

Original Article

Anticholinergic Burden in Geriatric Patients Attending Clinical Pharmacology Clinic — A Descriptive Cross-sectional Study in Eastern India

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Background : Anticholinergic burden in Geriatric population is of great concern throughout the Globe, yet often neglected. There are previous studies to assess the Anticholinergic burden, carried out in specific population, though its prevalence in general population is difficult to interpret. Polypharmacy remains one of the major causes contributing to the increased burden in Anticholinergic score among Geriatrics. Multiple co-morbidities and the prevalence of Multiple Chronic Diseases are the responsible factors which imbibe Multiple Drug Therapy in Geriatric population. Anticholinergic burden in older adults has been associated with Cognitive impairment, Delirium, Dizziness and Confusion, Falls and increased hospitalizations. However, Anticholinergic-acting drugs are often advised in Geriatric population. In this study an attempt was made to understand the Anticholinergic burden score among Geriatric population.

Methods : This study is a descriptive cross-sectional study, which was done, in a period of six months among 62 Geriatric patients attending a therapeutics clinic of a private clinical pharmacology OPD for first time. Patients were noted for their comorbidities and anticholinergic burden was calculated, based on the Anticholinergic Cognitive Burden scale. Results were statistically analyzed.

Results : Clinically significant anticholinergic burden was observed in 22.58% population. The most frequently prescribed drug was found to be alprazolam followed by amitriptyline and theophylline. Among the comorbidities hypertension and diabetes was commonly seen in majority of the population.

Conclusion : Co-professional care at clinical pharmacology OPD with assessment of anticholinergic burden of geriatric prescriptions and advices on rational de-prescribing with suggestions on safer alternatives would be beneficial for treating physicians to optimize therapy.

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Key words : Anticholinergic drugs, Anticholinergic burden, Polypharmacy, Geriatric population, Adverse effects.

Anticholinergic drugs target the muscarinic receptors and eventually block the neurotransmission of acetylcholine. Autonomic

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Editor's Comment :

- Elderly population is at high risk of developing adverse effects.
- Assessment of Anticholinergic burden in geriatric patients on multiple drugs may be helpful to minimize the adverse effects.
- Timely de-prescribing of drugs with high ACB or altering it with low ACB score using principles of clinical pharmacological review, reconciliation and feedback could prevent medication related atrocities.

nervous system plays an important role in maintaining multiple body functions. These body functions include learning and memory, urination, maintenance of heart rhythm etc. Integrity of the autonomic nervous system is to be maintained, for proper functioning of the various body functions. The drugs which act on this system are cumulatively known as Anticholinergic drugs and these drugs acts on its various receptors. These drugs not only bind to muscarinic receptors but also bind with other receptors based on its either agonistic activity or antagonistic activity, which makes different

therapeutic targets. Since cholinergic transmission is responsible for the activity of various physiological functions, particularly in neurotransmission, anticholinergic drugs do not escape adverse effects. These adverse effects may involve both the peripheral and central nervous systems. While Central Nervous System (CNS) related adverse effects primarily involves different cognitive domains, adverse effects of PNS include decrease in body's secretion which is manifested as dry mouth. The other PNS complication includes urinary retention, constipation, tachycardia and blurring of vision, among others.

