promise it held for new approaches to the diagnosis and early detection of health disorders, gene therapy treatments, and predictive guidance for existing drug treatments. Since then, the terms "pharmacogenomics," "pharmacogenetics," "precision medicine," and "personalized medicine" have appeared to describe how genes influence human physiology, and how they might be understood and used to inform on the improved effectiveness, efficiency, and safety of drug therapies. While some differences exist in how these terms are understood, the hope is that the best drug choices or individualized doses might be made based on these genetic profiles. Precision medicine, broadly, aims to tailor treatment decisions that appreciate individual "gene linked" differences, especially related to the metabolism and excretion of drugs, to improve their effectiveness and safety. Pharmacogenomics is the tool that enables this for prescription medication choices.

To appreciate how this works, it may help to understand that certain genes have been identified which code for the production of proteins in the body that influence the following:

1. How drugs are broken down, or metabolized, to ready them for excretion
2. How drugs are absorbed or distributed (in circulation)
3. Properties of specific drug receptors (targets for drug attachment and activation)
4. The progress of a biochemical pathway activated by a drug

For example, when a drug response for people who share a gene variation for its metabolism (more rapid or slower) is compared, it may be discovered that they need lower or higher doses of the same drug to achieve a therapeutic response, or to avoid an adverse effect. Without knowing that one possesses this gene variation, it would take time, money, and trial and error to discover this. With a genetic test in hand, a prescriber may select a drug or adjust its dose to spare the time, inconvenience, potential discomfort, and cost of such a trial.

An example of this can be found in predicting the safety and effectiveness of codeine, an opioid analgesic medication which must be converted to an active form (morphine) by a metabolic pathway in the liver called 2D6. Persons with the gene for "slow" metabolism of codeine in the 2D6 metabolic pathway are unable to convert enough codeine to morphine to provide pain relief and may be predicted to fail treatment. Persons with the gene for "rapid" metabolism of codeine may experience greater sedation, respiratory depression, and other side effects for the same medication.

At present, pharmacogenomic testing is not available for all medications, and not for most over-the-counter medications. Depending on the medications being considered, more than one test may be required to determine your predicted response.

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Drug of the Month

Voltaren Arthritis Pain (diclofenac sodium topical gel, 1%)

Voltaren Arthritis Pain (diclofenac sodium topical gel, 1%) is a branded, topical formulation of a non-steroidal anti-inflammatory drug (NSAID). Diclofenac is approved by the U.S. Food and Drug Administration (FDA) for temporary relief of osteoarthritis pain in joints amenable to topical treatment, such as knees and those of the hands.[1]

Diclofenac, and NSAIDs in general, act by inhibiting the activity of enzymes involved in the production of chemical messengers called prostaglandins that are involved in the signaling of pain. The topical application of diclofenac is thought to reduce the amount of the drug that reaches the bloodstream (compared to oral administration) and thereby minimize the risk of side effects.[2] "Systemic NSAIDs carry a risk of cardiovascular and kidney issues, stroke, bleeding, and ulcers," explains physiatrist Meredith Konya, MD. "The risk increases with the duration of treatment."[2] Voltaren Arthritis Pain Gel should be used at the lowest effective dose for the shortest duration of treatment consistent with individual treatment goals.[1]

Diclofenac is widely prescribed and was first approved for use in the U.S. in 1988. It is available in a variety of oral, injectable, and topical formulations for use, including tablets, gels, intramuscular and IV injections, and transdermal patches. There are several brand preparations, as well as generic and over-the-counter diclofenac products available in retail settings. Prescription-only Voltaren Gel was first approved for use by the FDA in 1997. It was announced on February 17, 2020 to be newly approved for over-the-counter availability as Voltaren Arthritis Pain Gel.[3] This would be the first prescription-strength NSAID topical gel available in the U.S. without a prescription, and provides more ready access to topical NSAID treatment. The makers of Voltaren Gel, GSK, anticipate that Voltaren Arthritis Pain will be available in U.S. retail settings in Spring 2020.[3] Pricing information for the new over-the-counter formulation was not available at the time of this publication.

1. Prescribing Information – Voltaren® Gel – Accessed at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/022122s010lbl.pdf on 3/11/2020
2. Cleveland Clinic – Health Essentials – Accessed at: https://health.clevelandclinic.org/why-topical-nsaids-could-be-a-safer-option-to-relieve-your-arthritis-pain/ on 3/11/2020
3. GlaxoSmithKline Press Release – February 17, 2020 – Accessed at: https://us.gsk.com/en-us/media/press-releases/fda-approves-gsk-s-voltaren-arthritis-pain-for-over-the-counter-use-in-the-united-states/ on 3/11/2020