

Prescription Medication Use in the Oldest Old of South-Central United States

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Abstract

Objectives: To evaluate medication use in the oldest old residing in Arkansas with a retrospective chart review at the University of Arkansas for Medical Sciences. Medical records from individuals aged 95 years or older treated at a medical center between January, 2011 and June, 2013 (n = 121) were reviewed to determine the frequency of medication use and category of medications used.

Results: Of the 121 individuals studied, 13.2 % (n=16) were not on any prescription or over-the-counter (OTC) medications. The remaining 105 patients consumed a mean of 4.8 ± 2.7 prescription medications daily. The most commonly used category of prescription medications were those for cardiovascular health. Seventy six percent of those taking any medication (n=80) took at least 1 antihypertensive daily (ranging from 1-5 daily). Approximately 46% (n=55) were on diuretics and about 11% (n=12) were prescribed an HMG-CoA reductase inhibitor. Medications for endocrine disorders, diabetes mellitus and hypothyroidism were taken by 27% of the subjects who were prescribed any medication. Other commonly prescribed medications for the 105 individuals taking medication included anti-depressants (47%) and opioids (29%). Aspirin was the most commonly used OTC medication at 44%, followed closely by acetaminophen and calcium & vitamin D supplements. Other high frequency OTC included laxatives (34%) and stool softeners (22%). Issues with polypharmacy appear to continue in the oldest nonagenarian and centenarian population. The fact that these individuals still survived beyond the ninth decade speaks to their resilience and favorable genetic profile.

KeyWords: Polypharmacy, Medication use, Oligopharmacy, Elderly, aging, cardiovascular

INTRODUCTION

During recent years, the changing population demographics have extended the range of the geriatric age-groups to include a sizable percentage of nonagenarian and centenarians. In fact, there are currently more than 72,000 centenarians in the U.S. (1-2) and the numbers are likely to rise because of better medical care and a reduction in death rate in both males and females (1-3). There is an inevitable increase of co-morbidity with age and patients over the age of 65 use an average of 2 to 6 prescribed medications and 1 to 3.4 non-prescribed medications (3-5). The prevalence of polypharmacy has been reported to be approximately 40% with a third of residents in long-term

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facilities using 9 or more medications(6-8). The elderly are also more susceptible to adverse drug effects (ADEs) because of multiple physiological changes, including decreased drug elimination rates due to a reduction in metabolism of most of the cytochrome p450 enzymes and reduced renal function (7-12). This frequently exacerbates ADEs in the elderly with unnecessary emergency room visits and hospitalization (10-12). Moreover, with treatment of each additional health condition, the chances of polypharmacy, drug-drug interactions, drug-gene interactions and adverse drug effects get magnified (7, 9-11). Although issues related to polypharmacy are well established in the elderly, there is still a dearth of literature on the use of medications in nonagenarians and centenarians in the U.S. (13-16). There is also sometimes a bias or reluctance of healthcare providers to treat the very old, resulting in oligopharmacy or non-pharmacy (17-18). Hence, under-prescription of potentially useful drugs can also have negative effects on health (17-19). Healthcare providers and pharmacists are becoming more aware of the fact that multiple co-morbid conditions and an altered aging physiology requires careful optimization of medications. Therefore, the emphasis currently is to try to reduce the use of potentially inappropriate medications (PIMs) in the elderly while still avoiding problems of polypharmacy or under-treatment (16-23).

The aim of this study was to evaluate the use of prescription and non-prescription medications in the nonagenarians and centenarians residing in Arkansas, in the relatively under-studied south-central part of the United States.

METHODS

After approval from the University of Arkansas for Medical Sciences Institutional Review Board (UAMS IRB), the researchers conducted a retrospective chart review of the oldest patients treated at the UAMS medical center (IRB protocol # 201959). Electronic medical records (EMRs) were evaluated for patients meeting the inclusion criteria for individuals 95 years of age or older who were seen at least once in the clinic and/or the hospital at the UAMS during the period of January 1, 2011 to June 13, 2013. Medications were defined as prescription and over-the-counter [OTC] products, regardless of the route of administration. Demographic and medication data were collected. Medication information included number of medications per patient and class/category of each medication.

