USE OF AN OREXIN ANTAGONIST FOR SUBACUTE DELIRIUM

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CASE

Mr. A 65-year-old man with a history of DLBC lymphoma and unipolar depression, admitted w/ febrile neutropenia and 2-wks of **hallucinations and** impaired alertness, attention, memory, and sleep-wake cycle

- **D2** Low potency D2 blockade (Seroquel PO, then Thorazine IV) precipitated catatonia
- **BDZ** Lorazepam effectively lysed catatonia however exacerbated underlying confusion
- **α Block** Clonidine patch and trazodone led to hypotension
- **M Options** Mirtazapine and then melatonin failed to regulate his sleep cycle
- **VPA** IV Valproic acid: drowsy, cognition slowed, and sleep cycle remained dysregulated

Discharged AMA w persistent delirium symptoms

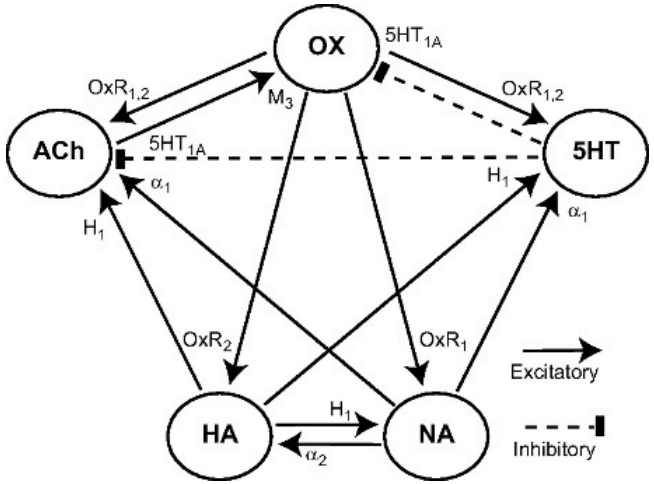
- **OA** As an outpatient, oral orexin antagonist, Suvorexant, allowed for restful sleep and behavioral control without adverse effects

Once Suvorexant was prematurely stopped days later, symptoms returned

BACKGROUND

Current evidence supports the use of orexin antagonists (OA) in cases of hospital delirium[1,2,3], and for subthreshold delirium in hospitalized patients.[4] Furthermore, OAs are not considered deliriogenic or catatonogenic.[1] To our knowledge, no reports exist documenting its role in the management of subacute delirium.

OREXIN PATHWAY



DISCUSSION

For Mr. A, modulation of serotonin, histamine, and melatonin pathways did not improve the symptoms of delirium, yet he suffered from all the side effects associated with alpha-1, D2, NMDA/glutamate blockade, and GABA agonism. In contrast, an OA controlled these symptoms without any reported side effects. Furthermore, its discontinuation led to the re-emergence of initial symptoms.

PROPOSAL

What: OAs are well-tolerated soporifics with mild side effect profile that includes sedation, headache, dizziness, and abnormal dreams

Who: Patients with disordered sleep and delirium risk, particularly: age >65, dementia, cancer, postoperative, ICU admission, with neuroinflammatory risk

When: (a) Want to promote sleep AND:

- Avoid using a Z drug or anticholinergic / Melatonin failure, insufficient
- D2 blockade is contraindicated or not preferred (i.e., high-risk EPS/Catatonia, LBD, HIV/AIDs, Cancer)
- High risk for alpha-1 antagonism associated fall-risk

(b) Aim for sedation and sleep regulation during hyperactive delirium

Why: Delirium/inflammation/neuronal aging dysregulates melatonin and orexin pathways leading to circadian rhythm reversal

Where: Inpatient general hospital, ICU, Home

How long: **For delirium:** The duration of delirium episode, ~7 days

How Long: **For Sleep or Subacute/Subthreshold Delirium:** studied up to 4 weeks, perhaps longer, but risks exist for tolerance among other adverse effects

CONCLUSIONS

CL Psychiatrists should familiarize themselves with OAs, a relatively new class of medication. Its efficacy and safety in treating the complications of delirium warrant its inclusion in their armamentarium, and its tolerability suits medically vulnerable patients and subsyndromal/subacute delirium, both inpatient and outpatient.

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