Individual Variations in Drug Responses

Peggy Ward-Smith

Other health care conditions, cultural factors, lifestyle, race, and ethnicity are all variables that impact individual response to any medication regime. These individual variations must be considere whenever recommending treatment and may be the reason dosages have to be altered to achieve the desired effect. As advances are made in the field of genetics, this knowledge must also be included when determining which drug and dosage will provide appropriate treatment. Genetic make-up, race, and ethnicity cannot be altered. Therefore, specific assessment should focus on detecting the presence of other health care conditions, lifestyle, and cultural practices that may alter use, compliance, and metabolism of medications (Jarvis, 2008). The purpose of this article is to review the literature on the effect race, ethnicity, health care conditions, and lifestyle choices have on drug responses.

Objectives

1. Describe influences on drug responses that cannot be altered.
2. Describe influences on drug responses that can be altered.
3. Discuss ways nurses can influence compliance and pharmacologic adherence in patients of different races and cultures.

Influences that Cannot Be Altered

Genomics is the focused area of research created by the Human Genome Project (U.S. Department of Energy Human Genome Program, 2009). Wasinger, Cordwell, and Wilkins (1995) state that this new knowledge has enabled researchers to re-formulate the chemical formulas of many drugs to enhance their effect while minimizing adverse reactions. Pharmacogenetics is the term used when reporting how genetic variables affect drug response in a specific group of people (Mosby, 2009).

Current testing focuses on the P-450 enzyme system. These enzymes are located within the liver and assist with drug metabolism. Specifically, these enzymes decrease the toxicity of many drugs, making them easier for the body to excrete (National Cancer Institute, 2009). Cytochrome P450, or CYP, is a genetically influenced enzyme that accounts for about 75% of total drug metabolism (Guengerich, 2008). While it is outside the scope of this article to detail the clinical impact P-450 or CYP enzymes have on pharmacogenetics, testing to identify carriers of this enzyme is useful and may be used to recommend one drug versus another and to identify the appropriate dose. According to a technological report from the Agency for Healthcare Research and Quality (2007), there is a

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Note: Objectives and CNE Evaluation Form appear on page 28.

This article provides an overview of the modifiable and non-modifiable variables that influence drug responses. Knowledge of these issues need to be known by nurses to assure adequate medication is prescribed and treatment adherence occurs.

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paucity of quality data correlating testing for CYP450 polymorphisms and clinical outcomes. Thus, not enough is known at this time to make clinical, personal, or public health decisions using CYP450 polymorphisms or based on CYP450 enzyme information.

Race has been shown to impact drug responses (Jarvis, 2008). This is known as genetic polymorphism (Kudzma, 1999). According to Kudzma (1999), genetic polymorphism is controlled primarily by genes that perform liver metabolism. Individuals who insufficiently metabolize medications are called slow or poor metabolizers. Those whose livers metabolize medications quickly are known as rapid or extensive metabolizers. In general, three types of polymorphism have been identified, the result of multiple clinical drug trials. These include debrisoquine, mephenytoin, and acetylation polymorphism (Kudzma, 1999).

Debrisoquine polymorphism was initially identified when evaluating treatment response to debrisoquine, an antihypertensive medication. Poor metabolizers were identified among 3% to 9% of Caucasians from the United States, Canada, Britain, Denmark, Sweden, and Switzerland. Debrisoquine has an even lower percentage of poor metabolizers among individuals from China, Malaysia, and Thailand, where rates range from 0% to 2% (Lin, Poland, & Silver, 1993). Knowledge of these responses is clinically significant. Some narcotics, antihypertensives, antipsychotics, and antidepressants are physiologically metabolized in manners similar to debrisoquine (Kudzma, 1999). This may explain why Chinese, Japanese, and Malaysian individuals may obtain sufficient pain control with lower doses of codeine (Jarvis, 2008).

Mephenytoin polymorphism describes the differences in metabolizing mephenytoin, an anticonvulsant medication. Other medications, such as some barbiturates and diazepam, are metabolized similarly to mephenytoin. Individuals of Chinese and Japanese descent are 20% more likely to poorly metabolize medications with this ingredient than other ethnicities (Pi & Simpson, 2005).

