Psychiatric Briefs

Treatment of the Interictal Psychoses

Blumer D, Wakhlu S, Montouris G, et al.

Background: The interictal "schizophrenia-like" psychoses of epilepsy conventionally are treated with antipsychotic medication with uncertain results. In patients with these psychoses, a preceding and concomitant dysphoric disorder usually can be documented. Effectiveness of the pharmacologic treatment by the combination of drugs that is effective for severe interictal dysphoric disorders is demonstrated in a series of patients with interictal psychosis. ***Method:*** Patients were treated with the combination of a tricyclic antidepressant and a selective serotonin reuptake inhibitor, enhanced if necessary by a small amount of the atypical neuroleptic risperidone. The series consisted of 8 consecutive patients with interictal psychosis seen over a 20-month period. Two additional patients seen over the past 10 years who required a different therapeutic intervention were also included. ***Results:*** Five of the 8 consecutive patients achieved full remission of their psychosis; 3 patients could not be reached for the full treatment effort. One patient with a malignant psychosis had been treated successfully (prior to the series reported) by surgical removal of a left frontal epileptogenic zone; a second patient (treated after the series) recovered only upon elimination of the antiepileptic drug that had suppressed clinical seizures but had resulted in an alternating psychosis. ***Conclusion:*** Interictal psychoses can be viewed as severe interictal dysphoric disorders with psychotic features. The same combination of psychotropic medication that is effective for severe interictal dysphoric disorders serves as the primary therapy for interictal psychoses. The interictal psychiatric disorders presumably result from seizure-suppressing mechanisms that are the targets of the proconvulsant drugs. Upon suppression of seizures, some patients with interictal psychosis may require modification of the antiepileptic medication responsible for excessive inhibition. Complete surgical removal of the epileptogenic zone can eliminate a chronic interictal psychosis upon postoperative fading of inhibitory mechanisms.

(J Clin Psychiatry 2000;61:110–122)

Sertraline-Induced Anorgasmia Reversed by Nefazodone

Michael A, Tubbe PA, Praseedom A

One commonly encountered side effect of antidepressant medications is delayed or absent ejaculation and/or orgasm. Efforts to reverse this effect with cyproheptadine, amantadine, methylphenidate, yohimbine, lowering antidepressant doses, and drug holidays have had limited effectiveness. The authors report a case of sertraline-induced anorgasmia reversed with nefazodone augmentation. Mr. A, a 60-year-old married man, had been referred with a moderate depressive episode lasting 3 months. Sexually active prior to the onset of depression, he experienced a moderate decrease in libido and a mild decrease in the frequency of sexual intercourse. Although his depression improved with sertraline, 10 mg/day for 4 weeks, his libido continued to be low and he experienced an inability to achieve ejaculation and orgasm. When nefazodone, 100 mg h.s., was added, Mr. A returned immediately to his former ejaculatory function, and he and his wife had a higher frequency of sexual intercourse during the next 2 weeks. At the end of that 2-week period, Mr. A attempted sexual intercourse without nefazodone but was unable to achieve orgasm. Thereafter Mr. A used adjunctive nefazodone 1 hour before sexual intercourse on an "as needed" basis. Controlled trials are necessary before nefazodone can be recommended routinely for the treatment of antidepressant-induced anorgasmia.

(Br J Psychiatry 1999;175:491)

Sildenafil for Sexual Dysfunction in Women Taking Antidepressants

Nurnberg HG, Lauriello J, Hensley PL, et al.

