Clozapine in Black Patients with Tardive Dyskinesia: Results of a 24 Week Open Label Clinical Trial

Tiffany Khieu, PharmD[1]; Matthew Glassman, MS[2]; Fang Liu, MA[2]; Bethany A DiPaula, PharmD, BCPP[1]; Deanna L. Kelly, PharmD, BCPP[2]
[1]University of Maryland School of Pharmacy; [2]Maryland Psychiatric Research Center, University of Maryland School of Medicine

Background

- Tardive dyskinesia (TD) is characterized by involuntary movements associated with neuroleptic medications and is potentially irreversible[1]
- Treatment options include dose reductions of the current psychotropic or switching to a different agent
- Clozapine has been shown to reduce severity and seldom exacerbates TD[2]
- Current literature is limited in determining risk factors associated with TD and predictors of response using clozapine, especially in Black patients
- To our knowledge, our data is the largest Black population with schizophrenia treated with clozapine to date

Objectives

Determine risk factors for TD in Black patients

Examine rate of clinical response for TD in Black patients when switching from baseline antipsychotic to clozapine

Methods

- Secondary analysis of a three-center prospective open-label study
- 274 enrolled patients treated with clozapine for six months
- Occurrence of TD at baseline defined as a score of ≥ 3 on the Abnormal Involuntary Movement Scale (AIMS)
- Examination of clinical variables associated with TD included:
  - Demographics
  - Smoking status
  - Substance use history
  - *ACKR1* genotype
  - Diagnosis
  - Medication use
  - Extrapyramidal symptoms (Simpson Angus Scale [SAS])
  - Psychiatric symptoms (Brief Psychiatric Rating Scale [BPRS])
- Examination of efficacy of clozapine in reducing TD
- TD response was defined as 50% reduction in total AIMS scores

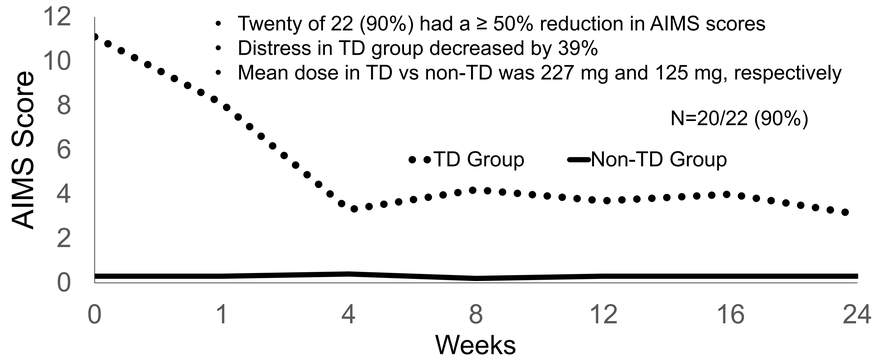
Table 1. Baseline Demographics

	TD (N=22)	Non TD (N=249)	p-value
Age in years, mean	**49**	**40**	**<0.001**
Sex, male, n (%)	11 (4%)	155 (59%)	0.258
Race, n (%)			
White	0 (0%)	6 (2%)	
Black	20 (7%)	232 (86%)	0.700
American/Indian	0 (0%)	1 (1%)	
Asian	0 (0%)	1 (1%)	
Mixed	2 (1%)	9 (3%)	
Smoker, n (%)			
Current	5 (2%)	65 (24%)	0.729
History	6 (2%)	111 (41%)	0.116
Substance Use, n (%)			
Alcohol	6 (2%)	62 (23%)	0.750
Marijuana	6 (2%)	74 (28%)	0.829
Stimulants	1 (1%)	2 (1%)	0.101
Cocaine	4 (2%)	36 (14%)	0.604
ACKR1 Gene, n (%)			
CCtype	15 (6%)	181 (74%)	0.945
CT/TT type	4 (2%)	46 (19%)	
Medications, n (%)			
FGA	**9 (3%)**	**164 (61%)**	**0.016**
SGA	17 (6%)	174 (65%)	0.499
Mood Stabilizer	9 (3%)	102 (38%)	0.972
Anticholinergic	8 (3%)	126 (57%)	0.188
Antihistamine	2 (2%)	76 (40%)	0.032
Sedatives	1 (1%)	30 (11%)	0.285
Vitamins	12 (5)	74 (28%)	0.018
Scales, mean			
Simpson-Angus Scale	**4**	**2**	**0.007**
Brief Psychiatric Rating Scale	40	39	0.687

Table 2. Predictors of TD 22/271 (8%) Met Criteria

Predictors	Odds Ratio (95% CI)	X^2	p-value
Age	**1.086 (1.032-1.142)**	**10.19**	**0.001**
Simpson-Angus Scale (SAS)	**1.143 (1.004-1.302)**	**4.06**	**0.044**
Body Mass Index	0.917 (0.838-1.004)	3.50	0.062
First Generation Antipsychotic	1.572 (0.557-4.440)	0.73	0.393

Figure 1. Mean Reduction of Tardive Dyskinesia



- Twenty of 22 (90%) had a ≥ 50% reduction in AIMS scores
- Distress in TD group decreased by 39%
- Mean dose in TD vs non-TD was 227 mg and 125 mg, respectively

Table 4. Predictors of Response to TD

Predictors of Response	Odds Ratio (95% CI)	X^2	p-value
Age	0.979 (0.920-1.042)	0.50	0.480
Anticholinergic Medications	4.185 (0.777-22.528)	3.06	0.080
Clozapine Dose	**1.007 (1.002-1.012)**	**4.73**	**0.030**

Discussion

- Low rate of TD (8%) suggesting rates of TD in chronic patients ready for clozapine is lower than reported elsewhere
- May be due to multiple different raters or differences in criteria used
- Participants meeting criteria for TD more likely to be older and had extrapyramidal side effects prior to clozapine treatment
- Having TD was associated with lower use of first-generation antipsychotics, less antihistamine use, and higher vitamin usage
- Robust response to clozapine as over 90% at baseline with TD had ≥ 50% reduction and average of 70% reduction in total scores from baseline
- Clozapine is a highly effective treatment for chronic patients with TD, particularly as seen in this Black population

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References

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