Follow-up research among those with tuberculosis treatment with isoniazid resulted in the identification of acetylation polymorphism (Hughes, Biehl, Jones, & Schmidt, 1954). Acetylation polymorphism describes the subset of individuals who metabolize isoniazid slowly, resulting in elevated serum levels of isoniazid, increased pharmacologic effects, and drug toxicity (Hughes et al., 1954). Hein and associates (2000) determined that demographically, individuals of European and African descent have an equal number of slow and rapid metabolizers, while Japanese and Inuit populations have a greater number of rapid metabolizers.

Ethnicity influences access to health care, recommendations, and compliance with treatment plans (Jarvis, 2008). The Centers for Disease Control and Prevention (CDC) reports that disease patterns vary among different ethnicities. This report also states that heredity, or ethnicity, influences medication absorption, efficacy, treatment response, and the incidence and severity of adverse side effects (CDC, 1993).

The ethnic composition of the United States is rapidly changing, with statistical estimates from the U.S. Census Bureau (2009) reflecting a 31.2% increase in the number of Hispanics between 2000 and 2010. It is estimated that during this time frame, the number of African Americans will increase by 11.6%, Native Americans will increase by 12.9%, Asian Americans and Pacific Islanders will increase by 36.1%, and the population of Caucasians will increase by 2.7% (U.S. Census Bureau, 2009). This represents a profound shift in ethnicity, making it imperative that clinicians include ethnicity knowledge in treatment plans.

The terms race and ethnicity are frequently used interchangeably, yet each has a different meaning. Race and ethnicity categories were redefined by the U.S. Census Bureau (2009) in 1997 to reflect changes in the U.S. population, and new categories were added. Description of race now includes six possible categories: 1) American Indian or Alaskan native, 2) Asian, 3) Black or African American, 4) Native Hawaiian or Other Pacific Islander, 5) White, and 6) Some Other Race. Ethnicity has two categories: 1) Hispanic or Latino and 2) Not Hispanic or Latino. These categories allow researchers to describe their study population and are used to collect census data.

Despite the additional categories, the term Hispanic or Latino is used to describe 39 million Americans who may actually be Puerto Rican, Mexican, Peruvian, and Chilean (U.S. Census Bureau, 2009). The Asian category includes individuals who are Korean, Chinese, Japanese, Indian, Pakistani, or Vietnamese (U.S. Census Bureau, 2009). These limitations inhibit the ability to generalize research findings. No research is found demonstrating a connection between culture and genetics. The ability to provide culturally respectful care is also hampered by these categories. According to Munoz and Hilgenberg (2006), culturally competent care includes an awareness of how individuals will respond to treatment, including drug therapies.

Race has been defined as “a class of persons of a common lineage. In genetics, races are considered as populations having different distributions of gene frequencies” (Dictionary.com, 2009). Race is generally used to describe the geographical origins
of ancestry. Historically, ethnicity has been used in the U.S. to describe people with shared origins, cultural bonds, and traditions (Answers Corporation, 2009). Ethnicity should not be used to classify individuals by race. Leininger (2002) describes ethnicity as an integrated system of learned beliefs, values, and customs common to a particular group of people and typically passed down from generation to generation.

The study of the effects of ethnicity on treatment and drug responses is defined as ethnopharmacology (Munoz & Hillegenberg, 2006). According to these authors, the effect of ethnicity on drug therapy is challenged by two separate issues. The first challenge based on ethnicity or race is the lack of precision in self-describing one's ethnic and racial background. Previous research and treatment violations against racial and ethnic minorities may make some individuals reluctant to self-disclose their ethnicity. The second challenge is the result of clinical trials being performed using Caucasian adult male participants. These results were then generalized to all people (Munoz & Hillegenberg, 2006). Research by Lin and Smith (2000) and Nicol (2003) concluded that ethnicity influences response to some medications. Burroughs, Maxey, and Levy (2002) have identified significant differences in the metabolism of certain medications based on ethnicity. The majority of research within this area has focused on antihypertensive and psychotropic medications.

The increased prevalence of hypertension among African Americans has resulted in research related to the effect of race and ethnicity on treatment. These studies report the effectiveness of and response to antihypertensive medications, which varies among Caucasian and African-American individuals (Materson, 2007).

