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Original Article

The drug burden index medication use in older people in north-east Nigeria

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ABSTRACT

Background and Aims: Evidence has shown that physical and cognitive impairment in older people is linked with the Drug Burden Index (DBI). The study aimed to describe the prescription pattern of DBI medications, estimate the frequency of contraindicated DBI medication use, determine the rate of exposure to high-risk DBI medications, and identify the potential predictors of exposure to high-risk DBI medications..

Methods: This one-year retrospective study was conducted in a secondary healthcare facility. It included patients over 65 years of age who were prescribed at least one anticholinergic and/or sedative medication. The study data were summarized using descriptive statistics, while multivariable logistic regression analysis was used to identify potential predictors of exposure to high-risk DBI medications. Statistically, a significant level was set at $p < 0.05$.

Results: Most patients were exposed to cardiovascular drugs (57.5%) followed by antihistamines (25.8%). A total of 23 (6.3%) contraindicated DBI medications were identified. Sixty (19.6%) older patients were prescribed high-risk DBI medications. Patients over 70 years were 3.08 times significantly more likely to be exposed to high-risk DBI medications. Also, patients with a low number of non-DBI co-medications (adjusted odds ratio [AOR] 3.40, 95% CI 1.03 - 11.23), polypharmacy (AOR 7.38, 95% CI 2.20 – 24.73), and those that had contraindicated DBI medications (AOR 3.93, 95% CI 1.14 – 13.53) were significantly more likely to be exposed to high-risk DBI medications.

Conclusion: The study demonstrated that most older people in the study were exposed to anticholinergic medications. A considerable proportion of these older people were exposed to contraindicated and high-risk DBI medications. Patients over 70 years of age, a low number of non-DBI co-medications, polypharmacy, and contraindicated DBI prescriptions were the significant predictors of exposure to high-risk DBI medications.

Keywords: Anticholinergic Medications; Sedative Medications; Drug Burden Index; Older People; North-East, Nigeria

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INTRODUCTION

Medications with sedative and anticholinergic effects pose considerable risk of negative health outcomes in older people (Sumukadas, McMurdo, & Mangoni, 2014). These medications are used to treat a variety of conditions that commonly occur in later life, such as sleep disturbances, nausea, pain, and urinary incontinence (Kouladjian, Gnjidic, & Chen, 2014). It is worth noting that an altered response to medications, in terms of efficacy as well as adverse drug events (ADEs), is an important aspect of the human aging process (Le Couteur, McLachlan, & de Cabo, 2012). The observation that older people are at higher risk of drug-drug interactions, increased comorbidities, and polypharmacy due to age-related alterations in pharmacokinetics and pharmacodynamics, is of clinical importance (McLean, & Le Couteur, 2004; Tinetti, Bogardus, & Agostini, 2004; Hilmer, McLachlan & Le Couteur, 2007). Polypharmacy is the most significant medication-related risk factor for ADEs that require hospitalization (Mannesse, Derkx, & de Ridder, 2000; Onder, et al., 2002; Leendertse, Egberts, & Stoker, 2008; Olivier, et al, 2009). To reduce medication-related problems (MRPs) in the older population, Beers et al. developed criteria that can be used to assess potentially inappropriate prescribing in this population (The American Geriatrics Society, 2019).

Aside from other MRPs, medications with sedative and anticholinergic effects pose significant risks to older people. Older people's exposure to anticholinergic medications is linked to decreased cognitive performance, physical performance, and functional status (Mulsant, et al, 2003; Lechevallier-Michel, Molimard, & Dartigues, 2005; Landi, et al., 2007; Nebes, Pollock, & Halligan, 2007; Han, Agostini, & Allore, 2008). Sedative medications have also been linked to ADEs in older people, including lower levels of physical function, falls, fractures, and cognitive impairment (Cumming, & Le Couteur, 2003; Hilmer, et al., 2007; Hartikainen, Lonnroos, & Louhivuori, 2007; Gnjidic, et al., 2009; Hilmer, et al., 2009). As a result, high-risk prescribing, such as polypharmacy and exposure to medications that increase the drug burden index (DBI), contribute to the downward spiral in physical and cognitive function in older people (Gnjidic, et al., 2009; Hilmer, et al., 2009; Xue, 2011; Lowry, Woodman, & Soiza, 2011). However, in a bid to formulate measures to reduce the irrational use of sedative and anticholinergic medications in older people, a valid method of quantifying the issue and identifying areas for enhanced rational prescribing is required.

