Research Briefs

Anxiety Drug Shortage Challenges Patients

The sudden shortage of buspirone, one of the safest anti-anxiety medications, has alarmed patients who rely on it daily to prevent panic attacks or to simply function. Physicians are also concerned because no one seems to know when supplies will resume.

Having to come off the drug and take a new one can be less suitable for several reasons, including addiction, and there is no equivalent medication to buspirone that works in the same manner. Maryland psychiatrist Dr. Dennis Glick says the shortage could disrupt patients' clinical stability, many of whom have complicated regimens. In 34 years of practice, he says, such issues only began affecting care a couple of years ago.

In the last few years there have been countless shortages of drugs, from morphine to drugs for schizophrenia to intravenous fluids. Often, the worst shortages are of generics, like buspirone, whose prices are now so low that some manufacturers claim they are no longer profitable to produce.

Twenty percent of Americans had an anxiety disorder in the last year, although not many use buspirone. Doctors have mixed feeling about its effectiveness; experts say it is far safer than benzodiazepines like Valium and Xanax. It is unlikely to cause harm from an overdose; it is not addictive; it doesn't cause sexual dysfunction; and it is very inexpensive.

Anxiety and depression often overlap and in many cases, it is better to avoid benzodiazepines, which can also be depressants. Buspirone can be a much safer choice. Unfortunately, Buspar, the brand-name version, is no longer made, leaving patients with no option of paying more to obtain the brand-name drug.

It seems the main reason behind the buspirone shortage is a halt in production at a Mylan Pharmaceuticals factory in West Virginia, which produces about one-third of the U.S.' supply. The FDA said the facility was not clean and that Mylan did not follow quality control procedures. The company says the date for resuming production is "T.B.D." As companies don't have to inform the FDA of how long a shortage is going to last, planning care becomes much harder for doctors and patients.

Although the FDA does not consider drugs like buspirone to be critical or lifesaving, millions of lives are affected each year by depression and anxiety.

Source: *The New York Times*, February 1, 2019

When a Patient Turns Down the Antidepressant

If an antidepressant hasn't worked for a patient after four to six weeks, guidelines suggest reconsidering the treatment. But what if the patient doesn't want to try a second one?

In a study evaluating the addition of mirtazapine to a serotonin and norepinephrine reuptake inhibitor (SNRI) or selective serotonin reuptake inhibitor (SSRI), researchers from Keele University in England, embedded a second, qualitative study to explore patients' perspectives on being invited to participate in a trial of a second antidepressant.

The most common reason for declining (49%) was not wanting to take part in a trial. About one-third of the invitees didn't want to take mirtazapine, although the researchers didn't know whether this was because of prior experience with the drug. One-fifth of the invitees didn't want to take more than one antidepressant.

Interestingly, the researchers say, 17% of the respondents indicated that they were not taking an antidepressant—even though they were being prescribed one. Some patients (10%) said they were too busy, and 7% said they were not depressed.

Of the invitees, 39% said they planned to stop taking the current antidepressant.

The researchers found some key themes in the responses. One was "the hard work of managing depression." They received "rich descriptions" of endeavors to manage mental health. Many respondents described delays in recognizing the cause of their depression, outlining repeated investigation for physical problems "until a diagnosis of depression was achieved by default," the researchers say.

Patients were also uncertain about the value of a second antidepressant, and concerned about attaining and maintaining a hard-won equilibrium. Some were reluctant to try a second antidepressant for fear of additional side effects.

Some respondents expressed skepticism about the "chemical imbalance story" they were told to explain why a tablet would help their mood. They couldn't see the logic behind a combination, and wondered why a second antidepressant would help if the first one hadn't.

When patients did agree to participate, it was often because they felt they were at a crisis point—where they were not only eager but even desperate to try something else.

The researchers say general practitioners, who often see patients when they are at that crisis point, should explore with patients their views on antidepressants, what other strategies they've used to manage symptoms, and whether they feel they're at a crisis point or at equilibrium. Understanding the patient's perceptions, they say, is key to negotiating the right treatment.

Source: *BMC Family Practice*, December 14, 2018

Getting the Right Numbers for Native American Drug-Overdose Deaths

More Native Americans have died from a drug overdose than members of any other racial or ethnic group in the U.S.—which as a whole has seen drug-overdose deaths triple since 1999. But little is known about the regional impact of opioids in tribal and urban American Indian/Alaska Native (AI/AN) communities, according to Indian Health Service researchers in Portland, Oregon. They examined death records from the Washington State Center for Health Statistics to identify trends and disparities in drug, opioid-involved, and heroin-involved overdose deaths for AIs/ANs and non-Hispanic whites in Washington.

