

The evaluation of relationship between polypharmacy and anticholinergic burden scales

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ABSTRACT

OBJECTIVE: Polypharmacy and anticholinergic burden are the indicators for the evaluation of the quality of pharmacotherapy in older adults. The aim of this study was to consider which anticholinergic burden scales are more related with polypharmacy among older patients.

METHODS: Four hundred and twenty older adults were evaluated retrospectively in this cross-sectional study. The patient's demographic data, comorbidities, the drugs, and number of drugs were recorded. Anticholinergic burden scales were calculated by a tool named anticholinergic burden calculator.

RESULTS: The participants' mean age was 73.08±8.71. The prevalence of polypharmacy was 32.14%. The highest relationship with polypharmacy was observed for drug burden index (DBI) (odds ratio 10.87, p<0.001).

CONCLUSION: Our study demonstrated that polypharmacy and DBI scores were more related than other anticholinergic burden scales in older adults.

Keywords: Anticholinergic burden scales, Elderly, Polypharmacy

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The world's population of older people is growing especially in developing regions [1]. As populations grow older, developing multiple chronic diseases and associated high consumption of drugs among older adults also increases [2]. In this case, it brings major health problems in older adults such as polypharmacy [3], inappropriate drug use [4, 5], and exposure to anticholinergic burden [6]. Polypharmacy results in adverse clinical events, such as depression, cognitive impairment, urine continence problems, malnutrition, and loss of

functionality [7, 8]. For that reason, the assessment of medications of older people is a major and essential part of comprehensive geriatric assessment (CGA).

Older people are frequently exposed to medicines that have anticholinergic properties [9]. The term anticholinergic burden means to point out the cumulative exposure to multiple medicines with anticholinergic properties concomitantly. The anticholinergic burden effect have a wide spectrum of side effects such as dizziness, blurred vision, urinary retention, constipation,



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confusion, and delirium [10, 11]. Higher anticholinergic burden increase the hospitalization risk, functional loss, cognitive decline, morbidity, and mortality [11, 12]. There are several anticholinergic risk scales that have been validated. Anticholinergic risk scale (ARS) [13], anticholinergic drug scale (ADS) [14], anticholinergic cognitive burden scale (ACB) [15], chew scale [16], and drug burden index (DBI) [17] are among these scales. Anticholinergic burden scales differ in their rationale, use and association with clinical outcomes [18] and have weak agreement between each other as they contain different medicines so that comparing the results is so hard [9, 19].

CGA is a time-consuming assessment which can be difficult to spare time for the evaluation of anticholinergic burden of an elderly with all anticholinergic burden scales during a busy clinical day. Understanding the relationship with polypharmacy and anticholinergic burden may help clinicians determine which anticholinergic burden scale can be chosen as a part of CGA. As far as we know, there is no clear evidence about the relationship between these two concepts, polypharmacy and anticholinergic burden. Therefore, the present study aimed to evaluate the relationship between polypharmacy and anticholinergic burden scales among older patients.

MATERIALS AND METHODS

This study included 420 outpatients aged 60 and over. Patients' medical records were inspected retrospectively. Approval was provided from the Dokuz Eylul University Non-Interventional Research Ethics Committee. This study had no exclusion criteria.

Patients' Characteristics

Socio-demographic variables (age, gender, and education), self-reported comorbidities (hypertension, peripheral vascular disease, diabetes, coronary artery disease, cerebrovascular disease, congestive heart failure, hyperlipidemia, thyroid disease, chronic obstructive pulmonary disease, and osteoporosis), and history of falls were evaluated. The Charlson comorbidity index (CCI) was used to evaluate patients' comorbidity status.

The Evaluation of Polypharmacy and Anticholinergic Burden

All drugs used by the patients were evaluated with anticholinergic burden scales and number of drugs was

Highlight key points

- Polypharmacy and anticholinergic burden are both common problems in older adults.
- The prevalence of polypharmacy was 32.14% in this study.
- The highest relationship between polypharmacy and anticholinergic burden scales was with Drug Burden Index (DBI) score.

recorded. Polypharmacy was considered as taking five or more medications daily [20]. Anticholinergic burden is characterized as using medications with anticholinergic adverse effects [21]. Anticholinergic burden scales are the medication lists which classify drugs in accordance with the anticholinergic potency of these drugs. The summation of anticholinergic activity scores of the drugs listed in each scale reflects the potential for negative outcomes [22].