The DBI is a pharmacological measure of an individual's exposure to medications with anticholinergic and sedative effects (Hilmer, et al., 2007). This measure provides a model for the measurement of the effects of cumulative exposure to both anticholinergic and sedative medications on physical and cognitive function in older people. The DBI as a clinical risk assessment tool was developed to estimate the risk of physical and cognitive impairment from medications in older people. It is an easy-to-use, evidence-based prescribing tool that can enhance the quality of drug use in older people.

A review of the literature revealed some previous studies on older people's exposure to anticholinergic and sedative medications in some non-African countries (Gnjidic, et al., 2009; Hilmer, et al., 2009; Wouters, van der Meer, & Taxis, 2017; Jamieson, et al., 2018). The paucity of such data from Africa, including Nigeria, justified the need for this study. Therefore, the present study aimed to describe the prescription pattern of DBI medications, estimate the frequency of contraindicated DBI medication use, determine the rate of exposure to high-risk DBI medications, and identify the potential predictors of exposure to high-risk DBI medications.

MATERIALS AND METHODS

Study design and setting

This retrospective study was conducted at a public secondary hospital in Maiduguri, Nigeria. This hospital is currently a 460-bed healthcare facility. It is the primary service and referral hospital for the Maiduguri Metropolis and the entire Borno State in North-East Nigeria. The hospital's General Out-patients' Department (GOPD) served as the study site.

Sample size and patients' selection

The study included all patients that were 65 years old or older who were prescribed at least a sedative or anticholinergic medication in the study hospital's GOPD between January 1, 2019, and December 31, 2019.

Data collection and measurements

A master list of available medications with potential sedative and/or anticholinergic effects in Nigeria was developed (Appendix I) by reviewing previously published studies (Ness, Hoth, & Barnett, 2006; Landi, et al., 2007; Cao, et al., 2008; Duran, Azermai, & Vander Stichele, 2013; Gnjidic, et al., 2013; Salahudeen, Hilmer, & Nishtala, 2015; Byrne, et al., 2018; O'Connell, et al., 2018; Zhang, Zhou, & Li, 2019). Data were taken at a one-time point for each participant. For those who had repeated visits, only data on their last visit were collected. Data including age, sex, marital status, religion, comorbidities, prescribed medications, and dosages were extracted from the patient's medical records.

Definition of variables and data processing

In the present study, medications without anticholinergic or sedative medications were considered as co-medications. Polypharmacy was defined as the presence of five or more medications in a prescription, including anticholinergic and/or sedative medications following previous studies (Bosboom, Alfonso, & Almeida, 2012; Best, Gnjidic, & Hilmer, 2013; Saka, Oosthuizen, & Nlooto, 2018; Akande-Sholabi, Adebusoye, & Olowookere, 2018; Alhawassi, Alatawi, & Alwhaibi, 2019; Assefa, Kedir, & Kahaliw, 2020; Seixas, & Freitas, 2021). The 2019 updated American Geriatrics Society Beers Criteria were used to assess for contraindicated DBI medications (The American Geriatric Society, 2019). An individual's DBI was calculated by adding the burdens from all sedative and anticholinergic medications they take regularly, using the equation below (Hilmer, et al., 2007):

$$\sum D/(\delta+D)$$

Where D is the dose taken in a day, and δ is the lowest licensed dose/day, which is used as an estimate of the dose/

day needed to elicit half of the highest effect at a steady state. In this study, the lowest effective dose for each of the sedative or anticholinergic medications was determined using a Nigerian drug formulary (EMDEX, 2019). For medications administered intravenously, the lowest effective dose/day for the oral route was used. Also, for medications available as combined products, the lowest effective dose/day for the sedative or anticholinergic medication only was used to define the lowest effective dose/day.

The DBI score for a patient is the sum of scores for his or her number of DBI medications in a prescription. In other words, for each patient, the DBI for each medication with anticholinergic and sedative effects in a prescription was calculated and added together. In this study, the DBI score was categorized dichotomously as low-risk (0 > 1), and high-risk (≥ 1). The DBI score 0 > 1 received zero points for logistic regression analysis, while the DBI score ≥ 1 received one point. The variables that were taken into account were classified as follows: age (categorized into 65 - 70 years [reference], and >70 years), gender (female [reference], and male), polypharmacy (no [reference], and yes), anticholinergic exposure (no [reference], and yes), sedative exposure (no [reference], and yes), and Beers criteria (not contraindicated [reference], and contraindicated).

