metabolizers. Genetic differences in metabolizing capacity have been associated with poor response and adverse effects in some patients. However, evaluation of the clinical usefulness of CYP testing has been conducted mainly in industry-sponsored studies of patients with major depression.

Researchers led by Gesche Jürgens, M.D., Ph.D., associate professor in the Clinical Pharmacology Unit at Zealand University Hospital in Denmark, conducted a study to determine whether routine genetic testing for CYP2D6 and CYP2C19 affects the tolerability and effectiveness of antipsychotic treatment in patients with schizophrenia.

**Study methods**

The randomized prospective trial recruited adult patients from outpatient psychiatric clinics in Denmark who met ICD-10 criteria for a schizophrenia spectrum disorder. Participants were divided into three groups: antipsychotic treatment guided by CYP testing, antipsychotic treatment guided by structural clinical monitoring, and a control group receiving usual clinical care. Members of the intervention groups received at least a quarterly evaluation of medication-adverse effects and factors affecting compliance during the one-year study; these evaluations did not take place in the control group.

The primary outcome was antipsychotic treatment persistence, a measure of tolerability calculated as the time in days to the first modification of the initial antipsychotic drug and/or dose. Secondary outcomes included the number of drug changes, the change in global rating of hallucinations and delusion severity as measured by the Scale for the Assessment of Positive Symptoms, and the change in severity of adverse events as measured by the Udvalg af Kliniske Undersøgelser (UKU) Side Effects Rating Scale. The researchers assessed for potential confounding factors such as age, gender, duration of illness, and baseline symptom severity.

**Results**

A total of 311 participants were randomized to one of the three study groups. Participants’ median age was 41 years, with a median duration of illness of 6 years; paranoid schizophrenia was the most common diagnosis.

Neither treatment guided by CYP testing nor structured clinical monitoring showed a significant difference in antipsychotic treatment persistence compared with the control group. Odds ratios for at least one medication change were also similar in the two intervention groups compared with the control group.

**Implications**

“The most important finding is that in a clinical everyday setting there is no indication that the routine use of [a] CYP test contributes to a more effective or tolerable pharmacological treatment of patients with schizophrenia when compared to clinical monitoring.”

Gesche Jürgens, M.D., Ph.D.

There was no significant effect on hallucinations in either the CYP testing or structured clinical monitoring groups, and there were similar nonsignificant effects on delusions in the two groups, the researchers reported.

**Genotyping** (continued from page 1)

**RESEARCH ROUNDUP**

**Study suggests fluvoxamine may limit deterioration from COVID-19**

Clinical deterioration from COVID-19 occurs most often in the second week of the illness, with an excessive inflammatory response thought to contribute to lung damage from the virus. Because sigma-1 receptor (SIR) agonism is a potential mechanism for immune modulation, researchers conducted a study to examine the effect of the SIR agonist fluvoxamine on clinical outcomes for patients in the early stage of COVID-19. The randomized, double-blind, placebo-controlled trial involved adult outpatients with confirmed coronavirus infection. Among the exclusion criteria were COVID-19 illness that required hospitalization and severe underlying lung disease, such as chronic obstructive pulmonary disease. Participants were randomized to fluvoxamine or placebo at a dose of 100 mg three times a day for 15 days, after a starting dose of 50 mg after baseline assessment followed by 100 mg twice a day for 2 days. The primary outcome was clinical...
deterioration, defined as the presence of
or hospitalization for shortness of breath and a decrease in oxygen saturation on room air or the need to receive supplemental oxygen in order to maintain oxygen saturation of 92% or greater. A secondary outcome was the severity of the participant’s most severe baseline symptom during the 15-day treatment period. A total of 152 participants with a mean age of 46 years entered the study. Clinical deterioration occurred in zero of 80 participants in the fluvoxamine group and six of 72 participants in the placebo group. Clinical deterioration in the placebo group occurred between 1 and 7 days following randomization and between 3 and 12 days after onset of COVID-19 symptoms. Only one patient in each group required hospital or emergency department care in the 30 days following the 15-day trial. The prevalence of adverse events was comparable in the two participant groups, with pneumonia and gastrointestinal symptoms more common in the placebo group. Because this was a small study with a number of endpoints, the researchers stated that the results should be considered preliminary until larger trials with more definitive outcome measures are conducted. [Lenze E, et al. JAMA 2020; published online Nov 12; doi: 10.1001/jama.2020.22760]

