

THE IMPACT OF ANTICHOLINERGIC BURDEN ON COGNITIVE FUNCTIONING IN SEVERE MENTAL DISORDERS: A COMPARATIVE STUDY.

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ABSTRACT:

Background: Anticholinergic medications are commonly prescribed in the management of psychiatric disorders, yet their potential adverse effects on cognitive functioning remain a topic of concern. This study aims to investigate the correlation between Anticholinergic Cognitive Burden (ACB) and cognitive functioning in individuals diagnosed with Schizophrenia, Bipolar Affective Disorder and Major Depressive Disorder.

Methods: A correlation analysis was conducted on data obtained from 120 participants (40 per each group) who underwent cognitive assessment and ACB scoring. Pearson's correlation coefficient (r) was used to examine the relationship between overall ACB scores and various cognitive measures, including KOHS Block Score, Passalong Score, Pattern Drawing Score, Immediate Memory Score, Picture Drawing Score and Total cognitive score.

Results: The findings reveal significant negative correlation between overall ACB scores and Total cognitive scores across all three psychiatric disorders (Schizophrenia: $r = -0.462$, $p = 0.003$; Bipolar Affective Disorder: $r = -0.399$, $p = 0.011$; Major Depressive Disorder: $r = -0.352$, $p = 0.026$), indicating that higher ACB scores are associated with lower overall cognitive scores and specific cognitive measures, such as KOHS Block Score and passalong score, in certain disorder groups, highlighting domain-specific effects of anticholinergic medications on cognitive performance.

Conclusion: Our findings underscore the detrimental impact of Anticholinergic Cognitive Burden on cognitive functioning in individuals with psychiatric disorders. Healthcare providers should carefully consider the potential cognitive effects of anticholinergic medications when prescribing treatment regimens for these populations. Future research should further elucidate the mechanisms underlying these associations and explore targeted interventions to mitigate cognitive impairment in individuals receiving anticholinergic therapy for psychiatric conditions.

Key words: Anticholinergics, Anticholinergic burden, Cognition, Schizophrenia, Bipolar Disorder, Major Depressive Disorder, Passalong test.

INTRODUCTION:

Cognitive disorders are pervasive in psychiatric disorders such as schizophrenia, bipolar disorders and depressive disorder. Profoundly impacting patients' daily functioning and quality of life. While antipsychotic medications are often integral to managing symptoms, their use can lead to extrapyramidal side effects (EPS) necessitating the concurrent prescription of anticholinergic medications. Unfortunately, the administration of anticholinergic drugs, while alleviating extrapyramidal symptoms, poses a conundrum as it may exacerbate cognitive decline in these patient populations (Eum, S et al.,2017; Bartus et al.,1982; Everitt and Robbins.,1997). The central anticholinergic system, crucial for memory and cognitive processes, is susceptible to suppression through the blockade of muscarinic cholinergic receptors by anticholinergic medications.

In Schizophrenia, the burden of anticholinergic medication is substantial and prevalent across various medication classes, with notable associations with cognitive impairments spanning all cognitive domains (Joshi et al., 2021). Notably, a threshold effect of anticholinergic burden on cognition has been delineated in clinically stable individuals with schizophrenia, a phenomenon not consistently observed in affective psychoses (Eum, S. et al., 2017). This suggests that patients with schizophrenia may exhibit heightened cognitive susceptibility to anticholinergic medications, necessitating a nuanced consideration of medication regimens in clinical practice.

In bipolar disorders and depressive disorder, while the use of anticholinergic medications may not be as prevalent as in schizophrenia, it still represents a significant aspect of treatment management. Previous research has shown that individuals with bipolar disorders and depressive disorder may also experience cognitive impairments associated with anticholinergic burden, albeit to varying degrees (Eum, S. et al., 2017; Satabdi Chatterjee et al., 2019). However, the precise impact and threshold effect of anticholinergic burden on cognition in these disorders remains less explored compared to schizophrenia. Understanding the cognitive consequences of anticholinergic burden across diverse psychiatric populations is crucial for optimizing treatment strategies and improving patient outcomes. Therefore, our present study aims to bridge this gap by investigating and comparing the impact of anticholinergic burden on cognitive functioning in schizophrenia, bipolar disorders, and depressive disorder. By elucidating the differential cognitive effects of anticholinergic medications across these psychiatric conditions, our study aims to inform more tailored and nuanced treatment approaches in clinical settings.

METHODS:

Subjects: This cross-sectional study was conducted at the Outpatient Department of the Department of Psychiatry, Government General Hospital, Anantapur. A total of 120 patients diagnosed with Major Depressive Disorder (MDD), Bipolar disorder (BD), and Schizophrenia (SZ) were recruited for the study, with 40 patients in each diagnostic group. Participants met the diagnostic criteria outlined in the International Classification of Diseases, 10th Revision (ICD-10), and had been compliant with their prescribed medications for a minimum duration of 2 years. Inclusion criteria encompassed individuals aged 18 years or older, free from neurological disorders, head injuries, and major medical conditions known to impact cognitive function. The study protocol was approved by the Ethics Committee of Government Medical

College, and all participants provided written informed consent following a comprehensive explanation of the study objectives and procedures.