Statistical analysis

Descriptive statistics for continuous data, such as age and DBI scores, were reported as mean ± standard deviation. The frequencies and percentages were used to express categorical data. The association between categorical variables was investigated using Chi-square or Fisher's exact test, as appropriate. The association between patient's variables (sex, age group, and the number of non-DBI co-medications, polypharmacy, anticholinergic prescriptions, sedative prescriptions, and contraindicated DBI prescriptions) and exposure to high-risk DBI medications was investigated using logistic regression. The statistical analysis was done using SPSS (IBM) Statistics for Windows, Version 21.0 (Armonk, NY: IBM Corp). A statistically significant level was set at $p < 0.05$.

RESULTS

The study included 306 patients that were 65 years old or older and were prescribed at least one anticholinergic and/or sedative medication in 2019. A high proportion (64.4%, n=197/306) of the patients were between the ages of 65 and 70 years. Males made up the majority (53.9%, n=165/306), 58.8% (180/306) were married and 92.2% (282/306) practice Islam. The most common chronic disease in the study population was hypertension (52.3%, n=160/306), followed by arthritis (10.5%, n=32/306) (Table 1).

The majority of patients were exposed to cardiovascular drugs (57.5%) and antihistamines (25.8%) (Figure 1).

Out of the 194 cardiovascular medications prescribed, 33.3% were for furosemide and 15.5% were for nifedipine. Out of the 82 antihistamines prescriptions, loratadine constituted 17.4%, promethazine 3.0%, and meclizine 0.8% (Table 2).

Table 1. Background Characteristics of the Study Population (n=306).

Variable	n (%)
Age Group (years)	
65 – 70	197 (64.4)
≥ 70	109 (35.6)
Sex	
Female	137 (44.8)
Male	165 (53.9)
Unreported	4 (1.3)
Marital Status	
Single/Widowed	40 (13.1)
Married	180 (58.8)
Unreported	86 (28.1)
Religion	
Christianity	21 (6.8)
Islam	282 (92.2)
Unreported	3 (1.0)
[+]**Chronic Diseases**	
None	110 (36.0)
Hypertension	160 (52.3)
Arthritis	32 (10.5)
Chronic kidney disease	20 (6.5)
Diabetes mellitus	19 (6.2)
Heart failure	15 (4.9)
Being prostate hyperplasia	10 (3.3)
Asthma	5 (1.6)
[#]Others	8 (2.6)
Number of Co-medications (those without anticholinergic or sedative effects)	
0 – 2	142 (46.4)
> 2	164 (53.6)
Polypharmacy (all medications including those with anticholinergic or sedative effects)	
Yes	122 (39.9)
No	184 (60.1)

[+]Some patients had multiple chronic diseases;
[#]Others=Osteoporosis, Chronic liver disease, Angina, Stroke, Pyelonephritis, and Cancer

Most of the patients (80.1%) were prescribed one DBI medication per prescription, followed by two (19.6%) as shown in Figure 2.

Furosemide was the highest (29.7%) mono DBI medication prescribed followed by loratadine (15.7%), while furosemide and loratadine were the highest (3.3%) among the dual DBI therapy followed by loratadine and codeine (2.9%). The only

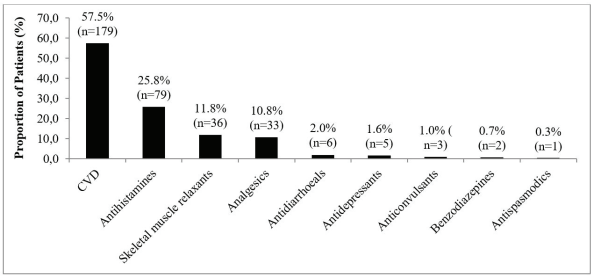

Figure 1. The Distribution of Patients Exposure to DBI Medication Classes (N=306)