We used ten previously published lists (briefly mentioned below) to determine the anticholinergic burden of the drugs that regularly used. ACB categorizes drugs on a score of 0–3, according to their anticholinergic effects. ACB score 0 represents no anticholinergic effect, ACB score 1 means possible, and ACB scores 2 and 3 show definite anticholinergic effects [15, 23]. ARS [13] consists of 49 drugs with anticholinergic effects and the scale ranks drugs for anticholinergic potency such as score of 0 means no or low risk; score of 1 or 2 means moderate risk; and score of 3 or higher means high anticholinergic potential. Chew's list [16] consists of 107 drugs with anticholinergic activities which were determined in vitro and scores range from 0 to +++; score of 0/+ shows no or minimal anticholinergic activity (AA) and classified as 0.5. ADS [14] is the largest scale which includes 536 drugs and scores of the scale range from 0 (means no known anticholinergic effects) to 3 (means remarkably anticholinergic effects). Anticholinergic activity scale (AAS) [24] is based on serum anticholinergic activity of 107 drugs commonly prescribed for the elderly with Parkinson's disease and scores of the scale range from 0 to 4. Anticholinergic load scale (ALS) [25] is also based on serum anticholinergic activity. The scoring ranges of the Clinician-rated anticholinergic scale (CrAS) [26] and Duran's scale [27] are 0 (no anticholinergic effect) to 3 (strong anticholinergic effect). DBI [17] is a formula to determine the anticholinergic potency by calculating the ratio between the prescribed dose and the sum of the minimum effective dose and the prescribed dose of the drug and consider the daily

TABLE 1. Characteristics and comorbid diseases of the study population (n=420)

Characteristic	Polypharmacy (n=135)	Non-polypharmacy (n=285)	P ₁	P ₂
Age, mean±SD	76.85±7.87	71.5±8.57	<0.001	–
Education years, mean±SD	6.3±4.61	8.35±4.75	<0.001	0.008
Female, %	72	63	0.13	–
Number of drugs, mean±SD	8.1±2.89	1.98±1.5	<0.001	–
Comorbid diseases, %				
Hypertension	77.8	42	<0.001	<0.001
Ischemic heart disease	27.8	5.3	<0.001	<0.001
Congestive heart failure	2.6	3.2	1.0	–
Cerebrovascular disease	11.1	3.2	0.003	0.016
Peripheral artery disease	10.3	4.2	0.003	0.118
Diabetes mellitus	39.3	10.2	<0.001	<0.001
Hyperlipidemia	23.1	11	0.003	0.002
Dementia	23.9	9.1	<0.001	0.004
COPD	22.4	3.5	<0.001	<0.001
Thyroid disease	25.6	12.7	0.003	0.002
Osteoporosis	38.2	17.7	<0.001	<0.001
Falls	45.3	22.3	<0.001	<0.001
CCI, mean±SD	1.34±1.02	0.53±0.86	<0.001	<0.001

SD: Standard deviation; CCI: Charlson comorbidity index; COPD: Chronic obstructive pulmonary disease; SD: Standard deviation; P₁: P-values for comparison of two groups; P₂: P-values for comparison of polypharmacy and non-polypharmacy group after adjusted for age.

dose and the minimum recommended daily dose of the drugs. Anticholinergic burden classification (ABC) [28] is based on the review of serum anticholinergic activity of 27 drugs and scores of the scale range from 0 to 3. Ten anticholinergic burden scales described above were administered for each of the patients' medications by a tool named Anticholinergic Burden Calculator. Anticholinergic Burden Calculator is a web portal software program (www.anticholinergicscales.es/) [29].

Statistical Analysis

Descriptive statistics are presented as mean ± standard deviations (SDs) or percentages. Nominal variables were analyzed with Pearson χ^2 -test or Fisher exact test. Normally and non-normally distributed continuous variables were assessed with t-test and Mann–Whitney U-test, respectively. Age-adjustment analysis was performed with binary logistic regression analysis (P₂-value). Then, the relationships between polypharmacy and each anticholinergic burden scale were analyzed with the binary logistic regression. P<0.05 was considered statistically significant. All statistical analyses were carried out with SPSS version 22.0.