After reviewing each chart and abstracting the appropriate data, the number of medications per individual was calculated. The percent medication utilization by the sample population was evaluated. Also, drugs with the same class/category were combined to assess the most commonly utilized medication in each class/category among the oldest old. Finally, t-tests were run on the data, with significance defined as $p \geq 0.05$.

RESULTS

While the majority of the studied individuals were between 95-98 years old (74%), over 26% were 99 years of age or older. 71% of the subjects were White, non-Hispanic, and 28% were African American. Only 1 subject (0.8%) was identified as Hispanic. The majority of studied individuals were female (83%), while only 17% were male (Table 1). Of the 121 individuals studied, 13.2 % (n=16) were not on any prescription or over-the-counter (OTC) medications (Group A, Table 2). Most of these subjects were 95-98 years of age (62%), White, non-Hispanic (81%), and/or male (69%). The remaining 105 patients (Group B) used a mean of 4.8 ± 2.7 prescription medications daily. They also consumed an average of 3.3 ± 2.1 OTC items each day. The use of a medication in one category did not preclude use of medications in other categories. The most commonly used category of prescription medications were those for cardiovascular health (Table 3). Seventy six percent

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of Group B (n=80) took at least 1 antihypertensive daily (ranging from 1-5 daily). Approximately 46% of this group (n=55) were on diuretics, and about 11% (n=12) were prescribed an HMG-CoA reductase inhibitor. Medications for endocrine disorders, diabetes mellitus and hypothyroidism were taken by 27% of Group B subjects. There were limited prescriptions for insulin (n = 3; 2.6%), metformin (n=2; 1.7%), and levothyroxine (n=9; 7.8%). Other commonly prescribed medications included anti-depressants and opioids; 44.7% (n=47) and 27 % (n=29) respectively. Subjects in Group B were infrequently on medications for dementia and Parkinson's (~22%).

Table 1. Demographics (All subjects)

	N	%
AGE		
95-98	89	73.6
Over 99	32	26.4
RACE		
White	86	71.1
African-American	34	28.1
Hispanic	1	0.83
GENDER		
Male	21	17.4
Female	100	82.6

Table 2. Subjects not on any documented prescribed medications or supplements (Group A). N=16 (13.2%)

	N
AGE	
95-98	10
Over 99	6
RACE	
White	13
African-American	2
Hispanic	1
GENDER	
Male	11
Female	5

Over-the-counter, non-prescription medications were also analyzed (Table 4). Aspirin was the most commonly used OTC medication for Group B at 43.8%, followed closely by acetaminophen (39%) and calcium & vitamin D supplements (38%). Other high frequency OTC included laxatives (34%) and stool softeners (22%).

We also had data on the metabolic profile of this cohort (24). When we compared the sixteen subjects in Group A who took no prescription medications to the rest of the study subjects in Group B, we found that there was a tendency towards higher mean hemoglobin levels (Hb =12.6 ±1.6) and slightly lower triglycerides (TG =106±40.9) in Group A as compared to Group B (Hb=11.7±1.7; TG=121± 82.7). However, these differences were not significant (t-test).

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Table 3. Prescription medication categories for Group B(N=105)

Category	Number of Prescription medications, N	Number of Subjects treated, N (%)
Antihypertensive	110	80 (76.1)
Anti-lipid	12	12 (11.4)
Antiplatelet	6	6(5.7)
Anticoagulants	10	10(9.5)
Antiarrhythmic	10	10 (9.5)
Anti-anginal, nitrates	4	4(3.8)
Diuretics	55	49(46.6)
Antidiabetic	8	7(6.6)
Thyroid replacement	22	22 (20.9)
Acid-suppressants	12	12 (11.4)
Dementia	19	19 (18.9)
Anti-Parkinson's	4	4 (3.3)
Anti-psychotic	6	6 (5.7)
Antidepressant	47	47 (44.7)
Benzodiazepine	11	11 (10.5)
Bisphosphonates	12	12 (11.4)
Inhalers	23	21 (20)
Opioid analgesics	31	29(27.6)
Non-opioid pain (gabapentin)	10	10 (9.5)
Overactive bladder medications	6	6(5.7)
BPH therapy	12	12 (11.4)
Eye	35	18 (17.1)
Antihistamines	20	19 (18)
Anti-cancer, tamoxifen	1	1(0.9)
Anti-seizure (not gabapentin)	4	4 (3.8)
Anti-gout	2	2 (1.9)