CVD: Cardiovascular Drugs

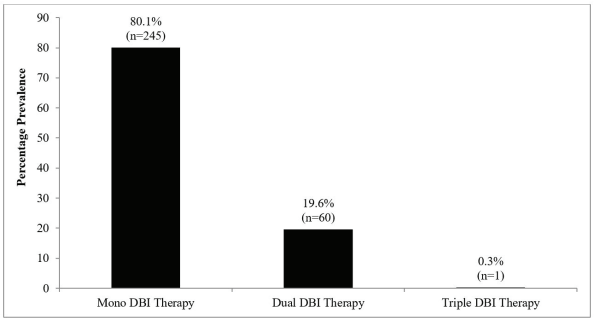

Figure 2. The Distribution of Patients Based on the Number of DBI Medications/ Prescription (n=306).

three DBI medications prescribed concomitantly were nifedipine, furosemide, and codeine (0.3%) as presented in Table 3.

The study identified a total of 23/368 (6.3%) contraindicated DBI medications according to the 2019 updated Beers criteria. The most frequently potentially inappropriate DBI medication in the study population was promethazine (47.8%, n=11/23), followed by amitriptyline (17.4%, n=4/23) (Figure 3).

The average DBI score in the cohort was 0.72 ± 0.28. Out of the 306 individuals prescribed DBI medications in 2019, 296 (96.7%) were exposed to anticholinergic medications, and 41 (13.4%) were exposed to sedative medications alone. Thirty-one (10.1%) were exposed to both anticholinergic and sedative medications. Two hundred and forty-six (80.4%) of the patients were prescribed low-risk DBI medications, while 60 (19.6%) were prescribed high-risk DBI medications. The analysis of prescriptions of both sexes for DBI score medications did not show any significant difference. In contrast, patients aged 70 years or older or with polypharmacy were more often prescribed high-risk DBI drugs ($p < 0.05$) (Table 4).

After adjusting for confounders, the multivariate logistic analysis revealed that patients over 70 years of age, with a low number of co-medications, polypharmacy, and contraindicated DBI medication prescribing were significantly associated with exposure to high-risk DBI medications ($p < 0.05$). Patients over 70 years of age were 3.08 times significantly more likely to be exposed to high-risk DBI medications compared to those 70 years and younger ($p = 0.006$). Patients that had a low number of co-medications were significantly more likely (adjusted odds ratio [AOR] 3.40, 95% CI=1.03 - 11.23, $p = 0.045$) to be exposed to high-risk DBI medications. Similarly, patients with

Table 3. Prescriptions Patterns Based on the Number of Individual DBI Medications Prescribed Per Encounter in 2019 (n=306).

Medication	n (%)
Mono DBI Therapy (n=245)	
Furosemide	91 (30.0)
Loratadine	48 (15.7)
Nifedipine	38 (12.4)
Tizanidine	30 (9.8)
Codeine	8 (2.6)
Hydrochlorothiazide	8 (2.6)
Promethazine	7 (2.3)
Loperamide	4 (1.3)
Amitriptyline	4 (1.3)
Lorazepam	1 (0.3)
Pregabalin	1 (0.3)
Orphenadrine	1 (0.3)
Diazepam	1 (0.3)
Hyoscine	1 (0.3)
Cimetidine	1 (0.3)
Cetrizine	1 (0.3)
Dual DBI Therapy (n = 60)	
Furosemide + Nifedipine	10 (3.3)
Loratadine + Codeine	9 (2.9)
Furosemide + Codeine	7 (2.3)
Furosemide + Loratadine	6 (2.0)
Nifedipine + Codeine	5 (1.6)
Codeine + Tizanidine	3 (1.0)
Furosemide + Hydrochlorothiazide	2 (0.7)
Nifedipine + Hydrochlorothiazide	2 (0.7)
Furosemide + Meclizine	2 (0.7)
Codeine + Hydrochlorothiazide	2 (0.7)
Promethazine + Codeine	2 (0.7)
Furosemide + Pregabaline	1 (0.3)
Nifedipine + Meclizine	1 (0.3)
Furosemide + Tizanidine	1 (0.3)
Furosemide + Cetrizine	1 (0.3)
Furosemide + Baclofen	1 (0.3)
Nifedipine + Amitriptyline	1 (0.3)
Promethazine + Loperamide	1 (0.3)
Promethazine + Gabapentin	1 (0.3)
Tizanidine + Methocarbamol	1 (0.3)
Loratadine + Loperamide	1 (0.3)
Triple DBI Therapy (n=1)	
Nifedipine + Furosemide + Codeine	1 (0.3)