Of the side effects associated with antidepressants, particularly selective serotonin reuptake inhibitors, sexual dysfunction is among the most common and troubling. Sexual dysfunction often leads to switching, discontinuation, or reduced dose levels of the antidepressant. The authors report an open-label study of 10 female patients treated with sildenafil after developing symptoms of sexual dysfunction as a consequence of antidepressant treatment. Eligible subjects were female patients aged 18 to 60 years who were in stable relationships, who had normal premorbid sexual functioning, and who had experienced sexual dysfunction, particularly anorgasmia—whether accompanied by additional sexual disturbances—during successful treatment with an antidepressant medication. The subjects must have been taking the antidepressant for at least 6 weeks, receiving a stable antidepressant dose, improving with regard to the presenting condition (most often depression, anxiety, or both), and experiencing sexual dysfunction continuously for longer than 4 weeks. Patients with comorbid unexplained medical illness, poor overall physical health, a history of sexual dysfunction not induced by antidepressant therapy, a psychiatric illness not under control, former or current alcohol or substance abuse and dependence, diabetes mellitus, neurologic disorders, or genital anatomical defects were excluded. Subjects were also explicitly excluded if they had a history of stroke, myocardial infarction, or use or likely use of any nitrate. Patients received three 50-mg tablets of sildenafil each, with instructions to take 1 tablet no more than 2 hours and no less than 1 hour before coitus was anticipated. If ineffective, the patient was to take sildenafil, 100 mg, no more than 2 hours and no less than 1 hour before the next sexual interaction. Nine of 10 subjects reported a complete or very substantial improvement of sexual functioning, including arousal, lubrication, and orgasmic function. Significant side

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effects were limited to mild, transient headache or dizziness. The reports of male sexual dysfunction reversed with sildenafil are augmented by our findings.

(Am J Psychiatry 1999;156:1664)

Addiction, Part II: Identification and Management of the Drug-Seeking Patient

Longo LP, Parran T Jr, Johnson B, et al.

A dilemma exists in the treatment of pain and anxiety: the fear that patients will abuse controlled substances—especially opioid analgesics, sedative-hypnotics, and stimulants—leads physicians to underprescribe these medications. Conversely, physicians are susceptible to being duped by individuals seeking these drugs for recreational use. Furthermore, treatment of patients with acute or chronic pain, anxiety disorders, or attention-deficit disorder is complicated by the fact that these patients are at risk for comorbid addiction. Thus, the authors recommend that physicians acquire the knowledge and experience to be able to discern when treatment with these medications is and is not appropriate. The authors describe 4 characteristics of drug-seeking individuals: escalating drug use, drug-seeking behavior, doctor-shopping, and scamming. They also identify 4 characteristics of overprescribing physicians—dated, duped, dishonest, and disabled—and warn of the fine line that exists for physicians between appropriate empathy with the patient and destructive codependency. Specific recommendations are offered for wise prescription of controlled substances. For example, physicians should ask patients about their history of substance use, including alcohol, illicit drugs, and prescription drugs. In addition, physicians should steadfastly say "no" to patients who exert pressure on them to obtain a prescription. Finally, physicians can improve clinical care and outcomes with these medications by maintaining a current knowledge base, documenting the decisions that constitute the treatment process, and consulting peers, supervisors, and others with specialized expertise.

(Am Fam Physician 2000;61:2401–2408)

Premenstrual Exacerbation and Suicidal Behavior in Patients With Panic Disorder

Basoglu C, Çetin M, Basar Semiz Ü, et al.

Background: In clinical observations, a relationship has been found between suicidal behavior and the menstrual cycle in patients with panic disorder. ***Method:*** The authors examined the connection between premenstrual exacerbation of panic disorder and suicidality in 70 female patients with DSM-III-R panic disorder. Panic symptoms were assessed in 28 patients who reported premenstrual exacerbation in the severity and frequency of panic attacks and 42 without such exacerbation using a 5-point self-rating measure based on DSM-IV criteria and the Clinical Global Impressions scale (CGI). Suicidality was measured by the Schedule for Affective Disorders and Schizophrenia (SADS). ***Results:*** Patients with premenstrual exacerbation had panic of significantly greater severity as measured by self-report ($p < .05$) and the CGI ($p < .001$). The mean suicidality score on the SADS was significantly higher for patients with than without premenstrual exacerbation ($p < .05$), and patients with premenstrual exacerbation were more likely to be rated as suicidal by this measure ($p < .05$). ***Conclusion:*** For patients with panic disorder, premenstrual exacerbation of panic symptoms may be a risk factor for suicidal behavior independent of major depression.