A meta-analysis of cardiovascular medicine literature was performed by McDowell, Coleman, and Ferrer (2006). The result of this analysis indicates that African-American patients displayed a higher relative risk of angioedema, and East-Asian patients exhibited a higher risk for cough from the use of angiotension-coverting enzyme (ACE) inhibitor medications. In an effort to determine the effect race has on medication response, Sowinski, Burlew, and Johnson (1995) administered propranolol to individuals who were not hypertensive. Results of this study demonstrated that healthy African-American and Caucasian participants had fewer side effects if not hypertensive – indicating that the decreases in urine, increased blood volume, and elevated concentrations of sodium and calcium may be the result of hypertension rather than the medication used to treat this health condition.

Yet, many major classes of antihypertensive medications are effective in African Americans (diuretics, beta blockers, ACE inhibitors, and calcium channel blockers). Some medications appear to be more effective or more reliable (McDowell et al., 2006). African Americans respond better to diuretics than to beta blockers and ACE inhibitors (Denberg, 2003). Evidence-based research should guide treatment decision making and evaluating treatment outcomes. Racial differences in medication response may need to be included in patient education. Keltner and Folks (2001) conclude that metabolism and efficacy of antipsychotics and anti-anxiety medications appear effective when using comparable doses in African-American, Caucasian, or Hispanic individuals. Kuno and Rothbard (2002) state that Asian individuals may require lower doses of some medications (such as haloperidol) because of the increased possibility for adverse effects when “routine” doses are administered. Diazepam (Valium) is poorly metabolized in Chinese and Japanese individuals, causing a rapid drug build up, increasing the possibility for drug toxicity (Bumoughs et al., 2002). Close monitoring is required when medications within this category are prescribed to ethnically diverse individuals.

Influences That Can Be Altered

One universal dietary substance that inhibits the ability of enzymes to metabolize drugs is grapefruit (Kiani & Imam, 2007). Grapefruit appears to block the ability of intestinal wall enzymes to decrease the absorption of drugs. The ingestion of grapefruit increases blood levels of drugs. The mechanism of this interaction is not known, but it affects calcium channel blockers, statins, and antihistamines (Munoz & Hillegenberg, 2006).

Uses of substances that result in health care conditions are also culturally influenced. Tobacco and alcohol impact the absorption of some medications (Strickland et al., 1991). Frackiewicz, Sramek, Herrera, and Cutler (1997) correlated smoking with a decrease in serum levels of traditional antipsychotics. They hypothesized the decreased medication levels to be the result of the effects smoking has on liver enzymes. Societal affairs associated with alcohol ingestion are also culturally influenced, and the propensity toward alcohol abuse has cultural and genetic components (Bobo & Husten, 2000).

Culture influences the desire and ability to access the health care system (Jarvis, 2008). Holistic health beliefs are a part of traditional Native American and Chinese American cultures where disease is considered a result of personal imbalance. Resolving the imbalance is necessary for cure or included as a part of treatment. Any treatment
plan may include exercise, herbal remedies, nutrition, dietary changes, and medication. Knowledge of the use of herbal remedies, and complementary and alternative treatments should be known to all health care providers because the use of these remedies impacts compliance with and the ability to metabolize drugs (Pavlovich-Danis, 1999).

Body size and body mass index (BMI) information are becoming more important as the incidence of overweight and obese individuals increases (World Health Organization [WHO], 2006). The WHO (2006) recognized obesity as a global pandemic, with estimates of 700 million obese people by 2015. In the U.S., obesity, defined as a BMI of equal to or greater than 30 kg/m², doubled among adults older than 20 years of age between 1980 and 2002 (CDC, 2009). Most drug dosage recommendations are made by the pharmaceutical industry, with the assumption that all adults weigh between 150 and 170 pounds (Pai & Bearden, 2007). According to DeRyke, Lee, Kutl, and Nicolaou (2006), the absorption of drugs does not appear to be modified by obesity. Thus, increased or decreased medication dosage may be required for those with increased or decreased body size. Youngkin, Sawin, Kissinger, and Iseal (2005) state that calculating the appropriate drug dosage using a dosing strategy provides more accurate dosing, and monitoring is necessary to assure appropriate amounts of the drug are present.