AI/AN and white people had similar overdose-related death rates during 1999 and 2001, but then the deaths began to multiply faster among the Native Americans: Between 2013 and 2015, Native Americans were dying at nearly three times that rate from drug and opioid-related overdoses. Heroin-related deaths were four times higher.

During 2013–2015, 184 AI/AN people died from drug overdoses in Washington, 126 of them from opioids. Most deaths occurred in urban communities, both Native American and white. Men were almost twice as likely as women to die of an overdose, and adults 25 to 54 years old had the highest death rates. Age-specific drug overdose mortality rates among AIs/ANs were almost twice those among whites.

The death rates are disturbing enough, but the researchers also found that death certificates that were not corrected for misclassification of AI/AN race underestimated the mortality rates among AI/AN people by approximately 40%. For example, uncorrected data showed 28.7 drug-overdose deaths in Washington. The corrected number was actually 40.9. In contrast, the uncorrected number for whites was 15.7, versus 15.1.

Even before correction for misclassification, AIs/ANs in Washington had higher overdose mortality rates than did whites in Washington and AIs/ANs in the U.S.

The researchers note that misclassification of AIs/ANs in public health data can obscure the prevalence of disease and result in suppression of health statistics because of small numbers. That, in turn, can affect the ability of state and federal programs to direct the resources needed for a "robust public health response to this epidemic."

Source: *MMWR*, December 21, 2018

HHS Seeks Public Input on HIPAA Rules

The Department of Health and Human Services (HHS) has issued a request for information seeking public input on how Health Insurance Portability and Accountability Act (HIPAA) rules, particularly the privacy rule, can be modified to promote "coordinated, value-based healthcare."

HIPAA was developed to protect the privacy and security of individuals' health information, while allowing the information to be shared when needed. However, the Office for Civil Rights (OCR) has heard calls to revisit aspects of the rules that may limit or discourage information-sharing needed for coordinated care, according to HHS. OCR is looking for "candid feedback about how the existing HIPAA regulations are working in the real world and how we can improve them."

"In addressing the opioid crisis," Deputy Secretary Eric Hargan says, "we've heard stories about how the privacy rule can get in the way of patients and families getting the help they need. We've also heard how the rule may impede other forms of care coordination that can drive value."

HHS is also seeking input on specific areas of the privacy rule, such as facilitating parental involvement in care; accounting for disclosures of protected health information for treatment, payment, and health care operations as required by HITECH; and changing the requirement for certain providers to make a good-faith effort to obtain an acknowledgment of receipt of the Notice of Privacy Practices.

Source: HHS, December 12, 2018

Crisis Communication for Multilingual Communities

What happens when an emergency involves someone who doesn't speak English, or is deaf, visually impaired, or illiterate? Civil rights laws mandate that federally funded emergency response and recovery services are accessible to all Americans. But at least 350 languages are spoken in the U.S., according to the Census Bureau, and millions of people have hearing or vision problems, or can't read.

The recent, devastating fires, hurricanes, and earthquakes have underscored the need for clear communication during disasters. HHS has unveiled a "plain language checklist" to help first responders ensure important information is shared.

The checklist, developed through the HHS Language Access Steering Committee, complements a 2016 emergency preparedness checklist. It includes recommendations, action steps, and resources to help first responders provide on-the-ground language assistance. One key recommendation is to not only identify languages and dialects spoken in the community, but specific types of sign language. Action steps include accessing state and local demographic data, and identifying public spaces serving people who lack English proficiency, such as libraries that offer language-access resources.

The checklist also provides practical tips for working with interpreters, such as speaking directly in the first person to the individual (not the interpreter) and avoiding idioms, acronyms, and double negatives. Red flags include interpreters who need repeated clarifications or overuse English terms, and whose interpretations seem overly long or short compared with the interpreted statements.

HHS also recommends collaborating with Centers for Independent Living and other groups who work with people with disabilities; identifying local partners, such as hospitals, faith-based organizations, and legal services; and coordinating with TV, print, radio, and online media to share plain-language, culturally appropriate emergency information.

Sources: HHS, December 4, 2018; ASPR blog, November 29, 2018

Sleep Apnea Doubles Risk of Hypertension for African-Americans

Sleep apnea doubles the risk of hard-to-treat hypertension in African-Americans, according to the Jackson Heart Study. The study, said leader Dayna Johnson, PhD, identifies a risk factor that until now has gone underrecognized in African-Americans.

The results are even more consequential as African-Americans have a disproportionately high rate of uncontrolled hypertension. Approximately 75% of African-American adults are likely to develop high blood pressure by the age of 55, compared to 55% of white men and 40% of white women.