Table 4. Over-the-counter medication categories for Group B(N=105)

Category	Number of Over-the-counter medications used, N.	Number of subjects using OTC medications, N (%)
Laxatives	34	34 (32.3)
Stool softeners	22	22 (20.9)
Calcium & Vitamin D	59	40 (38.1)
MVI	38	38 (36.1)
Iron	9	9 (8.5)
Vitamin B	33	33 (31.4)
Omega-3 fatty acids	2	2 (1.9)
Aspirin	46	46 (43.8)
NSAIDs	16	16 (15.2)
Acetaminophen	41	41 (39.0)
Sleep aids	13	13 (12.3)
Acid suppressants	17	17 (16.1)

DISCUSSION

Prescription medication use among nonagenarians and centenarians remains an understudied area in the United States and Europe (13-15). However, with the world's rapidly changing demographics, even developed and developing countries in the East are facing the challenges of polypharmacy (16, 17).

We had previously reported on the well-preserved metabolic health of nonagenarians and centenarians from Arkansas (25). In the current paper, we evaluated all the prescription and the non-prescription or over-the-counter (OTC) medications used by the same cohort of nonagenarians and centenarians and found that the daily prescription medication per individual was slightly lower than expected at 4.8 ± 2.7 prescriptions per person. Interestingly, in our population, there were 13.2% subjects who were not on any documented prescription or OTC medications at all (Group A). Although the number of patients in Group A was too small to be statistically significant ($n=16$), the patients appeared to have a healthier hemoglobin and lipid profile compared to those in Group B, even those who were taking only a single medication. A few studies have reported that centenarians have varying levels of polypharmacy in certain categories, such as cardiovascular medications (27). In a recent large centenarian study from the United Kingdom, a mean of 7 prescription medications/patient were documented (18). In contrast, centenarian Polish consumed a mean of only 2.5 medications (13). A number of factors could have impacted these variations in prescription medications, including cultural differences in populations, physician training, beliefs or biases, health of the population and socioeconomic factors.

The most commonly consumed medications among our study cohort were medications utilized for cardiovascular health. This is consistent with findings currently documented within the United States and Europe, especially considering that cardiovascular disease is the number one killer in the Western hemisphere (6, 13-15, 18, 27). Hence, the high prevalence of hypertension, cardiac arrhythmia, and hyperlipidemia in the elderly might help to drive the justification for cardiovascular medications being used in the very old (6, 26-32). Not surprisingly, over three quarters (76%) of Group B were on anti-hypertensives, the most common being an ace-inhibitor. The findings from the recent Sprint study suggest that intensive control of blood pressure to systolic ≤ 120 in generally healthy elderly was associated with greater reduction in morbidity and mortality (26). Whether this will also apply to the very old will require further investigation. Our previous data on this cohort had revealed a mean systolic blood pressure of 141 ± 24 mmHg and a diastolic of 72.5 ± 12 (25). The use of statins is also controversial in the very old and although moderate doses of simvastatin have demonstrated reduction in rates of myocardial infarction, stroke and revascularisation by about 25% in high risk patients; these findings have not been validated in the nonagenarian and centenarian population (29, 30).

A much smaller segment of patients in our study consumed medications for endocrine disorders. The limited treatment of endocrine disorders within the oldest old population is consistent with other studies and our own data in this cohort demonstrating well maintained metabolic health with generally normal ranges of HbA1C, thyroid function and vitamin D levels (25).