The prevalence of chronic diseases, like Diabetes, Hypertension and Osteoarthritis, in geriatric population is quite common. These diseases are not only associated with considerable illness, and is also associated with increased overall medication use, decreased quality of life, and ultimately increased cost of therapy¹. As age progresses impairment in cognition, autonomic dysfunction, falls and dementia cannot be do away with but these geriatric symptoms are not always directly related to the process of ageing, it may be also contributed due to the anticholinergic adverse effects of the prescribed medications in older adults^{2,3}. Geriatric population are at higher risk to experience adverse effects due to age-related modifications of Pharmacokinetic and Pharmacodynamic Parameters. Children and younger adults are not an exception as, adverse effects due to anticholinergic medications can affect them, but to a lesser extent. To be more specific, the adverse effects due to Anticholinergic drugs, targeting both at the peripheral and the central level, have greater impact in Geriatric population⁴⁻⁷. Among the different types of anticholinergic medications prescribed, the anticholinergic activity varies. Some possess more anticholinergic activity, while others have less anticholinergic activity. Sedating antihistamines and tricyclic antidepressants have strong anticholinergic side effects. In common practice the treating physician may not be aware that some commonly prescribed diuretics and other cardiac medications (eg, anticoagulants, antihypertensives) also have Anticholinergic properties. Also while prescribing; the physician should realize that taking multiple medications with weaker anticholinergic properties can have an additive effect⁸⁻¹⁰. It is evident from previous research that the cumulative exposure during as little as 1 to 2 years impairs memory and performance of activities of daily living¹¹. Long-term use of medications with high Anticholinergic burden score is associated with an increased incidence of Alzheimer disease and Dementia¹²⁻¹⁴. The risk of anticholinergic-

related cognitive impairment has been found independent of the underlying comorbid disease burden or severity of illness¹⁵. Conversely, effect of cumulated drug burden in increasing risk of hospitalization or mortality was not clear, with studies reporting conflicting results in different populations¹⁶.

Anticholinergic Drugs :

Anticholinergic drugs have several Therapeutic indications, which include urinary abnormalities, gastrointestinal diseases like Peptic Ulcer Disease and Irritable Bowel Syndrome, nervous system disorders like Parkinson's disease. Also, anticholinergics are frequently used as anesthetic agents and for Neurologic and Psychiatric conditions.

The main properties of Anticholinergic drugs are based on their affinity with central or peripheral cholinergic receptors¹⁷. These actions can affect cognition, which can be mistakenly diagnosed as a sequela of normal aging process¹⁸. Several drugs have a high ACB score but few drugs like amoxicillin, lansoprazole, metformin, fentanyl, furosemide, diazepam, digoxin, duloxetine, phenytoin and topiramate is associate with AA at high doses¹⁹. It has been observed that, the combination of several drugs, which may include even nutritional supplements can cause or enhance the adverse events of a prescribed anticholinergic medication. The prescription of Anticholinergic drugs may be considered inappropriate in certain scenario. "Potentially inadequate anticholinergic drug use in older adults" has already been discussed in the Beers (American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012) and the STOPP-START criteria²⁰. However, for certain clinical situations the benefits of anticholinergic outweighs their risks and their prescription may be considered appropriate in selected cases of Geriatric population, after making Risk benefit analysis.

Pathophysiology :

The various deleterious anticholinergic effects can be related to the various muscarinic receptors in our body. These receptors are of five types M1 to M5, out of which M1, M2, M4 are responsible for the various anticholinergic deleterious effects. M1 receptors are primary located in the CNS and have important role in execution of various functions. It is also responsible for maintaining episodic memory in hippocampus and pre-frontal cortex²¹. While M2 receptors are responsible for processing memory, M4 receptors are involved in regulating the levels of acetylcholine. The receptor antagonism of these receptors is associated with cognitive disturbance and cell death²². Cognitive

effects not only depend on anticholinergic burden, baseline cognitive function, but also on individual pharmacokinetics and pharmacodynamics variability. Cognitive effects can also be influenced by alterations in metabolism²³. Central effects of the various Anticholinergic drugs depend on the penetration power of the drug through the blood brain barrier. In diabetic patients and multiple sclerosis patients the blood brain permeability is increased and the drugs such as loperamide, simvastatin, clonidine, or methyl dopa can exhibit their central side effects.

Prolonged anticholinergic drug therapy can cause brain changes, partly simulating Alzheimer's Disease (AD). Cognitive dysfunction in AD is related with multiple aspects, such as reduction in cholinergic neurons, acetylcholine receptor dysfunction and altered signal transmission. Severity of disease is proportional to the changes in the cholinergic system²⁴. In this context a study has shown, that both amyloid plaques and neurofibrillary tangles were increased in Parkinson patients on prolonged anticholinergic medications²⁵. Another study, reveals that cholinergic receptor blockade for prolonged duration is associated with increased in beta-amyloid peptide in various parts of the brain including Amygdale, Cortex and Hippocampus²⁶. Accordingly, another longitudinal study found higher rates of atrophy in the total cerebral volume and in the gray matter associated to anticholinergic drug consumption²⁷.