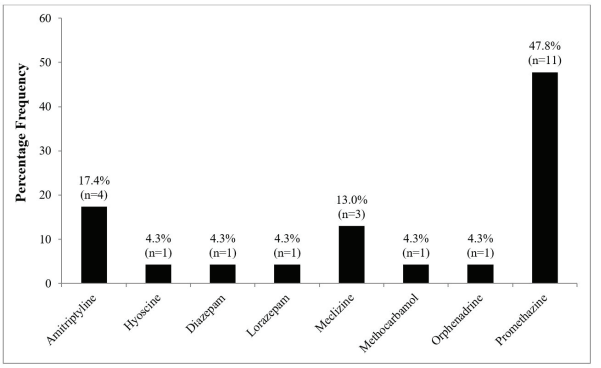

Figure 3. The Distribution of Contraindicated DBI Medications in the Study Population.

polypharmacy were significantly more likely (AOR 7.38, 95% CI = 2.20 - 24.73, p = 0.001) to be exposed to high-risk DBI medications than those with no polypharmacy. Also, patients prescribed contraindicated DBI medications were more likely (AOR 3.93, 95% CI = 1.14 - 13.53, p = 0.030) to be exposed to high-risk DBI medications as compared to those that received recommended DBI medications (Table 5).

DISCUSSION

The study found that most of the patients were exposed to anticholinergic medications with cardiovascular drugs being the most frequently prescribed class followed by antihistamines. More than two-thirds of the study population was prescribed one DBI medication per encounter. In the study population, some contraindicated DBI medications were found, while an appreciable proportion of older people were exposed to high-risk DBI medications, particularly those over 70 years, and those with polypharmacy. Furthermore, after adjusting for confounders, over 70 years of age, low number of co-medications, polypharmacy, and contraindicated DBI medication prescriptions were all found to be significant predictors of exposure to high-risk DBI medications.

In our study, patients' exposure to cardiovascular medications (57.5%, n = 179/306) was significantly higher compared to other DBI medications. This was most likely due to the high prevalence of cardiovascular diseases in the study population. This finding emphasized the importance of prescribing this medication class with caution to older people to avoid adverse effects. A systematic review of hospitalization due to various MRPs identified cardiovascular disease medications as one of the main therapeutic categories linked with MRPs (Al Hamid, Ghaleb, & Aljadhey, 2013). In contrast, the highest exposure to antipsychotics (56.0%, n = 298/532) was observed in the older population in Ireland (O'Connell, et al., 2018), antidepressants other than selective serotonin reuptake inhibitors and sympathomimetics (15.3%, n = 90/589, respectively) in Australia (Gnjidic, et al., 2009), and analgesics in France (Dauphinot, et al., 2014). This variation could be due to varying disease burdens in the study populations. The high exposure to antihistamines (25.8%, n = 79/306) is also noteworthy. Consistent with our result, high use of antiallergic medications (23.2%, n = 184/792) was reported previously in the study area (Okoro, & Shekari, 2013). This may be due to the incessant air pollution of our semi-arid study area with allergens (dust). This finding also highlights the need for rational prescribing of this medication class to older people to prevent negative health outcomes.

In the present study, a considerable proportion of patients (19.9%, n = 61/306) concomitantly used two or more DBI medi-

Table 4. The Distribution of Patients Based on DBI Categories (n=306).

Variables	All Patients n (%)	DBI Category		p-value
		Low (0 > 1) n (%)	High (≥ 1) n (%)	
Sex				
Female	137 (45.4)	111 (45.5)	26 (44.8)	0.927
Male	165 (54.6)	133 (54.5)	32 (55.2)	
Age Group (Years)				
65-70	197 (64.4)	168 (68.3)	29 (48.3)	0.004*
>70	109 (35.6)	78 (31.7)	31 (51.7)	
Number of Co-medications (those without anticholinergic or sedative effects)				
0 – 2	142 (46.4)	112 (45.5)	30 (50.0)	0.553
> 2	164 (53.6)	134 (54.5)	30 (50.0)	
Polypharmacy (all medications including those with anticholinergic or sedative effects)				
Yes	122 (39.9)	91 (37.0)	31 (51.7)	0.037*
No	184 (60.1)	155 (63.0)	29 (48.3)	
Exposure to Anticholinergics				
Yes	296 (96.7)	236 (95.9)	60 (100.0)	0.219
No	10 (3.3)	10 (4.1)	0 (0.0)	
Exposure to Sedatives				
Yes	41 (13.4)	11 (4.5)	30 (50.0)	< 0.001*
No	265 (86.6)	235 (95.5)	30 (50.0)	
Beer's Criteria				
Contra-indicated DBI medication	23 (7.5)	15 (6.1)	8 (13.3)	0.057
Indicated DBI medication	283 (92.5)	231 (93.9)	52 (86.7)	

