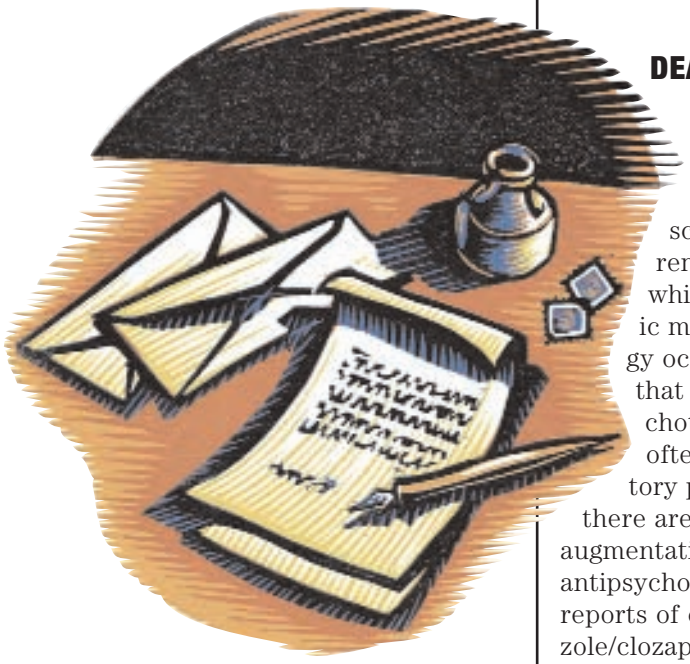
ARIPIPRAZOLE AUGMENTATION OF CLOZAPINE *in Refractory Schizophrenia*



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DEAR EDITOR:

It is not uncommon for patients with psychotic disorders, and specifically schizophrenia, to remain symptomatic while taking antipsychotic medication. One strategy occasionally employed is that of combining antipsychotics.[1] Clozapine is often reserved for refractory patients, but to date there are only a few reports of augmentation with atypical antipsychotics.[2–6] There are no reports of combination aripiprazole/clozapine for any purpose. I report here the first two cases of this combination to treat schizophrenia.

Ms. W. is a 22-year-old Caucasian woman with undifferentiated schizophrenia who had failed extended trials of high FDA-approved doses of haloperidol, fluphenazine, lithium, risperidone, olanzapine, quetiapine, and ziprasidone, and who was a partial responder to clozapine 800mg/day. Unfortunately, she experienced a 45-pound weight gain and sialorrhea. Aripiprazole was added up to 90mg/day, which allowed for reduction of clozapine to 700mg/day. This combination reduced side effects dramatically. The patient lost 40 pounds and began looking for employment as she experienced a profound clinical improvement despite the refractory nature of her disease and not being able to discontinue clozapine entirely. She has been stable on this combination for over one year.

Mr. T. is a 25-year-old Caucasian man with undifferentiated schizophrenia whose illness led him to drop out of college at the age of 19 and neglect bathing and basic personal hygiene for over one year. He was oversedated for several months on risperidone 1.5mg/day and failed a therapeutic dose of divalproex sodium. At the family's request, clozapine was begun, and he demonstrated marked clinical improvement but experienced sialorrhea and sedation at 400mg/day. Aripiprazole augmentation at 15mg/day provided full remission of schizophrenia allowing him to live independently and become a retail operations manager. In addition, aripiprazole augmentation allowed him to reduce his clozapine dose to 150mg/day. He has been successful with this combination of aripiprazole and clozapine for nine months.

These cases describe significant response in patients with refractory schizophrenia using the previously unreported combination of aripiprazole/clozapine. In fact, aripiprazole allowed for a reduction, but not discontinuation, of clozapine, which produced enhanced tolerability as well. It is not clear what aripiprazole augmentation is providing neurochemically that clozapine is not, but perhaps the dopamine partial agonist effect helps limit dopamine suppression and, therefore, minimize side effects while enhancing

attention, cognition, and mental clarity. These patients described this phenomenon and felt this was the defining advantage of this combination. Limitations include lack of placebo-control along with small sample size. Nevertheless, the prolonged treatment response experienced by these chronically ill individuals suggests that this combination may be helpful for some patients with schizophrenia. Further research using this combination would help to define the extent of benefit. Until then, use of the combination of atypical antipsychotic with clozapine may be a reasonable treatment strategy for selected patients and may not only enhance efficacy but also reduce clozapine-induced side effects.

With regards,
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