Impaired driving performance among antidepressant users subsides over time

Older classes of antidepressant, such as tricyclic and tetracyclic drugs, can cause psychomotor and cognitive impairment, exacerbating the risk of motor vehicle accidents. Some studies have suggested that the level of impairment that can result from the use of tricyclics is comparable to that from a blood alcohol concentration of 0.5. A multi-center trial in the Netherlands compared driving performance among individuals using older-generation antidepressants for more than 6 months and a group of healthy controls. The researchers recruited 38 long-term users of antidepressants; 25 used mirtazapine and 13 used amitriptyline. These individuals were divided into groups using the antidepressant for more than 3 years and less than 3 years. Heavy alcohol use and smoking were among the exclusion criteria. Members of the control group were of comparable age, gender, and driving experience. Participants completed an on-road driving test, requiring maintenance of a consistent speed and lateral position, and neurocognitive tests measuring variables such as attention, processing speed, visual orientation, and reaction time. A practice session and a test session were conducted within one week of each other. There was no significant difference in standard deviation of lateral position between antidepressant users and healthy controls, but those using an antidepressant for less than 3 years showed clinically significant impairment. None of the groups showed a significant difference in results on the neurocognitive tests. The study’s authors wrote that the findings on driving performance “suggests mitigation of driving-related impairment over time, which corresponds with a decreasing accident risk found in epidemiological studies following long-term antidepressant treatment.” They added that the results support the idea that duration of treatment can be considered when evaluating the impact of long-term medication use on driving performance.

[van der Sluiszen N, et al. Hum Psychopharmacol Clin Exp 2020; published online Oct 1; doi: 10.1002/hup.2762]

Antiseizure drugs used in pregnancy show varying levels of risk

Research has shown an increased risk of adverse birth outcomes and neurodevelopmental disorders associated with maternal use of antiseizure medications during pregnancy, but most studies have not sufficiently adjusted for confounding factors. A new study used data from Swedish birth registers to examine the association between maternal use of antiseizure medications during pregnancy and childhood risk of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). The researchers examined records of children born to mothers with epilepsy from 1996–2011 and followed up on them through 2013. They examined mothers’ reports of any antiseizure medication use in the first trimester of pregnancy, and also looked at the most commonly reported individual drugs of carbamazepine, lamotrigine, and valproic acid. They accounted for potential confounding factors, such as maternal and paternal characteristics at the time of the child’s birth, parental psychiatric and behavioral problems detected before pregnancy, and socioeconomic factors. Children whose mothers reported use of any antiseizure medication had an elevated risk of ASD and ADHD, with ASD risk more pronounced. Differences were found when observing the risk associated with the individual medications. Risk of ASD and ADHD was most pronounced with valproic acid, whereas adjustment for covariates showed a completely attenuated risk with lamotrigine. There was an elevated risk of ASD with carbamazepine that was substantially attenuated by adjustment for confounders, and a weak association with ADHD. The study’s authors wrote that these findings highlight “the importance of research on individual drugs in that our results supported the hypothesis that certain [antiseizure medications] may be associated with greater risk to fetal development.” They added, however, that these results should be interpreted with caution because they could not rule out all possible sources of confounding. [Wiggs K, et al. Neurol 2020; published online Oct 28; doi: 10.1212/WNL.0000000000010993]

Some cancer patients at risk for nonmedical use of opioids

Nonmedical use of opioids can have a significant effect on cancer pain management, but there has been little information on how often this behavior occurs and what factors can predict it. A prognostic study was launched to address these questions. Cancer patients who were taking prescribed opioids and received an initial outpatient supportive care consultation between Feb. 12, 2016 and July 15, 2018 were eligible for inclusion; those who had no follow-up visits within 3 months of their initial consultation were excluded. The researchers reviewed documentation of the supportive care encounters for the presence of any of 14 factors that could suggest nonmedical use of opioids and used the Screener and Opioid Assessment for Patients with Pain (SOAPP) to assess risk for nonmedical use. A total of 1,554 patients were included in the analysis. Twenty-one percent of the patients had a SOAPP score that indicated elevated risk of nonmedical use of opioids, and 19% exhibited at least one nonmedical use behavior. The most common of these behaviors was an unscheduled clinic visit for inappropriate refills of medication. Factors associated with a higher risk of nonmedical use of opioids were being