Measurements: The anticholinergic properties of all prescribed medications were assessed using the Anticholinergic Drug Scale (ADS), a validated tool for quantifying the anticholinergic burden of medications. This scale categorizes drugs based on their potential negative impact on cognition, ranging from zero (no anticholinergic activity) to possible and finally to definite anticholinergic activity, with scores ranging from zero to three. The Anticholinergic Cognitive Burden Scale identifies 88 medicines with known anticholinergic activity. The scores for each medication were summed to calculate a total ADS burden score for each participant, which was subsequently analyzed in conjunction with cognitive assessments using the Bhatia Battery, which is developed by C.M. Bhatia in 1955.

Statistical analysis: Clinical variables with a normal distribution were compared using one-way analyses of variance (ANOVAS), while non-normally distributed clinical data were analyzed using Kruskal-Wallis nonparametric ANOVAS. Gender differences were evaluated using the chi-square test. Correlations between Anticholinergic Cognitive Burden (ACB) scores and subcategory as well as total cognitive scores of psychiatric illnesses were examined using Pearson's correlation coefficient. Statistical analyses were performed using SPSS software, with differences considered significant at a p-value < 0.05.

This methodological approach ensured rigorous evaluation of the relationship between anticholinergic burden and cognitive functioning across different psychiatric disorders, facilitating comprehensive insights into impact of medication regimens on cognitive outcomes in this patient populations.

RESULTS:

Variable	Schizophrenia (N=40)	Bipolar Affective Disorder (N=40)	Major depressive Disorder (N=40)	p-value
Age (Mean ± SD)	38.3 ± 10.4	39.0 ± 9.99	35.3 ± 9.34	0.216 [#] ; NS
Gender				
Male	21 (52.5%)	24 (60%)	16 (40%)	0.195 ^{\$} ; NS
Female	19 (47.5%)	16 (40%)	24 (60%)	
Religion				
Hindu	33 (82.5%)	26 (65%)	30 (75%)	0.479 [€] ; NS
Muslim	3 (7.5%)	8 (20%)	8 (20%)	
Christian	4 (10%)	6 (15%)	2 (5%)	
Educational status				
Illiterate & Primary	21 (52.5%)	22 (55%)	17 (42.5%)	0.306 ^{\$} ; NS
Secondary & High school	14 (35%)	12 (30%)	11 (27.5%)	
Intermediate and above	5 (12.5%)	6 (15%)	12 (30%)	
Relationship status				

Married & staying with spouse	25 (62.5%)	28 (70%)	29 (72.5%)	0.606 [§] ; NS
Unmarried/ separated	15 (37.5%)	12 (30%)	11 (27.5%)	
Occupation				
Skilled & above	9 (22.5%)	16 (40%)	13 (32.5%)	0.510 [§] ; NS
Unskilled	22 (55%)	15 (37.5%)	18 (45%)	
Unemployed	9 (22.5%)	9 (22.5%)	9 (22.5%)	
Income	8000	9500	9500	0.414 [£] ; NS
(Median with IQR)	(5000 - 10000)	(6000 - 12000)	(6000 -15000)	

Table:1. Describes the socio demographic data of the participants.

SD = Standard deviation; **IQR** = Inter-quartile range; **NS** = Not Significant; **#** = ANOVA p-value; **§** = Chi-square test p-value; **€** = Yate's p-value; **£** = Kruskal-Wallis p-value

Variable	Schizophrenia (N=40)	Bipolar Affective Disorder (N=40)	Major depressive Disorder (N=40)	p-value
Duration of disease (Median with IQR)	7.0 (5.0 – 10.0)	5.5 (3.75 – 10.0)	4.0 (2.75 – 7.0)	<0.001 [¥] ; S
ACB score (Median with IQR)	6.0 (4.0 – 6.0)	2.0 (0.0 – 3.25)	3.0 (0.0 - 3.0)	<0.001 [§] ; S
KOHS block score (Median with IQR)	5.0 (4.0 – 5.0)	7.0 (6.0 – 8.0)	6.5 (5.75 – 7.0)	<0.001 [§] ; S
Passalong score (Median with IQR)	6.0 (5.0 – 6.25)	8.0 (7.0 – 8.25)	8.0 (7.0 – 9.0)	<0.001 [§] ; S
Pattern drawing score (Median with IQR)	4.0 (4.0 – 5.0)	5.0 (4.75 – 5.0)	5.0 (4.0 – 5.0)	<0.001 [¥] ; S
Immediate memory score (Median with IQR)	5.0 (4.0 – 6.0)	6.0 (6.0 – 7.0)	6.5 (6.0 – 7.0)	<0.001 [§] ; S
Picture drawing score (Median with IQR)	5.0 (4.0 – 5.0)	6.0 (5.0 – 7.0)	6.0 (5.75 – 7.25)	<0.001 [§] ; S
Total cognitive score (Median with IQR)	24.0 (22.0 – 27.0)	32.0 (30.0 – 34.0)	32.5 (29.5 – 34.3)	<0.001 [§] ; S

Table:2. The above table shows the clinical data of the participants with individual parameters of Bhatia battery and ACB scores in Schizophrenia, Bipolar Disorder and Major Depressive Disorders.