(Compr Psychiatry 2000;41:103–106)

The Role of Gender in Mixed Mania

Arnold LM, McElroy SL, Keck PE Jr

Reports have conflicted as to whether mixed mania is more common in women than in men. In this review of studies on mixed mania, the authors explored (1) whether mixed mania is more prevalent in women than in men and (2) whether differences exist for men and women with mixed mania in factors that separate mixed from classic mania: biological abnormalities, suicidality, illness outcome, and treatment response. The authors found that gender differences are found for mixed mania in direct proportion to the strictness of the criteria used to define mixed mania; that is, when a greater number of depressive symptoms are required, mixed mania is found more commonly in women. The authors found, however, no between-sex differences for the variables that distinguish mixed mania from classic mania.

(Compr Psychiatry 2000;41:83–87)

Gender and Bipolar Illness

Hendrick V, Altshuler LL, Gitlin MJ, et al.

Background: For major depression and schizophrenia, gender differences have been reported in symptom expression and course of illness. Gender differences in bipolar disorder are becoming increasingly apparent, but have been less studied. Research data on these differences will help determine whether gender is important in influencing illness variables such as course, symptom expression, and likelihood of comorbidity. ***Method:*** Charts of 131 patients (63 women and 68 men) with a DSM-IV diagnosis of bipolar disorder admitted to the University of California Los Angeles Mood Disorders Program over a 3-year period were reviewed to gather data on demographic variables and course of illness and to assess differences in the illness across genders. ***Results:*** No significant gender differences were found in the rate of bipolar I or bipolar II diagnoses, although women were overrepresented in the latter category. Also, no significant gender differences emerged in age at onset, number of depressive or manic episodes, and number of hospitalizations for depression. Women, however, had been hospitalized significantly more often than men for mania. Further, whereas bipolar men were significantly more likely than bipolar women to have a comorbid substance use disorder, women with bipolar disorder had 4 times the rate of alcohol use disorders and 7 times the rate of other substance use disorders than reported in women from community-derived samples. ***Conclusion:*** For bipolar disorder, course of illness variables such as age at onset

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and number of affective episodes of each polarity do not seem to differ across genders. Women, however, may be more likely than men to be hospitalized for manic episodes. While both men and women with the illness have high rates of comorbidity with alcohol and other substance use disorders, women with bipolar disorder are at a particularly high risk for comorbidity with these conditions.

(J Clin Psychiatry 2000;61:393–396)

Serum Valproate Levels in 6 Breastfeeding Mother-Infant Pairs

Piontek CM, Baab S, Peindl KS, et al.

Background: Women with bipolar disorder are at high risk for recurrence of an affective episode in the postpartum period, and treatment with a mood stabilizer may be indicated. Few data are available to inform the risk-benefit decision regarding the use of valproate for women with bipolar disorder who elect to breastfeed. ***Method:*** Serum valproate levels were obtained from 6 breastfeeding mother-infant pairs. All mothers had a diagnosis of bipolar disorder (Research Diagnostic Criteria) and were taking divalproex sodium as prophylaxis for or treatment of a recurrent affective episode. None of the mothers received valproate during pregnancy. ***Results:*** The mothers had serum valproate levels near or within the therapeutic range (39.4 to 79.0 μg/mL). Infant serum levels were low, ranging from 0.7 to 1.5 μg/mL (0.9%–2.3% of maternal serum levels). No adverse clinical effects were observed in the infants. ***Conclusion:*** Serum valproate levels were low in nurslings of mothers treated with valproate. These data can be used to inform clinical decisions regarding the use of valproate during breastfeeding.

(J Clin Psychiatry 2000;61:170–172)

Trends in the Prescribing of Psychotropic Medications to Preschoolers

Zito JM, Safer DJ, dosReis S, et al.