MATERIAL AND METHODS

A descriptive cross-sectional study was conducted over a period of six months on all Geriatric patients attending a specialty Therapeutics clinic in eastern India. The study commenced after obtaining its due permission for conduct from the institutional ethics committee. All geriatric patients were evaluated for their anticholinergic burden using the Anticholinergic Cognitive Burden (ACB) scale. This scale is widely accepted and validated for adverse anticholinergic outcomes^{28,29}. The ACB scale was first published in the year 2008 and updated in the year 2012²⁸. A systematic review based study was done in-order to make a list of possible anticholinergic medications with notable Anticholinergic effects. Later the same list was identified and further evaluated and categorized by a team of clinical expert clinicians. The ACB scale categorizes drugs on a scale of 0 to 3, based on their anticholinergic activity. Detailed scoring uses the following criteria: (i) ACB score of 1 (possible anticholinergic effect) requires "evidence from in vitro data that the medication has antagonist activity at

muscarinic receptors", (ii) ACB score of 2 (definite anticholinergic effect) requires "evidence from literature, prescriber's information, or expert opinion of clinical anticholinergic effect", (iii) ACB score of 3 (definite anticholinergic effect) requires "evidence from literature, prescriber's information, or expert opinion of the medication causing delirium". All other medications have a score of 0. The total anticholinergic burden of a patient is calculated by summing the ACB scores from all the medications that patient receives concomitantly: anticholinergic burden ≥ 3 is considered clinically significant²⁹. Data collected were checked for completeness, tabulated and statistically analyzed using Microsoft Excel.

RESULTS

The study included a total of 62 geriatric patients who visited clinical pharmacology outpatient facility in a specialty clinic in eastern India. Out of the 62 patients 23 were females and rest were males. The mean age of the female patients was 60.6 ± 74.32 years and that of male patients was 70.92 ± 4.06 years. Clinically significant Anticholinergic burden with a ACB score of 3 or more was found in 14 (22.58%) of the patients, out which 6 were female and 8 were male. Presenting disease condition and drug usage pattern of anticholinergic medications was noted in all included individuals (Table 1).

While 53.23% Geriatric population had ACB score of 0, the study noted 22.58% population having clinically significant anticholinergic burden with score 3 or greater. 19.35% geriatrics had ACB score of 1 (Fig 1).

DISCUSSION

Anticholinergic burden in Geriatric population is often associated with various sideeffects like impairment in cognition, autonomic dysfunctions relating to problems in micturition in elderly males, drying of secretions and many more. ACB, though a common entity is often neglected. Elderly population is much more associated with multiple comorbidities which imbibe multiple drug therapies and thus polypharmacy is one of the major causes of poor compliance to drug treatment. In this descriptive cross-sectional study, we looked for the prevalence of Anticholinergic burden in Geriatric population attending for the first time in a therapeutic clinic. It has been found that overall anticholinergic burden is 22.5%, which is fairly high. Previous studies also have similar results which suggest that about one third of study population was associated with fairly high ACB score^{3,5}. About 27% of the male population has an