IQR = Inter-quartile range; **S** = Significant; **ACB** = Anticholinergic Cognitive Burden

Variable	Schizophrenia (N=40)		Bipolar Affective Disorder (N=40)		Major depressive Disorder (N=40)	
	Correlation coefficient (r)	p- value	Correlation coefficient (r)	p- value	Correlation coefficient (r)	p- value
Overall ACB scores with KOHS block score	-0.391	0.013; S	-0.253	0.115; NS	-0.311	0.051; NS
Overall ACB scores with Passalong score	-0.383	0.015; S	-0.476	0.002; S	-0.393	0.012; S
Overall ACB scores with Pattern drawing score	-0.168	0.300; NS	-0.039	0.810; NS	-0.141	0.386; NS
Overall ACB scores with Immediate memory score	-0.272	0.089; NS	-0.237	0.141; NS	-0.030	0.854; NS
Overall ACB scores with Picture drawing score	-0.322	0.043; S	0.073	0.656; NS	-0.154	0.342; NS
Overall ACB scores with Total cognitive score	-0.462	0.003; S	-0.399	0.011; S	-0.352	0.026; S

Table 3: The above table shows the correlation of ACB scores with individual parameters of Bhatia battery. In this data the passalong scores shoed significant negative correlation in schizophrenia, Bipolar Disorder and Major Depression Disorder.

NS = Not Significant; **S** = Significant; **ACB** = Anticholinergic Cognitive Burden

Negative symbol in correlation coefficient signifies that two variables are inversely related, that means unit increase in ACB scores will decrease the other scores in r (Pearson's correlation coefficient) times.

DISCUSSION:

Our study sheds light on the intricate relationship between anticholinergic burden and cognitive functioning across diverse severe mental illnesses namely schizophrenia, BPAD and major depressive disorders. The significant correlations observed between anticholinergic burden cause and cognitive performance in all three diagnostic groups highlight the widespread impact of anticholinergic medication on cognitive functioning in psychiatric population.

The current study explored the influence of sociodemographic factors on cognitive functioning across 3 diagnostic groups. While variables such as age, gender, education and marital status did not exhibit significant differences in cognitive performance among the 3 groups certain trends were observed. Although not statistically significant, cognitive impairment tended to be

more prevalent in older individuals and those with lower educational attainment. In line with existing literature our findings corroborate the substantial burden of anti-cholinergic medication usage in individuals with schizophrenia {Joshi et al 2021}. Notable schizophrenia patients are known to exhibit cognitive impairments associated with anti-cholinergic burden, as demonstrated in previous studies {Eum S et al 2017}.

Our results further emphasise the heightened cognitive susceptibility of individuals with schizophrenia to anti cholinergic medications, emphasizing the critical importance of considering the medication regimens in clinical decision making. Interestingly this study also unveils significant co relations between ACB scores and cognitive performance in individuals with bipolar disorder and major depressive disorder. While the prevalence of anti-cholinergic medication used may be lower in these populations as compared to schizophrenia even modest exposure to anticholinergic drugs appears to adversely affect the cognitive functioning in individuals with mood disorders {satabdi Chatterjee et al 2019}. This finding resonates with prior research highlighting the increased risk of cognitive impairment associated with anti-cholinergic use in the elderly individuals with depression {satabi chaterjee et al 2019}.

Significant correlation was seen with the ACB scores and cognitive performance across all three diagnostic groups associations with ACB scores highlights the relationship between these two variables of pass along test sub scale demonstrated sensitivity in detecting the cognitive disturbances associated with anti-cholinergic burden, this underscores the need for the cautious prescribing of anticholinergics medication in psychiatric population and suggests the potential of the pass along test as a valuable screening tool for cognitive deficits in these patients.

CONCLUSION:

In conclusion this study contributes to understanding the complex interplay between socio demographic factors, cognitive functioning and anticholinergic medication use in individuals with schizophrenia, BPAD and MDD. The significant correlation observed between ACB scores and cognitive performance highlight the importance of considering medication regimen in clinical decision making to mitigate cognitive impairment. Additionally, Passalong test emerges as a promising tool for routine cognitive screening in psychiatric patients. By understanding these relationships, the findings of this study facilitate the development of tailored treatment approaches aimed at improving cognitive outcomes and overall quality of life in individuals with psychiatric disorders.

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