The use of psychotropic medications to treat emotional and behavioral disorders in preschool-aged children has increased sharply in recent years, prompting concern about the safety and effectiveness of such treatments in this age group. The authors systematically identified patterns of use of psychotropic medications in preschoolers, pooling prescription records for the years 1991, 1993, and 1995 from 2 state Medicaid programs and 1 health maintenance organization (HMO) serving over 200,000 2- to 4-year-old children. Specifically, the authors calculated the prevalence of the use of 3 classes of medications (stimulants, antidepressants, and neuroleptics) and of the individual medications methylphenidate and clonidine. In 1995, the prevalence per 1000 enrollees in the 2 Medicaid programs was highest for stimulants (12.3 and 8.9), followed by antidepressants (3.2 and 1.6), clonidine (2.3 and 1.4), and neuroleptics (0.9 and 0.5). For enrollees in the HMO, the prevalence of clonidine use in 1995 was approximately 3 times greater than that for antidepressant use. Although the use of stimulants, antidepressants, and clonidine increased markedly from 1991 to 1995, only a slight increase occurred in the use of neuroleptic medications. The use of methylphenidate increased in all 3 groups between 1991 and 1995: 3-fold and 1.7-fold for the 2 Medicaid groups, 3.1-fold for the HMO enrollees. Although the authors found a decrease in the proportions of older stimulants and antidepressants used in this age group, the use of newer, less-established agents increased. Given the rise in the prescription of psychotropic medications in preschoolers noted in this study and the widespread use of these medications for off-label indications, the authors recommend systematic, prospective study of this phenomenon.

(JAMA 2000;283:1025–1030)

Trimethoprim-Sulfamethoxazole-Induced Hypoglycemia as a Cause of Altered Mental Status in an Elderly Patient

Mathews WA, Manint JE, Kleiss J

Even though drug-induced hypoglycemia is a rare event in the general population, it occurs more frequently in the elderly and in diabetic patients and thus should be considered in the differential diagnosis of altered mental status in these patient groups. In this case study, the authors describe a 91-year-old woman who was taken to the emergency department because of decreased consciousness while on a drug regimen that included once-daily triamterene-hydrochlorothiazide and twice-daily, double-strength trimethoprim-sulfamethoxazole (TMP-SMX). On arrival at the hospital, the patient had a plasma glucose value of 34 mg/dL along with an elevated creatine kinase level and a small tongue laceration. She was treated with a 50-mL ampule of 50% dextrose solution intravenously. She regained consciousness within 5 minutes after treatment and had a glucose level of 210 mg/dL 10 minutes later. The patient's rapid response to dextrose administration indicated hypoglycemia, which was the result of an overdosage of TMP-SMX combined with the effects of her thiazide diuretic. The authors caution physicians to keep in mind the decreased renal function of elderly patients when adjusting medication doses and to watch for potential side effects when combining medications in this patient group.

(J Am Board Fam Pract 2000;13:211–212)

An Approach to Drug Abuse, Intoxication and Withdrawal

Giannini AJ

Although physicians often misdiagnose symptoms of drug abuse, the author posits that the likelihood of accurate diagnosis can be increased when physicians recognize the unique clusters of symptoms produced by different classes of drugs based on how they affect different neurotransmitter systems. Drugs of abuse—including anticholinergics, dissociatives, opiates, psychedelics, sedative-hypnotics, and stimulants—can influence the action of 6 neurotransmitters (acetylcholine, β-endorphin, dopamine, γ-aminobutyric acid [GABA], norepinephrine, and serotonin), which act on their respective receptor sites to produce certain

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clinical effects. In addition to linking drugs from the 6 classes with the neurotransmitter systems they affect, the author identifies antidotes that can be administered to counter the effects of these drugs of abuse. The author cautions, however, that this ability of physicians to determine the class of drugs abused and counter the drug-induced effects must be supplemented by a willingness on the part of the abuser to undergo long-term treatment for addiction to these agents.

