

DO PSYCHIATRISTS KNOW?

Psychiatrists’ awareness of pharmacodynamic interactions in antipsychotic polypharmacy with aripiprazole. A national survey.

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Introduction

Guidelines recommend antipsychotic monotherapy for schizophrenia. But antipsychotic polypharmacy remains common in clinical practice. Aripiprazole, as partial dopamine agonist (PDA), may be co-prescribed with other antipsychotics, to mitigate metabolic issues, extrapyramidal side effects, sexual dysfunction, and negative symptoms. Due to its high affinity for the D2 receptor, Aripiprazole can displace other antipsychotics at the receptor level. Due to its inherent agonism this can reducing overall D2 receptor antagonism. There have been with several reports of a paradoxical worsening of psychotic symptoms in these settings, especially when patients have been prescribed high doses of high potency antipsychotics and have signs of dopamine supersensitivity.

We observed cases where this potential interaction in setting of relapse was missed. So we set out objectives to answer our queries.

Objectives

- To test if Maltese Psychiatrists and Specialist Trainees
1. Are cognisant of the pharmacodynamic interaction between Aripiprazole and high potency full dopamine antagonists (FDA)
 2. Can apply that knowledge to the clinical setting of a relapsing patient with FDA PDA polypharmacy

Methods

- Literature review
- Ethics approval
- Anonymous online questionnaire
- Sent to all psychiatrists and specialist trainees through the local specialist association and psychiatry department within the national mental health service
- Questionnaire containing
 - Demographics
 - Clinical Case - SBA
 - Knowledge questions - MCQs. Relating to specific relevant psychopharmacological knowledge

THE CASE

Joe is a 42 year old man. He was diagnosed with Schizophrenia age 23. He has been on various antipsychotics since, including risperidone and haloperidol (with response), having had approximately 4 relapses since diagnosis. His last relapse was 6 years ago. He improved on Olanzapine, having complete sustained resolution of symptoms once the dose was increased from 15mg to 20mg Nocte. For the last 3 years he has been prescribed Olanzapine 20mg Nocte and Aripiprazole 30mg Nocte. He presents with a 1 month history of recurring auditory hallucinations with running commentary, and a complex delusional system surrounding persons trying to harm him and his family. Treatment compliance is confirmed.

What is the most appropriate treatment option?

- Stop Olanzapine and start Haloperidol 5 mg BD
- Stop both drugs and start Clozapine
- Stop Aripiprazole
- Add Risperidone titrating to a maximum of 6mg Daily
- Increase Olanzapine to 30mg Nocte
- Increase Aripiprazole to 45mg Nocte