The researchers followed 664 participants, which is the largest investigation to date of the causes of cardiovascular disease in African-Americans. Sleep apnea tests revealed that more than 25% of participants had moderate or severe sleep apnea and that the condition had gone undiagnosed in most of them—94%.

The report underscores the need for studies to determine whether screening high-risk patients for sleep apnea would reduce the risk or severity of heart disease, says Michael Twery, PhD, director of the National Center on Sleep Disorders Research at the National Heart, Lung, and Blood Institute, which partly funded the study.

Source: NIH, December 10, 2018

CRP Can Help Guide Antibiotic Decisions

Using C-reactive protein- (CRP) based algorithms seems to reduce antibiotic treatment in neonates, and treatment initiation in adults, according to the first meta-analysis of the topic.

Researchers from the University of Western Ontario, McGill University, and Université de Montréal screened 15 studies. In five randomized, controlled trials in adult outpatients, the risk difference for starting antibiotics in the CRP group was –7%, with no difference in hospitalization rates. In neonates, CRP-based algorithms reduced treatment duration by roughly one day, with no difference in relapse rates.

CRP is an acute-phase reactant secreted in response to inflammation. The secretion is regulated by cytokines, with levels that begin to rise six hours after the initial stimulus and peak in 48 hours. After the bacterial trigger for inflammation is eliminated, CRP levels drop quickly; the half-life is approximately 19 hours.

In healthy adults, the median CRP concentration is 1.5 mg/L. Levels above 100 mg/L are associated with bacterial infection. In healthy-term neonates, normal CRP levels depend on age. Median levels gradually increase from 0.4 mg/L at birth to 2.7 mg/L at 48 hours, then decline to 1.4 mg/L at 96 hours. The researchers note that CRP values above 10 mg/L, the cut-off point most often used to diagnose neonatal sepsis, are not uncommon during the first 72 hours after birth, which may make CRP levels less useful for diagnosing early-onset sepsis or gauging the appropriateness of starting antibiotics in infants.

Based on their analysis, the researchers say the recommended CRP cutoff for stopping antibiotic treatment in newborns with neonatal sepsis is < 10 mg/L. In adult outpatients with respiratory tract infections, the recommended cutoffs are < 20 mg/L for antibiotic withholding and ≥ 100 mg/L for treatment initiation.

Importantly, the researchers conclude, the use of CRP algorithms to guide the duration of antibiotic treatment appears to be safe. Both adult and neonate studies showed no differences in mortality.

Source: BMJ Open, November 27, 2018

A Quick, Effective Screening Tool for Youth At Risk for Suicide

In 2016, more than 6,000 young people in the U.S. killed themselves, according to the Centers for Disease Control and Prevention (CDC). Most had visited a health care provider or medical setting in the month prior to their death, making health care settings ideal for suicide intervention efforts. Researchers from the National Institute of Mental Health (NIMH) offer advice on how hospitals can address the rising suicide rate in a way that "is flexible, and mindful of limited resources"—i.e., via an easily administered screening survey that provides an immediate, actionable response.

The NIMH report presents a three-tiered clinical pathway system, created by a subcommittee of the Pathways in Clinical Care workgroup of the Physically Ill Child Committee of the American Academy of Child and Adolescent Psychiatry.

The first step is an initial screen of all patients aged 10 to 24 years old (for those with mental health issues, below the age of 10), using the Ask Suicide-Screening Questions (ASQ) tool.

The first screening tool developed specifically for pediatric patients, ASQ is free and available in 14 languages. Four questions (e.g., "In the past few weeks, have you wished you were dead?") take about 20 seconds to administer. A "yes" to one or more identified 97% of youth at risk, in an NIMH study.

The second step is the most critical: a brief suicide-safety assessment, which takes 10 to 15 minutes to administer. This classifies a patient's risk of suicide based on survey responses and clinical judgment.

The third step, if deemed necessary, is a full comprehensive safety evaluation by a licensed mental health provider, with the goal of addressing safety issues and establishing an intervention plan.

One of the biggest barriers to screening, NIMH says, is how to effectively and efficiently manage the patients who screen positive. Therefore, NIMH recommends that each health care setting have a plan. The ASQ Toolkit is designed to help with such a plan and provide tools for managing care. The kit is organized according to medical setting: emergency department, inpatient medical/surgical unit, and outpatient primary care and specialty clinics. The kit includes information sheets, the Brief Suicide Safety Assessment Guide, nursing scripts, and information for parents and guardians.

The ASQ Toolkit is available at https://www.nimh.nih.gov/labs-at-nimh/asq-toolkit-materials/index.shtml.

Source: NIH, December 20, 2018 ■