*Chi-square or Fisher's exact test is significant at p < 0.05

Table 5. Independent Predictors of Older Peoples' Exposure to High-Risk DBI Medications (n=306).

Independent Variables	AOR (95% CI)	p-value
Sex		
Female	1.19 (0.53 to 2.66)	0.674
Male	1.00	
Age Group (Years)		
65 – 70	1.00	
> 70	3.08 (1.38 to 6.89)	0.006*
Number of Co-medications (those without anticholinergic or sedative effects)		
0 – 2	3.40 (1.03 to 11.23)	0.045*
> 2	1.00	
Polypharmacy (all medications including those with anticholinergic or sedative effects)		
Yes	7.38 (2.20 to 24.73)	0.001*
No	1.00	
Exposure to Anticholinergics		
Yes	-	-
No	-	
Exposure to Sedatives		
Yes	326.94 (39.30 to 272.00)	< 0.001*
No	1.00	
Beer's criteria		
Contraindicated DBI medication	3.93 (1.14 to 13.53)	0.030*
Indicated DBI medication	1.00	

*Significant at p < 0.05; AOR; Adjusted Odds Ratio; CI: Confidence Interval

cations comparable with a higher rate of 45.6% (n = 169/371) in a previous Australian study (Wilson, et al., 2011). Concomitant use of DBI medications is of particular concern when the additive effects that result in a high DBI score. It is already known that the older population is more susceptible to the negative outcomes of most medications (Sumukadas, et al., 2014). As a result, the cumulative effect of taking two or more DBI medications together could result in negative outcomes in older patients. Available evidence has demonstrated that increasing DBI is linked to decline in activities of daily living (DBI > 0.8 - 1.65: OR 0.17, 95% CI = 0.08 - 0.25, DBI > 1.65: OR 0.19, 95% CI = 0.09 - 0.29) (Wouters, et al., 2020), greater number of falls (incidence rate ratio [IRR] 1.56, 95% CI = 1.48 - 1.65) (Nishtala, Narayan, & Wang, 2014) and 2.11, 95% CI = 1.47 - 3.04) (Wilson, et al., 2011), greater number of general practitioner visits (IRR 1.13, 95% CI = 1.12 - 1.13) (Nishtala, et al., Narayan & Wang, 2014), increased risk of hospitalization (relative risk [RR] 1.26, 95% CI = 1.18 - 1.35) (Lo¨nnroos, et al., 2012), and mortality (hazard ratio [HR] 1.29, 95% CI = 1.25 - 1.33) (Nishtala, et al., 2014). These findings suggest that in older patients, deprescribing DBI medications might be an option. This is because older people's exposure to these medications may have a significant impact on their health. The rising number of chronic conditions and the aging population necessitates a greater number of medication regimens (or polypharmacy), which may contribute to MRPs in older people. However, the efficacy of some DBI medications is frequently insufficient to overlook the attendant consequences in older people (Glass, Lanctôt, & Herrmann, 2005; Nishtala, et al., 2014). Based on the available evidence, deprescribing some DBI medications may have a positive impact on an older patient's health (Cumming, & Le Couteur, 2003; Garfinkel, & Mangin, 2010). As a result, decreasing the irrational use of these medications in the older population is a critical public health concern.

The prevalence (7.5%) of contraindicated DBI medication noted in the present study population is considerable, although, our study did not assess patients' home medications which may have underestimated this prevalence. The most commonly prescribed contraindicated DBI medications in the study population were promethazine (47.8%, n = 11/23) and amitriptyline (17.4%, n = 4/23). These medications should be avoided in older people due to their highly anticholinergic effects, reduced clearance with advanced age, and higher risk of side effects such as confusion, dizziness, dry mouth, constipation, blurred vision, and other anticholinergic effects or toxicity (The American Geriatric Society, 2019). Therefore, evidence-based alternative medications, along with non-pharmacological approaches when appropriate are recommended to avoid these problems (The American Geriatric Society, 2019).

