The Anxiety-Psychosis Spectrum

Pattern of Comorbidity Among Anxious and Odd Personality Disorders: The Case of Obsessive-Compulsive Personality Disorder
A. Rossi, M. Grazia Marinangeli, G. Butti, A. Kalyvoka, and C. Petruzzi

Social Anxiety and Premorbid Personality Disorders in Paranoid Schizophrenic Patients Treated With Clozapine
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Anxiety as a Primary Symptom in Cycloid Psychosis
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CNS Spectrums
The International Journal of Neuropsychiatric Medicine

CNS Spectrums is indexed by EMBASE/Excerpta Medica, DIALOG, SilverPlatter, OVID, and Lexis-Nexis, and is the official journal of the International Neuropsychiatric Association.
In mild to moderate Alzheimer's disease

You see it as maintaining cognitive

* Individual responses to ARICEPT® may include improvement, stabilization, or decline.

† The most common adverse events in pivotal clinical trials with ARICEPT® were nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue, and anorexia. Pivotal clinical trials of ARICEPT® have shown no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding. Nevertheless, cholinesterase inhibitors may be expected to increase gastric acid secretion. Therefore, patients (especially those at increased risk for developing ulcers—eg, having a history of ulcer disease, receiving concurrent nonsteroidal anti-inflammatory drugs) should be monitored closely for gastrointestinal bleeding. In pivotal clinical trials, syncopal episodes have been reported in association with ARICEPT® (2% vs 1% for placebo).
She sees it as a bedtime story.

ARICEPT®. Helping to make a difference for people living with Alzheimer's

- Slows the worsening of symptoms*
- Proven to maintain cognition in placebo-controlled studies
- Well tolerated†
- Proven safety profile
- Once-daily dosing
- 3 years of real-world use

ONCE-A-DAY
ARICEPT®
(donepezil HCl)
5 MG AND 10 MG TABLETS

THERAPY TO REMEMBER™

Please see brief summary of prescribing information on adjacent page.
ARICEPT® (Donepezil Hydrochloride Tablets)

Summary - see package insert for full prescribing information. INDICATIONS AND USAGE ARICEPT® is indicated for the treatment of mild to moderate dementia of the Alzheimer's type. CONTRAINDICATIONS ARICEPT® is contraindicated in patients with a history of seizures, as it may be an epileptogenic agent. WARNINGS Anesthesia: ARICEPT® may cause a cholinesterase inhibitor, is likely to exaggerate suxamethonium-type muscle relaxation during anesthesia. Constipation/Depression: Constipation and depression have been reported in association with the use of ARICEPT®. Nausea: Nausea is a common gastrointestinal adverse reaction, cholinesterase inhibitors may have vagotonic effects on heart rate (e.g., tachycardia). The potential for this action may be particularly important to patients with "bradycardia syndrome" or other supranuclear cardiovascular conduction conditions. Syncope episodes have been reported in association with the use of ARICEPT®. Because of the potential for cholinergic action, cholinesterase inhibitors may be expected to increase gastric acid secretion due to increased cholinergic activity. Therefore, patients should be monitored closely for symptoms of acid or active gastrointestinal bleeding, especially those at increased risk for developing ulcers, e.g., those with a history of ulcers or those who receive concurrent nonsteroidal anti-inflammatory drugs (NSAIDs). Clinical studies of ARICEPT® have shown no increase, relative to placebo, in the incidence of either peptic ulcer or gastrointestinal bleeding. ARICEPT®, as a potential consequence of its pharmacological properties, has been shown to produce diarrhea, nausea, and vomiting. These effects, when they occur, appear more frequently with the 10 mg/day dose than with the 5 mg/day dose. In most cases, these effects have been mild and transient, and patients have continued to receive the ARICEPT® treatment.
Why expose your patients to the “ups and downs” of traditional carbamazepine therapy?

Peak-to-trough fluctuations in patients receiving immediate-release carbamazepine three times daily can be as great as 2.5 fold."
Switch to Carbatrol®—Second-generation delivery system design that targets the limitations of conventional carbamazepine

- Bioequivalent to immediate-release carbamazepine dosed rigidly Q6h
- Peak-to-trough fluctuations are not compromised
- Smooth, consistent plasma concentrations
- Extensive drug dispersion, dissolution, and absorption
- Predictable bioavailability
- BID dosing
- No generic equivalent

Absence seizures (petit mal) do not appear to be controlled by carbamazepine. The most frequently reported adverse events (particularly during the initial phases of therapy) are dizziness, drowsiness, unsteadiness, nausea, and vomiting. Adverse events can be minimized by initiating therapy at the lowest possible effective dose.