(Am Fam Physician 2000;61:2763–2774)

Critical Overview: Adverse Cutaneous Reactions to Psychotropic Medications

Kimyai-Asadi A, Harris JC, Nousari HC

Background: Adverse cutaneous reactions (ACRs) are common, potentially life-threatening or symptomatically and cosmetically unappealing side effects of psychotropic drugs. ***Data Sources:*** A MEDLINE search of the literature was employed to cite the association of various psychotropic drugs with specific cutaneous reactions. ***Data Synthesis:*** In addition to the common exanthematous eruption, the authors explored several serious reactions including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria, angioedema, anaphylaxis, hypersensitivity syndrome, hypersensitivity vasculitis, erythroderma, and drug-induced lupus erythematosus. Other side effects such as alopecia, pigmentary disorders, photosensitivity, lichenoid lesions, fixed drug eruptions, and psoriasiform, acneiform, and seborrheic eruptions are discussed. Attention is paid to the morphology and distribution, systemic findings, diagnosis, and treatment of these conditions. ***Conclusion:*** Awareness of ACRs will allow psychiatrists to deter their continuation or recurrence, educate patients who have them, and diagnose serious instances of them.

(J Clin Psychiatry 1999;60:714–725)

Underuse of Antidepressants in Major Depression: Prevalence and Correlates in a National Sample of Young Adults

Druss BG, Hoff RA, Rosenheck RA

Background: Epidemiologic studies have reported disturbingly low rates of treatment for major depression in the United States. To better understand this phenomenon, we studied the prevalence and predictors of antidepressant treatment in a national sample of individuals with major depression. ***Method:*** Between 1988 and 1994, 7589 individuals, aged 17–39 years and drawn from a national probability sample, were administered the Diagnostic Interview Schedule as part of the National Health and Nutrition Examination Survey. Interviewers asked about prescription drug use and checked medication bottles to record the name and type of medications. ***Results:*** A total of 312 individuals, or 4.1% of the sample, met DSM-III criteria for current major depression. Only 7.4% of those with current major depression were being treated with an antidepressant. Among individuals with current major depression, being insured and having a primary care provider each predicted a 4-fold increase in odds of antidepressant treatment; telling the primary provider about depressive symptoms predicted a 10-fold increase in treatment. ***Conclusion:*** The study's findings support the notion that a serious gap exists between the established efficacy of antidepressant medications and rates of treatment for major depression in the "real world." Underreporting of depressive symptoms to providers and problems with access to general medical care appear to be 2 major contributors to this problem.

(J Clin Psychiatry 2000;61:234–237)

Potential Treatment for Subthreshold and Mild Depression: A Comparison of St. John's Wort Extracts and Fluoxetine

Volz H-P, Laux P

Modern prescription antidepressant medications are the standard of care for severe depressive disorders. However, effective over-the-counter medications such as St. John's wort potentially constitute a readily available treatment for subthreshold depressive symptoms and mild depressive episodes that precede a clear diagnosis of depression. This study identified controlled studies employing St. John's wort or fluoxetine for the treatment of mild (Hamilton Rating Scale for Depression [HAM-D] score < 20) and moderate (HAM-D score from 20 to 24) depression and compared the efficacy of the 2 treatments as determined by decrease from baseline in HAM-D scores. No meaningful difference in antidepressant efficacy was found between the treatments: the mean reduction in HAM-D scores was 10.2 points (51.4% reduction from baseline) for St. John's wort and 12.5 points (55.5% reduction) for fluoxetine. Several limitations qualify the findings of this study: lack of a meta-analysis to more clearly identify efficacy in studies with widely varying numbers of patients, greater methodological sophistication in the fluoxetine versus the St. John's wort studies, and the use of different St. John's wort extracts in the different studies. Still, this study provides preliminary evidence that nonprescription medications such as St. John's wort can have efficacy equal to that of prescription antidepressants in the treatment of mild-to-moderate depressive symptoms.

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