Avoiding antipsychotic sedation can improve patient outcomes

Sleep disturbances and treatment-related sedation are common in patients with schizophrenia.[1] Many antipsychotic medications cause sedation but not all of these drugs have the same sedative effect and the sedation can be mistaken for a number of negative symptoms, including cognitive impairment, withdrawal, anhedonia and amotivation.[1]

Sedative effects have little relation to the potency of an antipsychotic at the dopamine D_2 receptor, but instead seem to have an association with each antipsychotic's highly variable affinity for the dopamine H_1 receptor.[2] This could explain why agents that are high affinity histamine H_1 antagonists, such as olanzapine, cause more sedation than antagonists with lower histamine H_1 receptor affinity such as ziprasidone.[2] In addition to affinity for histamine H_1 receptors, the amount of drug which induces a response at H_1 receptors appears to determine the sedative effect.

Medication	Common dosage (mg/day)	Sedation
Aripiprazole	15 – 30	Mild
Chlorpromazine	300 – 600	Moderate
Clozapine	250 – 500	Marked
Fluphenazine	4 – 20	Mild
Haloperidol	5 - 20	Mild
Olanzapine	15 – 30	Moderate
Risperidone	2 – 6	Mild
Ziprasidone	80 – 160	Mild

From Miller DD[2]

Although sedation may be required during short term treatment for patients with an acute relapse, during long term treatment it can have a negative impact on mental and social functioning and on treatment compliance.[3,4] Furthermore, the negative impact that sedation may have on communication and social interaction can prevent patients from benefiting from psychiatric rehabilitation and other treatments.[1,2] Sedation significantly increases patient's negative feelings and attitudes towards taking antipsychotic medications[6] and can be troublesome to patients who are trying to become reintegrated into society.[1]

Aripiprazole is an atypical antipsychotic with partial agonist activity at dopamine D_2 receptors; its moderate affinity for histamine H_1 receptors is consistent with the low incidence of sedation seen with the drug. In Kane's 4-week, double blind, multicentre study, 95% of patients receiving aripiprazole (15mg/day) did not report somnolence, compared with 96% taking placebo.[6]

The level of sedation experienced by patients should be monitored regularly and intervention is necessary if the sedation prevents patients taking an active role in daily life or there is a risk of non-compliance with their treatment. If this is the case, it is worthwhile ensuring that other sedating drugs or conditions have been ruled out, considering night time dosing or even switching the patient to a less sedating antipsychotic medication.[2]

Effective long term antipsychotic treatments that cause minimal or no sedation can help improve compliance and patients' quality of life - this in turn may lead to improved long term effectiveness.[2]

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References

1. *Miller DD. Atypical Antipsychotics: Sleep, Sedation, and Efficacy. Prim Care Companion J Clin Psychiatry 2004;6(2):3-7.*
2. *Miller DD. Sedation with antipsychotics. Curr Psychiatry 2007;6(8):38-42.*
3. *Bourin M. Aripiprazole, a new treatment for schizophrenia. Future Neurol 2006;1(4):373-388.*
4. *Fleischacker WW, Oehl MA, Hummer M. Factors Influencing Compliance in Schizophrenia Patients. J Clin Psychiatry 2003;64(suppl 16):10-13.*
5. *Hofer A, Kemmler G, Eder U, Honeder M, Hummer M, Fleischhacker WW. Attitudes Toward Antipsychotics Among Outpatient Clinic Attendees With Schizophrenia. J Clin Psychiatry 2002;63(1):49-53.*
6. *Kane JM, Carson WH, Saha AR et al. Efficacy and Safety of Aripiprazole and haloperidol Versus Placebo in Patients With Schizophrenia and Schizoaffective Disorder. J Clin Psychiatry 2002;63(9):763-771.*