Our study found that a considerable proportion (19.6%, n = 60) of the study population was exposed to high-risk DBI medications comparable with 33.3% (n = 22/66) in a Finnish study (Lo¨nnroos et al., 2012). In contrast, another study in Finland found a higher prevalence of 35.4% among 257 community-dwelling older people exposed to DBI medications (Gnjidic, Le Couteur, & Abernethy, 2012). Also, a study of 532 older adults with intellectual disabilities exposed to DBI medications in Ireland found a much higher proportion of 69.0% (O'Connell et al., 2018). The observed variations could be due to differences in disease burden, medications prescribed, and methods of prevalence calculation.

When the study data were analyzed for potential independent predictors of high-risk DBI medication exposure, it was discovered that patients over 70 years of age (OR 3.08, 95% CI = 1.38 - 6.89), those with low non-DBI co-medications (OR 3.40, 95% CI=1.03 - 11.23), polypharmacy (OR 7.38, 95% CI = 2.20 - 24.73), and contraindicated DBI medication (OR 3.93, 95% CI = 1.14 - 13.53) had significantly higher odds of exposure to high-risk DBI medications (p < 0.05). In agreement with the finding of the present study, a similar study linked increased DBI medication exposure with increasing age (OR 1.02, 95% CI = 1.02 - 1.02) (Nishtala, et al., 2014). The significantly increased likelihood of being exposed to high-risk DBI medication with a low number

of non-DBI co-medications confirmed that an increasing number of non-DBI co-medications do not translate to increased DBI. In addition, consistent with the finding of the present study, polypharmacy is significantly associated with increased DBI (OR 4.92, 95% CI = 4.86 - 4.98) (Nishtala, et al., 2014).

Furthermore, several studies demonstrated that inappropriate medication use, which included the use of sedative and anticholinergic medications, was linked to increased inpatient visits (OR 1.99, 95% CI = 1.76 - 2.26); increased outpatient visits (OR 1.53, 95% CI = 1.43 - 1.63); increased physician office visits (OR 1.89, 95% CI = 1.55 - 2.30); and increased emergency hospital room visits (OR 1.98; CI = 1.77 - 2.20) (Fick, Mion, & Beers, 2008), a shorter time to hospitalization (HR 1.20; 95% CI = 1.04 - 1.39) (Fillenbaum, et al., 2004), and a higher risk of at least one acute hospitalization (RR 2.03, 95% CI = 1.49 - 2.77) (Klarin, Wimo, & Fastbom 2005). Also, a study showed that a higher DBI was associated with an impairment in cognitive performance which corresponded to lower Mini-Mental State Exam scores (coefficient: –0.161, 95% CI = –0.250 - –0.071) (Kris, et al., 2017). These findings emphasized the potential benefit of clinical medication reviews to stop or reduce the prescribing of unnecessary medications, particularly DBI medications to this high-risk population. Targeted efforts involving a multidisciplinary approach are thus required to reduce irrational use of sedative and/or anticholinergic medications in older people.

The implications of the study findings for practice are: (i) the high use of cardiovascular disease medications and antihistamines, combined with an appreciable concomitant prescribing of two DBI medications, suggest that interventions to educate patients and physicians about the risks associated with sedative and anticholinergic medications in older people should be prioritized. (ii) Regular medication reviews by a clinical pharmacist should also be considered, with a particular emphasis on those over 70 years of age and those with polypharmacy. Also, the DBI can be deployed as a screening tool to identify older patients with high exposure to sedative and/or anticholinergic medications who may have compromised bodily or psychological functions (Wouters, et al., 2017).

To the best of our knowledge, this is the first study in Nigeria to investigate older peoples' exposure to sedative and anticholinergic medications. Secondly, a list of DBI medications formulated in this study may be useful for further DBI studies in Nigeria. The study had some limitations, which includes the inability to review patients' home medications due to a lack of information in the medical records and the retrospective study design. Secondly, a single-center study with a small sample size may have an impact on the generalizability of the findings. Thirdly, while all DBI medications prescribed were included in the analyses, it was impossible to ascertain whether they were dispensed and ingested by the patients, or how long they were consumed. As a result, the DBI calculations may not accurately reflect true exposure. Concerning intention to prescribe, the results, however, reflect prescribing practice. Finally, the DBI medication main list provided in this study was based on medications and dosages applicable to Nigeria.