THE PHARMACODYNAMIC QUESTION

Choose the correct answer

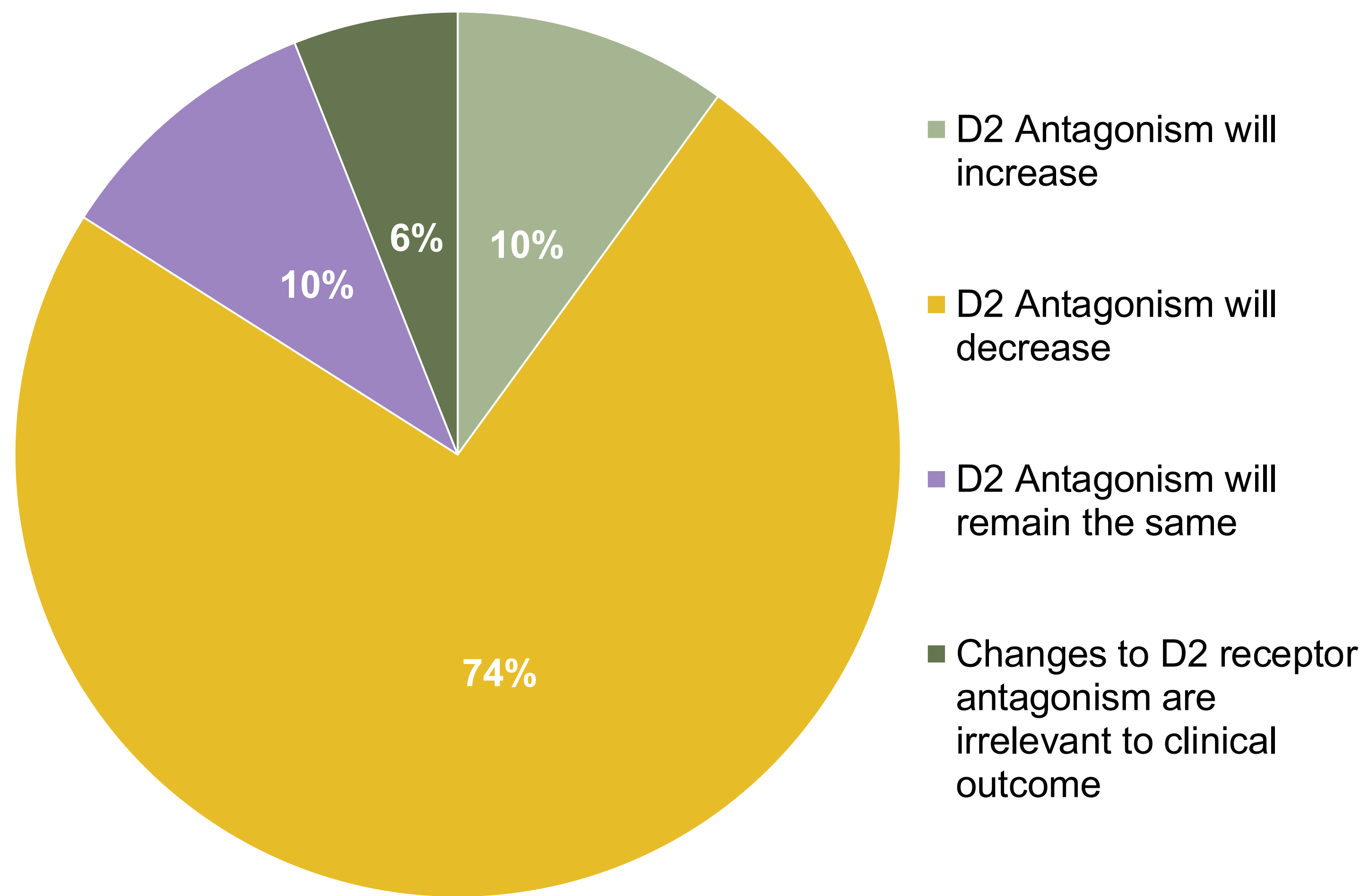
If a patient is prescribed Haloperidol or Olanzapine or Risperidone, and Aripiprazole is added

- D2 Antagonism will increase
- D2 Antagonism will decrease
- D2 Antagonism will remain the same
- Changes to D2 receptor antagonism are irrelevant to clinical outcome