Please see brief summary of prescribing information on adjacent pages. Carbatrol is a registered trademark of Shire Richwood Inc.
Drug Interactions

Carbatrol® interacts with the following drugs:

1. Antidepressants: Increase the level of clomipramine HCl; phenytoin, and primidone.


3. Anticoagulants: Drug interactions have been reported when carbamazepine is used with warfarin, heparin, or other anticoagulants.

4. Antiparkinsonian drugs: May increase the risk of severe extrapyramidal reactions in patients taking antiparkinsonian drugs and carbamazepine.

5. Barbiturates: May increase the risk of extrapyramidal reactions in patients taking antiparkinsonian drugs and carbamazepine.

6. CYP 3A4 inducers: Increase the risk of carbamazepine toxicity.

7. CYP 3A4 inhibitors: Decrease the risk of carbamazepine toxicity.

8. Contraceptives: May increase the risk of carbamazepine toxicity.

9. Other anticonvulsants: May increase the risk of extrapyramidal reactions in patients taking antiparkinsonian drugs and carbamazepine.

10. Other antipsychotics: May increase the risk of extrapyramidal reactions in patients taking antiparkinsonian drugs and carbamazepine.

11. Other antihistamines: May increase the risk of extrapyramidal reactions in patients taking antiparkinsonian drugs and carbamazepine.

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OBSESSIVE-COMPULSIVE PERSONALITY DISORDER: PART OF A SPECTRUM OR A DISTINCT NOSOLOGIC ENTITY?

page 23

“The organization of the eleven personality disorders into three broad clusters based on common underlying themes has been criticized by some authors as being atheoretical. However, several studies using factor analysis in an attempt to validate the three-cluster model obtained results substantially supporting such a model. It is interesting to note that when incongruences emerged from these studies, they concerned cluster C PDs, particularly OCPD. In fact, in their factor analytic studies, Kass and colleagues and later Hyler and Lyons demonstrated that OCPD defined a fourth factor and argued that it should stand on its own. In 1994, Mulder and colleagues found that the Tridimensional Personality Questionnaire dimensions associated with obsessive-compulsive symptoms support these findings, suggesting that obsessive-compulsive personality symptoms might be linked with cluster A PDs or form a separate cluster.”

ANXIETY: REENTERING THE SPOTLIGHT
page 29

“Approximately 43% to 45% of patients with schizophrenia also have an anxiety disorder; the disorders with the highest comorbidity rates are panic disorder (32.1%), obsessive-compulsive disorder (OCD) (17.0%), and social phobia (11.3%). Long-term treatment with high doses of traditional neuroleptics seems to be closely related to the manifestation of anxiety disorder, especially panic disorder, in patients with schizophrenia. Anxiety symptoms in patients with schizophrenia are sometimes difficult to recognize and may be confused with akathisia. Recently, evidence has been collected about anxiety disorders appearing during clozapine treatment. In fact, treatment with clozapine has been associated with the development (denovo) of obsessive-compulsive (OC) symptoms in up to 10% of adults and adolescents with schizophrenia; however, these symptoms seem responsive to an adjunctive selective serotonin reuptake inhibitor (SSRI) regimen.”

NEUROPHYSIOLOGIC-PSYCHOPATHOLOGIC LINKS IN CYCLOID PSYCHOSIS
page 47

“An important progress was made in the knowledge about P300 alterations in psychosis when a group of the Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised, schizophrenics was subdivided into cycloid psychoses (according to Leonhard's original descriptions and the criteria of Perris and Brockington) and the remaining core schizophrenics (chronic and subchronic course). Reduced amplitudes and right-lateralized P300 peaks were found in those with core schizophrenia, while patients with cycloid psychosis had increased amplitudes and normal (left-lateralized) P300 fields. Abnormal P300 asymmetry was confirmed in core schizophrenia in a replication study with an independent sample, as well as in significantly higher than normal amplitudes seen in another new, independent group of cycloid psychosis patients. While reduced P300 amplitudes are very common in psychiatric and neurologic patients, increased amplitudes had not been described before. The finding, therefore, is specific for this particular patient group and specularly inverse to the results seen in patients with schizophrenia, in whom cycloid psychosis is often perceived to be in affinity.”