CONCLUSION

This study demonstrates that most older people were exposed to anticholinergic medications, especially cardiovascular disease medications, and antihistamines. A considerable proportion of these older people had contraindicated DBI and high-risk DBI medications. The significant independent predictors of exposure to high-risk DBI medications identified in our study were over 70 years of age, low number of non-DBI co-medications, polypharmacy, and contraindicated DBI prescriptions. These findings suggest that there are opportunities for interventions targeting these identified significant predictors to ensure rational prescribing in this high-risk population. Future studies on the effects of DBI medications on health outcomes in older people in Nigeria are recommended. Interventional studies to reduce the irrational use of DBI medications in older people are also warranted.

Abbreviations

ADEs = Adverse Drug Events

AOR = Adjusted Odds Ratio

CI = Confidence Interval

CVD = Cardiovascular Drug

DBI= Drug Burden Index

GOPD = General Outpatients' Department

HR = Hazard Ratio

IRR = Incidence Rate Ratio

MRPs = Medication Related Problems

OR = Odds Ratio

RR = Relative Risk

Peer-review: Externally peer-reviewed.

Informed Consent: Written consent was obtained from the participants.

Author Contributions: Conception/Design of Study- R.N.O.; Data Acquisition- A.I.I.; Data Analysis/Interpretation- R.N.O., A.I.I.; Drafting Manuscript- R.N.O.; Critical Revision of Manuscript- R.N.O.; Final Approval and Accountability- R.N.O., A.I.I.

Conflict of Interest: The authors have no conflict of interest to declare.

Ethics Committee Approval: This study was approved by the State Specialist Hospital Research and Ethics Committee (No: SSH/GEN/641).

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Appendix I

Drug class	Anticholinergics	Sedatives
Cardiovascular drugs		
		Methyldopa
	Nifedipine	
		Prazosin
	Furosemide	
	Digoxin	
Antihistamines		
	Imipramine	Imipramine
		Cetirizine
	Chlorpheniramine	Chlorpheniramine
		Loratadine
	Meclizine	Meclizine
	Cimetidine	Cimetidine
	Clemastine	Clemastine
	Clomipramine	Clomipramine
	Prochlorperazine	Prochlorperazine
	Promethazine	Promethazine
	Ranitidine	
	Diphenhydramine	Diphenhydramine
	Hydroxyzine	Hydroxyzine
	Triprolidine	Triprolidine
	Cyproheptadine	Cyproheptadine
Skeletal muscle relaxants		
		Baclofen
	Methocarbamol	Methocarbamol
	Orphenadrine	
	Tizanidine	Tizanidine
Analgesics		
		Codeine
		Tramadol
		Pentazocine
Antidiarrhoeals		
	Loperamide	
Antidepressants		
	Amitriptyline	Amitriptyline
	Paroxetine	Paroxetine
		Citalopram
		Paroxetine
		Escitalopram
		Fluoxetine
		Sertraline
		Venlafaxine

Appendix I. Continue

Drug class	Anticholinergics	Sedatives
Anticonvulsants		
		Amobarbital
		Aprobarbital
		Benzylbutylbarbiturate
		Butabarbital
		Butalbital
		Gabapentin
		Phenobarbital
		Pregabalin
		Secobarbital
		Thiopental
	Carbamazepine	Carbamazepine
		Phenytoin
Benzodiazepines		
		Diazepam
		Bromazepam
		Clonazepam
		Flunitrazepam
		Lorazepam
		Nitrazepam
		Oxazepam
		Temazepam
		Estazolam
		Flurazepam
Antispasmodics		
	Propantheline	
	Oxybutynin	Oxybutynin
	Hyoscine Butylbromide	
	Trihexyphenidyl	
	Benztropine	
Antipsychotics		
	Chlorpromazine	Chlorpromazine
	Olanzapine	Olanzapine
	Fluphenazine	Fluphenazine
		Resperidone
	Trifluoperazine	Trifluoperazine
	Clozapine	Clozapine
	Thioridazine	Thioridazine
		Haloperidol