Pain is often under-appreciated in the elderly perhaps because of reduced communication by the older individual or provider bias or fear of prescribing centrally acting drugs which are considered potentially inappropriate medications (Beers list). In our study, surprisingly, antidepressants and opioids were fairly commonly prescribed medications. Based on our results and those of others, one could argue that the use of pain medications with careful monitoring is justified in the very old, and these drugs might actually add to the quality of life of these elderly individuals (7, 9-12, 32, 33). Personalized medication and pharmacogenetic testing can also help minimize drug-drug and drug-gene interactions in instances when the health provider has concerns about the efficacy or side-effects of a required medication in elderly subjects (7, 32, 33).

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The decreased polypharmacy among the oldest old is a likely factor contributing to their longevity which can be inferred from the high percentage of mortality attributed to polypharmacy in various studies (3-5, 10-12). However, molecular factors also influence the response to medications and longevity via their impact on inflammation, protein aggregation, metabolism and drug-gene interactions in various tissues (36-39). A large proportion of OTC medications used by our study population included anti-inflammatory drugs such as aspirin, acetaminophen and non-steroidal anti-inflammatory agents which testifies to the increased inflammation and the inflammatory theory of aging and debunks the telomere theory of longevity(36-39). Nevertheless, anti-inflammatory medications also need to be used with caution in the elderly and even acetaminophen has been associated with increased cardiovascular, gastrointestinal, renal and hepatic side-effects even below the maximum dose of 4 gms/day (40-42).

Other frequently used OTC medications in our study included laxatives, calcium and vitamin D supplements. Because of the changing physiology with age, reduced neural control of gut, slow intestinal transit, use of opioids and other constipating medications, use of laxatives is highly prevalent in the older population (43, 44). Calcium supplementation should also not be undertaken casually since calcium intake was shown to be significantly associated with development of white matter lesions on CT scans and dementia in women (45). On the beneficial side, a recent meta-analysis of studies in the elderly showed that calcium plus vitamin D supplementation produced a statistically significant 15% reduced risk of total fractures and a 30% reduced risk of hip fractures (46, 47). Hence, caution needs to be exercised in dispensing both prescription and non-prescription medications in the oldest old.

LIMITATIONS

A few limitations included the relatively small sample size, reduced representation of other ethnic groups and the retrospective nature of the study with some missing data. However, a unique strength of our study was the robust representation of African American subjects of approximately 30%, which is higher than the national average.

CONCLUSIONS

The results of our study suggest that polypharmacy is still an issue in the oldest old in Arkansas. Nevertheless, a subset of patients in this oldest old cohort were found to not be taking any medications and to still have preserved health. Hence it is entirely possible to be healthy and on no medications as nonagenarians or centenarians. Therefore, we need to exercise caution in prescribing medications in this age group, just as we would in relatively younger geriatric age groups. In addition, age per se should not be a factor in limiting prescription of appropriate medications to the oldest old. As healthcare providers it is our responsibility to evaluate the medication profile of every individual and match it with the physiological and emotional health of the person to ensure that they have the best possible quality of life in their remaining years.

DECLARATIONS

Ethics Approval: Approval from the University of Arkansas for Medical Sciences Institutional Review Board (IRB) was obtained before this retrospective chart review was initiated (IRB protocol # 201959).

Consent to Publish: All authors consent to the publishing of the materials presented in the manuscript.

Consent to Participate: As this was a retrospective analysis, the UAMS IRB determined that consent to participate was not applicable.

Availability of data: The anonymous, de-identified datasets used and/or analyzed during the current study may be available by consulting the corresponding author.

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

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Authors' Contributions: JLH and LJW analyzed some of the data and contributed to the writing. LCH and ETP provided consultation on the medications and the discussion section. AKP maintained the database, assisted with collecting demographic information and submitted the manuscript. JYW, the principal investigator on the grant and GA provided input as geriatricians and were responsible for the concept and design of the overall study, data analysis, and manuscript.

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