RESULTS

A total of 420 patients older than 60 years were included in the study, 72% of whom were female in polypharmacy group and 63% in non-polypharmacy group. 135 (32.14%) patients were in polypharmacy group and 285 (67.86%) patients were in non-polypharmacy group. Mean age (SD) was 73.08 (8.71). The mean number of drugs (SD) was 8.1 (2.89) and 1.98 (1.5) in polypharmacy and non-polypharmacy group, respectively. The participants' characteristics, comorbid diseases, and CCI are shown in Table 1. There was statistical significance between the two groups according to age, education years, number of drugs, and all of the self-reported comorbid diseases except congestive heart failure (p<0.05 for all). Furthermore, CCI and frequency of falls between the two groups were statistically significant (p<0.001). After the age adjustment analysis, education years and the self-reported comorbid diseases except peripheral artery disease were still significant between the two groups (p<0.05).

The highest relationship with polypharmacy was observed for DBI (OR 10.87, p<0.001). It is found

TABLE 2. The relationship between anticholinergic burden scales and polypharmacy

Scale	Odds ratios	95% CI	p
ACB	2.32	1.764–3.046	< 0.001
ARS	3.11	1.919–5.032	< 0.001
Chew	1.90	1.541–2.345	< 0.001
ADS	2.35	1.785–3.082	< 0.001
AAS	1.44	1.109–1.871	0.006
ALS	3.17	2.163–4.646	< 0.001
CrAS	3.3	2.229–4.871	< 0.001
Duran	3.46	2.173–5.519	< 0.001
ABC	2.14	1.417–3.238	< 0.001
DBI	10.87	5.446–21.680	< 0.001

All adjusted for age. AAS: Anticholinergic activity scale; ABC: Anticholinergic burden classification; ACB: Anticholinergic cognitive burden scale; ADS: Anticholinergic drug scale; ALS: Anticholinergic load scale; ARS: Anticholinergic risk scale; CI: Confidence interval; CrAS: Clinician-rated anticholinergic scale; DBI: Drug burden index.

that each unit increase in DBI increased the risk of polypharmacy 10.86 times. ARS, ALS, CrAS, and Duran scale showed moderate relation with polypharmacy (with odds ratio [ORs] 3.11; 3.17; 3.3; and 3.46, respectively). The relationship between anticholinergic burden scales and polypharmacy is shown in Table 2. The odds ratios of polypharmacy according to the anticholinergic burden scales are shown in Figure 1. The scores of the anticholinergic burden scales according to the polypharmacy and non-polypharmacy are shown in Table 3.

DISCUSSION

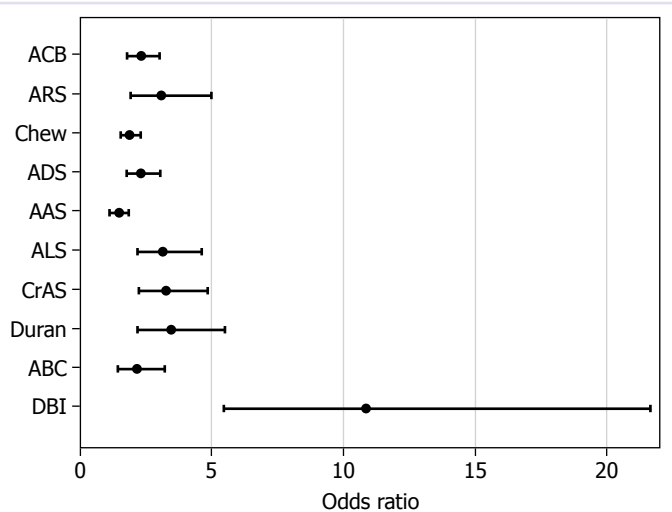
The results of the present study revealed that the highest relationship with polypharmacy was with DBI, while the lowest relationship was with AAS.

As a geriatric syndrome, polypharmacy is prevalent in the elderly and closely related with falls, mood disorders, cognitive, and functional decline [7, 20, 30]. Likewise, anticholinergic burden put older patients at increased risk of negative clinical outcomes such as falls, delirium, hospitalization, functional decline, and negative impact on cognitive functions [11, 12, 27]. Anticholinergic burden and polypharmacy lead in adverse outcomes and functional limitation of older adults and these two concepts are often in close relationship.

