DRUG INFORMATION CENTRE

St Mary's Hospital
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or 822331 ext.3771 [or bleep 468]

Dear Dr. Bailey,

Thought you might like a copy of the reference that I cited to you on the phone.

Best wishes,

Code A

2/2/96

With Compliments

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retardation receiving clonazepam (up to 10.5 mg/day) developed improvement in her aggressive behavior when trazodone 100 mg plus tryptophan 500 mg were given 3 times a week.[3] However, within 2 weeks she stopped eating, developed symptoms of psychosis or hypomania, and became drowsy and withdrawn. Although the reaction may have been caused by the combination of trazodone and tryptophan, you cannot rule out the possibility that clonazepam contributed to the problem (clonazepam concentrations were elevated during the reaction).

MANAGEMENT: Although trazodone plus tryptophan can be used with good results in patients with aggressive behavior, be alert for adverse effects when the combination is used.

References

1. Simpson DM et al. Improvement in organically disturbed behavior with trazodone treatment. J Clin Psychiatry. 1986;47:191.
2. Pinner E et al. Effects of trazodone on aggressive behavior in seven patients with organic mental disorders. Am J Psychiatry. 1988;145:1295.
3. Patterson BD et al. Severe anorexia and possible psychosis or hypomania after trazodone-tryptophan treatment of aggression. Lancet. 1989;1:1017. Letter.

FLUOXETINE (PROZAC) INTERACTIONS

Antidepressants

See page 480. Antidepressant Interactions: Fluoxetine (Prozac).

Lithium (Eskalith, Lithane, Lithobid)

SUMMARY: Some patients receiving lithium (Eskalith) and fluoxetine have developed neurotoxicity, but the incidence of this reaction is unknown.

MECHANISM: Not established.

CLINICAL SIGNIFICANCE: Several cases of neurotoxicity have been reported in patients receiving fluoxetine and lithium.[1-4] The toxicity generally occurred within a few days of starting concurrent therapy and consisted of confusion, ataxia, dizziness, stiffness of arms and legs, dysarthria, tremor and absence seizures. The order of administration of the drugs did not appear to be a factor in these cases. In one case, the neurotoxicity was associated with an increase in the serum lithium concentration from ≈1 mEq/L to 1.7 mEq/L,[4] but in another case the lithium did not reach toxic levels.[3] The latter patient subsequently achieved good results with lithium plus nortriptyline.[3] Some patients, however, appear to tolerate lithium plus fluoxetine without difficulty; no adverse effects were noted in one study of 5 patients with refractory depression given the combination.[5]

MANAGEMENT: Until additional information is available, monitor for evidence of neurotoxicity in patients receiving lithium and fluoxetine. Symptoms have included tremor, confusion, ataxia, dizziness, dysarthria, and absence seizures. Although it is not proven that standard cyclic antidepressants (e.g., nortriptyline, imipramine) are less likely than fluoxetine to produce neurotoxicity when combined with lithium, they may be safer alternatives.

References

1. Sacristan JA et al. Am J Psychiatry. 1991;148:146.
2. Austin LS et al. Toxicity resulting from lithium augmentation of antidepressant treatment in elderly patients. J Clin Psychiatry. 1990;51:344.
3. Noveske FG et al. Possible toxicity of combined fluoxetine and lithium. Am J Psychiatry. 1989;146:1515. Letter.
4. Salama AA et al. A case of severe lithium toxicity induced by combined fluoxetine and lithium carbonate. Am J Psychiatry. 1989;146:278. Letter.
5. Pope HG et al. Possible synergism between fluoxetine and lithium in refractory depression. Am J Psychiatry. 1988;145:1292.

Monoamine Oxidase Inhibitors (MAOIs)

SUMMARY: Severe or fatal reactions have been reported when monoamine oxidase inhibitors (MAOIs) and fluoxetine are coadministered; the combination should be avoided.

MECHANISM: Not established. Probably involves increased central nervous system serotonin.

CLINICAL SIGNIFICANCE: Several cases of serious or fatal reactions to tranylcypromine (Parnate) have occurred when tranylcypromine was initiated soon after fluoxetine had been discontinued.[1,2] Although a causal relationship cannot be established, the manufacturer warns against concurrent use of fluoxetine and an MAOI.[3] A 31-year-old woman with depression, anxiety, and obsessional thinking was given a trial of fluoxetine 20 mg/day, but it was discontinued after two weeks due to nausea and restlessness.[2] Two days later she was started on tranylcypromine 10 mg/day. On the fourth day of tranylcypromine therapy, she decided to take 20