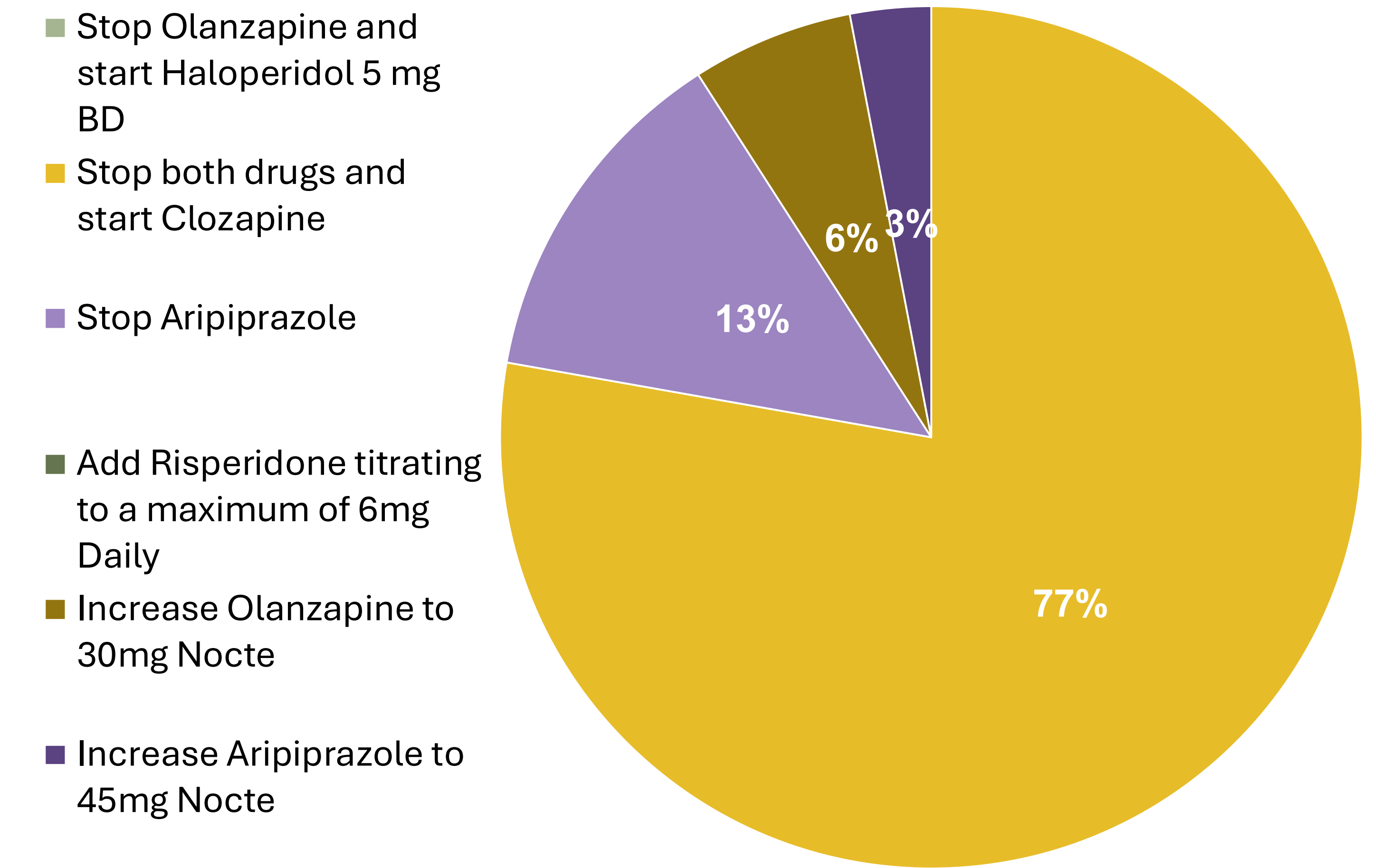
Results

Response 40/66 (61%) partial. 31/66 (47%) complete

Knowledge of Pharmacodynamic interaction



Clinical Decision



Discussion

This was a first of its kind study, bringing with it several strengths and weaknesses. The instrument used could not be validated, the sample size was limited with possible non-response bias. However, it does bring to light an interesting and unexpected conclusion. The gap between knowledge and the simulated clinical decision brings up several questions for further study. The current available literature on clinical decision making can provide some hypotheses to attempt to understand this gap. These include, reliance on intuitive "System 1" thinking, bounded rationality and satisfying, framing and premature closure.

Of note in additional questions related to D2 blockade requirements in different stages of illness, and the maximum D2 antagonistic occupancy that Aripiprazole can provide, knowledge was generally poor (although this did not statistically significantly correlate with responses to the clinical case)

Conclusion

Psychiatrists do possess the theoretical knowledge of FDA PDA pharmacodynamic interaction, but do not appear to apply this to their clinical decision.

To be sure why further study is needed.
To safeguard our patients, further training is needed.