TABLE 3. The scores of the anticholinergic burden scales

Scale	Polypharmacy	Non-polypharmacy
ACB	0.99±1.13	0.1±0.47
ARS	0.42±0.74	0.06±0.36
Chew	0.78±1.11	0.2±0.62
ADS	1.04±1.1	0.11±0.43
AAS	0.42±0.88	0.07±0.44
ALS	0.76±0.91	0.09±0.38
CrAS	0.77±0.95	0.08±0.36
Duran	0.6±0.98	0.06±0.3
ABC	0.33±0.92	0.02±0.25
DBI	1.36±1.21	0.04±0.18

AAS: Anticholinergic activity scale; ABC: Anticholinergic burden classification; ACB: Anticholinergic cognitive burden scale; ADS: Anticholinergic drug scale; ALS: Anticholinergic load scale; ARS: Anticholinergic risk scale; CrAS: Clinician-rated anticholinergic scale; DBI: Drug burden index. All data are expressed as means±standard deviations.

**FIGURE 1.** The odds ratios of polypharmacy according to the anticholinergic burden scales.

The prevalence of polypharmacy has been reported to range from 20% to 40% [31]. In this study, the prevalence of polypharmacy was 32.14%. This finding is similar to the previous studies that found the prevalence 30.5% in the United Kingdom [32] and 26.7% in Western countries such as Germany [33]. On the other hand, the prevalence of polypharmacy in the elderly was reported as 54.5% [2] and 55.3% [20] in the studies from Turkey, which is higher than the other European countries.

Several studies have assessed the concordance between anticholinergic burden scales [9, 34–36] and concordance between anticholinergics among potentially inappropriate medications and anticholinergic burden scales [37]. To the best of our knowledge, there are no studies which identified the relationship between polypharmacy and anticholinergic burden scales. We believe that to clarify the relationship between polypharmacy and anticholinergic burden, which are both related to the health status of older adults, will provide future researchers to better viewpoint for the factors affecting the functionality of the older adults exposed to polypharmacy and/or anticholinergic burden.

In the present study, DBI has the highest relationship with polypharmacy. DBI is an evidence-based tool used to evaluate a patient's cumulative exposure to anticholinergic and sedative medicines [17]. Recently, it was reported that number of medicines and the DBI scores were positively associated with evaluation of the level of polypharmacy [38]; on the other hand, population and methodology of this study are different from ours.

ARS, ALS, CrAS, and Duran scale showed moderate relationship with polypharmacy (OR range from 3.11 to 3.46); ACB, Chew, ADS, and ABC showed lower relationship with polypharmacy (OR range from 1.90 to 2.35) whereas the lowest relationship was found for AAS. We may have achieved these results because there are different drugs included in each anticholinergic scale. The number of common drugs in the scales has been reported to be 29 (ADS, ARS, and ACB) while 20 drugs remained if DBI and Summated Anticholinergic Medications Scale were included in the study [34]. ADS and ACB have an acceptable relation in view of the fact that the structure of both scales has identical data and both of them include similar anticholinergic medicines [35].

The large sample size and the usage of ten anticholinergic burden scales are the strengths of the present study. As far as we know, there is no study, which investigates the relationship between polypharmacy and anticholinergic burden assessed by ten different scales; however, there are still some limitations. These are that this study is retrospective, a single-center, and observational study.

Conclusion

The current study has demonstrated that polypharmacy and DBI scores were more related than other anticholinergic burden scales. Although polypharmacy and anticholinergic burden are two different concepts, they are

in close relationship. For a better understanding of polypharmacy and anticholinergic burden, further research is required to evaluate which one is more effective on the functionality and health status of older adults.

Ethics Committee Approval: The Dokuz Eylul University Non-Interventional Research Ethics Committee granted approval for this study (date: 13.09.2018, number: 2018/22-06).

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Authorship Contributions: Concept – ATI; Design – ATI; Supervision – PS; Data collection and/or processing – SKO, OD, AEA, SEK; Analysis and/or interpretation – OD; Literature review – SKO; Writing – SKO, ATI; Critical review – PS, ATI.

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