	Female		Male	
	Frequ- ency(N)	Perce- ntage(%)	Frequ- ency(N)	Perce- ntage(%)
Total Sample	23	37.09	39	62.90
Disease Condition :				
Type 2 Diabetes Mellitus	13	56.52	25	64.10
Hypertension	15	65.22	32	82.05
Chronic urticarial	3	13.04	0	0
COPD	6	26.09	10	25.64
Psychosis	2	8.70	0	0
GERD	1	4.35	0	0
Rheumatoid Arthritis	1	4.35	0	0
Benign prostatic hyperplasia	0	0	2	5.13
Asthma	0	0	1	2.56
Chronic Kidney Disease	0	0	5	12.82
Inflammatory Bowel Syndrome	0	0	1	2.56
Anticholinergic Burden (ACB) :				
ACB Score 0	13	56.52	20	51.28
ACB Score 1	4	17.39	8	20.51
ACB Score 2	0	0	3	7.69
ACB Score 3	2	8.70	2	5.13
ACB Score 4	2	8.70	3	7.69
ACB Score 5	0	0	0	0
ACB Score 6	1	4.35	2	5.13
ACB Score 7	1	4.35	1	2.56
Drug (with ACB) Usage Pattern :				
Amitriptyline	2	8.70	7	17.95
Ranitidine	1	4.35	5	12.82
Clemastine	1	4.35	0	0
Alprazolam	4	17.39	8	20.51
Prednisolone	1	4.35	2	5.13
Hydroxyzine	1	4.35	3	7.69
Quetiapine	2	8.70	0	0
Doxepin	2	8.70	3	7.69
Nortriptyline	3	13.04	0	0
Theophylline	0	0	4	10.26
Levocetirizine	0	0	4	10.26

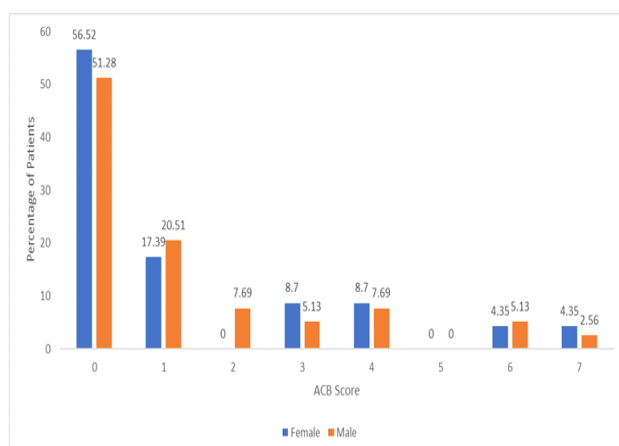


Fig 1 — Total Anticholinergic Burden in the Cohort

ACB score of ≥ 3 , 26% while female population had an ACB score ≥ 3 . Among the frequently prescribed drugs in both female and male population sedative and

hypnotics outnumbered others. The most frequently prescribed drug was found to be alprazolam followed by amitriptyline and theophylline. This is also a common finding in previous studies^{5,9}. Among the comorbidities Hypertension and Diabetes was commonly seen in majority of the population. However there has not been any notable adverse effect noted among the patients. All the patients were questioned about the possible adverse effects of anticholinergic medications, but most of them did not experience any notable adverse effect. In a study it was found that de-prescribing drugs having high Anticholinergic burden ameliorated the medication related problems that was developed due to prescribing cascade³⁰. In another study it was shown that de-prescribing drugs in clinical pharmacology clinic with high anticholinergic burden was beneficial in drug induced erectile dysfunction patients³¹. In diabetic patients suffering from Autonomic Neuropathy, drugs with anticholinergic burden, increases parasympathetic autonomic dysfunction. In one study it was depicted that timely identification and discontinuation of offending agent produce beneficial effect to the patient³².

CONCLUSION

Geriatric population warrants special care in prescribing. There are many things yet to be learned about the distribution of Anticholinergic burden in geriatric population, associated risk factors, and effective measures to assess and intervene if necessary. ACB scores of 3 or greater represent clinically relevant anticholinergic burden and it remains the wise decision of the treating physician to have balance between risk and potential benefits. Also screening may be helpful for early recognition of anticholinergic adverse effects and develop a plan to minimize anticholinergic drug exposure. This may eventually improve the health outcomes of Geriatric population by halting the progression of Functional decline and Geriatric syndromes, particularly cognitive impairment. Co-professional care at clinical pharmacology OPD with assessment of anticholinergic burden of geriatric prescriptions and advices on rational de-prescribing with suggestions on safer alternatives would be beneficial for treating Physicians to optimize therapy.

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