THE EMERGENCE OF A UNIQUE SUBTYPE OF POSTTRAUMATIC STRESS DISORDER
page 52

“When present, psychotic symptoms are associated with an increased severity of a number of other symptoms. Among veterans with PTSD-P, significantly higher levels of general psychopathology, paranoia, violent thoughts, feelings, and behaviors have been reported, as well as greater degrees of depression, anxiety, and anhedonia. Individuals with PTSD-P have levels of general psychopathology similar to those of patients suffering from chronic schizophrenia. This high level of impairment in PTSD-P vs PTSD without psychotic features is similar to the greater levels of social impairment reported in depressed patients with psychotic features vs those without psychotic features. It is interesting that the severity of PTSD symptoms, as measured by the Clinician-Administered PTSD Scale (CAPS), does not appear to be greater in patients with psychotic features. This suggests that PTSD-P may reflect a distinct subgroup of patients, rather than simply very severe PTSD. Likewise, the presence of psychotic symptoms in depression is not associated with more severe levels of depression.”

UNRAVELING HEMISPHERIC FUNCTIONING IN PSYCHIATRIC DISORDERS
page 58

“The lateralization patterns of neuromodulator projection systems have been examined by Tucker and Williamson, who reviewed evidence that the noradrenergic projection system is under greater control of the right hemisphere, while the dopaminergic system seems under greater control of the left hemisphere. As a consequence, the right hemisphere is involved in phasic arousal (simultaneous orienting to multiple parallel sensory channels), while the left hemisphere is involved in tonic arousal (focal attention—extended representation of few elements in the working memory). Increased left hemisphere activation may result in anxiety or hostility states with a redundancy bias that may produce cognitive and behavioral stereotypes, while increased right hemisphere activation may result in states of elated mood with a bias toward an expanded attention and memory access. The concept of increased/decreased activation is generally a relative one; in laterality studies, increased left activation implies decreased right activation, which means that either primary left hyperactivation or right hypoactivation may result in anxiety states.”
AMPHETAMINES HAVE A HIGH POTENTIAL FOR ABUSE. ADMINISTRATION OF AMPHETAMINES FOR PROLONGED PERIODS OF TIME MAY LEAD TO DRUG DEPENDENCE (TOLERANCE AND PHYSICAL DEPENDENCE) AND HABIT FORMATION. CONSEQUENCES OF THERAPEUTIC USE OF AMPHETAMINES DEFINITELY PREVENTED AND IMPLIES PATIENTS WITH SERIOUS DEPENDENT DISORDERS MUST BE ADEQUATELY TREATED WITH ANTI-DEPRESSANT AGENTS (SODIUM BICARBONATE, ETC.) INCREASE ABSORPTION OF AMPHETAMINES. URINARY EXCRETION OF AMPHETAMINES IS INCREASED, AND EFFICACY IS REDUCED, BY ACIDIFYING THE URINE. AMPHETAMINES SHOULD BE USED WITH CAUTION IN PATIENTS WITH ACUTE OBSTRUCTION TO URINARY OUTLET.

REFERENCES:

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5 mg, 10 mg, 20 mg & 30 mg TABLETS
Methylphenidate Sulfate
Methylphenidate Sulfate
Dextroamphetamine Salicylate
Dextroamphetamine Asparagine

BRIEF SUMMARY

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Methylphenidate Sulfate
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If methylphenidate (MPH) seems to be “working fine”...

Why make the switch to ADDERALL®?

- On average, ADDERALL is more effective than Ritalin® ($p<0.001$)\(^1\)
- ADDERALL was favored 3 to 1 over Ritalin by clinical staff for continued medication\(^1\)
- Ritalin patients were rated more deviant than ADDERALL, particularly on lower doses\(^1\)
- ADDERALL scored better than MPH on Clinical Global Impression (CGI) improvement ($p<0.05$)\(^2\)
- There were significantly more responders in the ADDERALL group than the MPH group ($p<0.01$)\(^3\)
- ADDERALL showed better scores than MPH for both inattention and hyperactivity ($p<0.05$)\(^2\)
- Clinical staff clearly preferred ADDERALL over MPH for continuation of treatment\(^6\)
- ADDERALL is dispensed for more ADHD patients than Ritalin\(^4\)
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ADDERALL is generally well tolerated—adverse reactions have seldom been reported (most frequently reported adverse reactions include anorexia, insomnia, stomach pain, headache, irritability, and weight loss).

