Off-Label Use of Atypical Antipsychotics: An Update

[EXCERPTS]

Overall, a class effect of the atypical antipsychotics for each disorder cannot be assumed, and for most atypicals, adequate supporting evidence for either efficacy or comparative effectiveness is still lacking for many indications. The trade-offs between risks and benefits (especially in the elderly) should be considered before instituting drug therapy, and careful monitoring for adverse effects is warranted.

Atypical antipsychotics can improve behavioral symptoms of dementia. Several atypical antipsychotics have approved indications in treatment of MDD, and additional members of the class show evidence of efficacy. There is a growing evidence base for the efficacy of atypicals, individually, in obsessive-compulsive disorder (OCD), combat-related post-traumatic stress disorder (PTSD), and generalized anxiety disorder. The evidence for efficacy in borderline personality disorders is too limited to estimate benefit, and the evidence is insufficient for treatment of Tourette's syndrome in adults. Evidence is stronger that atypical antipsychotics do not increase body weight in anorexia nervosa (although weight gain is a common adverse effect in other patients) or reduce substance abuse. There is little evidence about optimal dosages and durations of treatment in off-label use.

The risk of death in elderly patients (65 and older) is increased by both atypical and typical antipsychotics. Other adverse effects of the atypicals include an increased risk of weight gain, which is more common and severe with olanzapine. The risks for endocrine and metabolic abnormalities, including diabetes, are less certain, though measurable. Sedative effects of the atypicals are seen in adults of all age groups. The possibility of urinary adverse effects in elderly patients has appeared in studies of the atypical antipsychotics.

Table 1. Strength of Evidence for Efficacy of Atypical Antipsychotics for Off-Label Indications

[I] = the medication can improve symptoms; **[X]** = the medication does not improve symptoms

Indication	**Aripiprazole**	**Olanzapine**	**Quetiapine**	**Risperidone**
Dementia	Overall[a] **[I]** [evidence: moderate] Agitation **[I]** [evidence: low] Psychosis **[I]** [evidence: low]	Overall **[I]** [evidence: low] Agitation **[I]** [evidence: moderate] Psychosis **[X]** [evidence: low]	Overall **[I]** [evidence: low]	Overall **[I]** [evidence: high] Agitation **[I]** [evidence: high] Psychosis **[I]** [evidence: high]
MDD (augmentation)[b]	Approved indication	Approved indication	Approved indication[c]	**[I]** [evidence:

				moderate] Remission NNT = 8 Response NNT = 7
MDD (monotherapy)[d]	No trials	**[X]** [evidence: moderate]	**[I]** [evidence: moderate] Remission NNT = 13 Response NNT = 6	No trials
OCD (augmentation)[e]	No trials	**[I]** [evidence: low][f]	No trials	**[I]** [evidence: moderate] Response NNT = 5
PTSD (adjunctive)	No trials	[evidence: unavailable or does not permit conclusions]	[evidence: unavailable or does not permit conclusions]	**[I]** [evidence: moderate][g] (combat-related)
GAD	No trials	No trials	**[I]** [evidence: moderate] Response NNT = 8[h]	No trials
BPD[i]	**[I]** [evidence: low]	[evidence: unavailable or does not permit conclusions]	**[I]** [evidence: low]	No trials
Anorexia Nervosa (body weight)	No trials	**[X]** [evidence: moderate]	**[X]** [evidence: low]	No trials
Substance Abuse (reduction in use)	Alcohol **[X]** [evidence: moderate] Methamphetamine **[X]** [evidence: low]	Alcohol **[X]** [evidence: low] Cocaine **[X]** [evidence: low]	Alcohol **[X]** [evidence: low]	Cocaine **[X]** [evidence: low] Methadone **[X]** [evidence: low]

NNT, NNH = the number of patients that must be treated in order to see benefit (NNT) or harm (NNH) in one patient more than found in the comparison group, calculated from the difference in risk between the groups. The smaller the NNT or NNH value, the greater the effect attributable to the treatment.
BPD = borderline personality disorder; **GAD** = generalized anxiety disorder; **MDD** = major depressive disorder; **OCD** = obsessive-compulsive disorder; **PTSD** = post-traumatic stress disorder; 95% **CI** = 95-percent confidence interval, the range of statistically valid values for the result; $p < 0.05$ when the CI does not include 1.0.

[a] Overall = total/global scores, for each drug where listed.
[b] Augmentation of SSRIs (selective serotonin reuptake inhibitors) or SNRIs (serotonin-norepinephrine [reuptake] inhibitors); remission is defined as a score less than 7 on the HAM-D 17 (Hamilton Depression Rating Scale) or less than 8 on the HAM-D 24 over two consecutive visits; and response is defined as at least a 50% reduction in the HAM-D score.
[c] Approved for use in combination with fluoxetine.
[d] No atypical antipsychotic has been approved for use as a monotherapy for MDD.
[e] Augmentation of SSRIs; response is defined as at least a 25–35% improvement in the YBOCS (Yale-Brown Obsessive Compulsive Scale) score.
[f] Effect similar to risperidone in a head-to-head study.
[g] Mean difference of 7.8 points of improvement in the CAPS (Clinician Administered PTSD Scale) score.
[h] Response is defined as at least a 50% improvement in the HAM-A (Hamilton Anxiety Rating Scale) total score.
[i] The evidence for treatment of BPD is inadequate for meta-analysis and does not support conclusions about the statistical or clinical significance of the effect.