Individuals with a higher percentage of body fat, especially abdominal fat, have a greater risk toward developing heart disease, diabetes mellitus, gallbladder disease, stroke, and certain cancers (Wadden, Berkowitz, & Womble, 2005). The risk or presence of comorbid conditions should be considered since obesity has been demonstrated to influence kidney glomerular filtration rate (GFR) (Bosma, Krikken, Homan van der Heide, de Jong, & Narsis, 2006). Clinically, an obese individual may require an increased dose of a medicine, yet the presence of a comorbid condition may prevent the ability to provide an adequate dose or increase the risk of adverse effects. Careful attention is needed to assure appropriate dosing while minimizing the potential for drug-related complications (Youngkin et al., 2005).

The role of culture, health care providers, and adherence to medications cannot be overstated. An excellent overview article specific to urology is provide by Baum and Dowling (2007). The use of alternative and complementary medicine should be assessed and included in any medication history. There are specific research results that should be known to urology nurses. Research by Li and associates (2008) identified that all men, particularly Asian men, seek medical assistance only when erectile dysfunction impacts their quality of life. Zickerman and Ratanawong (2007) described self-injection of viscous materials into men’s penile shaft to increase its size or to correct erectile dysfunction. These authors also articulate the resistance of these individuals to initiate or undergo medical treatment(s).

**Nursing Implications and Interventions**

Nursing assessments provide a mechanism to identify variables that may impact or influence drug responses (Jarvis, 2008). These assessments should include alternative or complementary treatments, as well as the individual responses to previous treatments and medications (Youngkin et al., 2005). Nurses’ knowledge of patients’ individual needs and desires is necessary to advocate for a treatment that is culturally respectful, therapeutic, and appropriate. Developing interventions that include unmodifiable and modifiable variables assures compliance, prevents complications, and develops therapeutic relationships (Youngkin et al., 2005).

Several methods can be used to appropriately and respectfully assess race and ethnicity. The Sunrise Model depicts the different dimensions of the Culture Care Theory and includes the constructs of education, economics, family, social, political, technological, religious, philosophical, and cultural values, as well as beliefs and practices (Leininger, 2002). Bloch (1983) uses the Sunrise Enabler to guide clinical research and as a method to respectfully assess culture. According to Leininger (1997), care always occurs within a cultural context.

Giger and Davidhizar (2002) provide a Transcultural Assessment Model that focuses on six areas of cultural phenomena and provides assistance in understanding how culture affects the perspective of patients. The six areas of cultural phenomena within this model are communication, space, social organization, time, environmental control, and biologic variations (Giger & Davidhizar, 2002). Assessing each of these domains provides the accurate and appropriate assessment information necessary to understand the influence race, ethnicity, and culture have in health care.

These models provide guides that can used as the basis for research surrounding individual variations in drug responses, specifically as they relate to cultural differences. Knowledge of cultural diversity, if not used to guide practice, carries a greater influence on drug responses than non-modifiable variables (Kudzma, 1999). In this area of health care, nurses initially connected culture and health care. As leaders in this area, as well as
being the health care provider often perceived as non-judgmental, trustworthy, and able to develop successful patient/caregiver relationships, nurses are in a pivotal position to assess, identify, advocate, and assure that drug therapy is individualized. Lanza, Pomeranz, and Corey (1998) report that serious adverse drug reactions occur in an estimated 6.7% of hospitalizations and rank as the fourth to sixth cause of death. In addition, estimates by Wijnen, Op den Buijsch, and Dront (2007) predict that 25% to 60% of individuals respond as expected to commonly prescribed medications. The necessity of frequent assessment to detect adverse effects and routine monitoring to determine therapeutic doses specific to the individual may be essential to the remaining 40% to 75%. As primary health care providers, nurses are charged with administering and educating patients about their medications. Nurses should also encourage individuals to report side effects and adverse effects, mention previous negative responses to drugs, describe any complementary or alternative therapy, and complete all follow-up laboratory care to assess patient benefits from drug therapy while minimizing potential complications.

References


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**Individual Variations in Drug Responses**

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**OBJECTIVES**

This continuing nursing educational (CNE) activity is designed for nurses and other health care professionals who care for and educate patients and their families with an overview of the modifiable and non-modifiable variables that influence drug responses. After studying the information presented in this offer, you will be able to:

1. Describe influences on drug responses that cannot be altered.
2. Describe influences on drug responses that can be altered.
3. Discuss ways nurses can influence compliance and pharmacologic adherence in patients of different races and cultures.

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