As with most psychostimulants indicated for ADHD, the possibility of growth suppression and the potential for precipitating motor tics and Tourette’s syndrome exist with ADDERALL treatment and, in rare cases, exacerbations of psychosis have been reported. Since amphetamines may have a high potential for abuse, ADDERALL should only be prescribed as part of an overall multimodal treatment program for ADHD with close physician supervision.

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In two 6- to 8-week placebo-controlled clinical trials, spontaneously reported, treatment-emergent adverse events with an incidence of 5% or greater in at least one of the RISPERDAL groups and at least twice that of placebo were: anxiety, somnolence, extrapyramidal symptoms, dizziness, constipation, nausea, dyspepsia, rhinitis, rash, and tachycardia.

EPS with RISPERDAL, while dose-dependent, are comparable to placebo at doses ≤6 mg/day and differ significantly from placebo at doses >6 mg/day. Prescribing should be consistent with the need to minimize the risk of tardive dyskinesia; if its signs and symptoms appear, discontinuation of RISPERDAL should be considered.

Orthostatic hypotension was reported infrequently (<1%) in clinical trials; its risk may be minimized by following the recommended RISPERDAL dose titration regimen.

Reference:
1. IMS America, 12/99.

Please see brief summary of Prescribing Information on adjacent page.

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**INDICATIONS AND USAGE**

Risperidone is used for the treatment of schizophrenia, schizoaffective disorders, and bipolar I disorder. It is also effective in the acute treatment of mania associated with bipolar I disorder.

**CONTRAINdications**

Risperidone is contraindicated in patients with a known hypersensitivity to the product.

**WARNINGS**

Neuroleptic Malignant Syndrome (NMS)

A potentially fatal syndrome characterized primarily by hyperpyrexia, autonomic instability, and metabolic derangements. The syndrome occurs with varying degrees of frequency in patients taking antipsychotic drugs.

**cally evaluated. Given the primary CNS effects of risperidone, caution should occur in patients with severe renal impairment and in patients with severe close supervision of high risk patients should accompany drug therapy.

**Increased plasma concentrations of risperidone and 9-hydroxyrisperidone during chronic administration. Neither clinical studies nor epidemiologic may also occur in humans, and may mask signs and symptoms of over-**

**POTENTIAL FOR CARDIOVASCULAR EFFECTS**

Risperidone and 9-hydroxyrisperidone may increase the risk of QT prolongation in QT intervals of 480 to 500 milliseconds.

**Potential for Psychiatric Effects**

Risperidone and 9-hydroxyrisperidone may increase the risk of ventricular arrhythmias, including torsades de pointes.

**Body Temperature Regulation:**

**Seizures:**

**Laboratory Changes:**

**Vital Sign Changes:**

**Weight Changes:**

**Infections:**

**Additional Information:**

Risperidone has been shown to be effective in the acute treatment of aggression in patients with histories of violence.

**Drug Interactions:**

Risperidone is metabolized by cytochrome P450 to 9-hydroxyrisperidone, an active metabolite. The metabolism of both the parent compound and its active metabolite is known to be genetically variable, with a polymorphic relationship to the enzyme cytochrome P450.

**Overdosage:**

**Pharmacology:**

Risperidone is a neuroleptic, an antipsychotic, and an antiemetic.

**REFERENCES**

Clinical studies of Risperidone did not include adequate and well-controlled studies in pregnant women. However, there is no evidence of a teratogenic effect of Risperidone at doses equivalent to human doses. Risperidone has been shown to be effective in the acute treatment of aggression in patients with histories of violence.

**ADVERSE REACTIONS**

**INFORMATION FOR PATIENTS**

Risperidone recipients should be advised to contact their health care provider if they develop a potential adverse event or experience changes in specific adverse events.

**ADDITIONAL INFORMATION**

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