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Original Article

Gender difference in drug use in hospitalized elderly patients

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ABSTRACT

Purpose: The aims of this study were to evaluate whether or not there are gender differences in drug use at hospital admission and prescription at discharge and to evaluate the effect of hospitalization on medication patterns in the elderly.
Method: In-patients aged >65 years included in the REPOSI registry during a recruitment period of 3 years (2008–2010–2012) were analyzed in order to evaluate drug use at hospital admission and prescription at discharge according to gender.
Results: A total of 3473 patients, 52% women and 48% men, were considered. Polypharmacy (>5 drugs) is more frequent in men both at hospital admission and discharge. At hospital discharge, the number of prescriptions increased in both sexes at all age groups. Neuropsychiatric drugs were significantly more prescribed in women ($p < 0.0001$). At admission men were more likely to be on antiplatelets (41.7% vs 36.7%; $p = 0.0029$), ACE-inhibitors (28.7% vs 24.7%; $p = 0.0072$) and statins (22.9% vs 18.3%; $p = 0.0008$). At discharge, antiplatelets (43.7% vs 37.3%; $p = 0.0003$) and statins (25,2% vs 19.6%; $p < 0.0001$) continued to be prescribed more often in men, while women were given beta-blockers more often than men (21.8% vs 18.9%; $p = 0.0340$). Proton pump inhibitors were the most prescribed drugs regardless of gender. At discharge, the medication pattern did not change according to gender.
Conclusion: Our study showed a gender difference in overall medications pattern in the hospitalized elderly. Hospitalization, while increasing the number of prescriptions, did not change drug distribution by sex.

1. Introduction

Elderly are the largest medication users in the general population, often taking several different drugs on a regular basis [1,2] Although polypharmacy is the consequence of multiple chronic conditions, socio-demographic factors (including age, sex, education, living and functional status) may have a role in the medication needs and use [3,4]. Gender and sex differences in medication use and prescription represent a complex issue, pertaining also to sex-related physiologic characteristics of drugs metabolism and response [5–8]. In addition, factors such as socio-demographic profiles and living arrangements might play a contributing role in medication pattern in elderly women, in whom widowhood and loneliness are often associated with depressed mood and over-utilization of neuropsychiatric drugs [9–12]. Finally, differences between sexes in risk factor distribution [13] and clinical manifestations [14] of the most frequent chronic conditions such as cardiovascular and inflammatory diseases might have contributed to a model of medication prescription based on physician's misperception of disease gender specificity [15–17]. Women and the elderly are historically under-represented in large clinical trials of pharmacological intervention, mainly in the cardiovascular field, despite the disease global burden being equally represented in women and men [18]. As a consequence, specific pharmacological treatments in women and in the elderly are frequently administered on the basis of indirect evidence. Furthermore until recently epidemiological studies and clinical trials failed to systematically report gender differences in medication profile, leading to a knowledge gap that contributed to an increase of the risk of inappropriate medication use [19,20]. With this background, the REPOSI

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registry [21] was finalized to investigate issues related to multimorbidity and polypharmacy in elderly patients (>65 years) acutely admitted to internal medicine and geriatrics wards in Italy. The aims of this study were to describe whether or not there were gender differences in drug use at hospital admission and in prescription discharge, and to evaluate the effect of hospitalization on medication patterns in the elderly women and men included in this registry.

2. Methods

The REPOSI (REgistro POliterapie SIMI) is a collaborative and independent study of the Italian Society of Internal Medicine (SIMI), IRCCS Fondazione Cà Granda Policlinico and the IRCCS—Istituto di Ricerche Farmacologiche "Mario Negri". The design was described in details elsewhere [21]. Briefly, patients aged 65 years or older consecutively admitted to internal medicine and geriatric wards during 2008, 2010 and 2012 in four periods of four weeks each 3 months apart from each other were included in the registry. Participation was voluntary and all patients provided signed informed consent. The study was approved by the Ethical Committes of the IRCCS Cà Granda Maggiore Policlinico Hospital Foundation, Milan, and of all participating hospitals. All data of the patients included in the 3 years of the REPOSI registry were analyzed according to gender. Medications recorded at hospital admission and discharge were considered and compared between sexes. All drugs were encoded according to the Anatomical Therapeutic Chemical classification system (ATC) (WHO 1990), by first and third levels. Drug distribution by gender at hospital admission and discharge has also been analyzed according to age subgroups (65–69, 70–74, 75–79, 80–84, 85+). Out of a whole population of 4035 subjects recruited in the 3-year study, 3473 were included in this analysis, after exclusion of 158 cases who died in hospital, 339 transferred to other wards, 29 in critical conditions and 36 missing at discharge for whom we didn't have information about drugs at discharge.

Number of diagnoses at admission and discharge was also evaluated by gender. Socio-demographic variables (such as age, education, marital status and living arrangement) were all considered. Data were analyzed according to the cognitive status and mood disorders, as tested by the Short Blessed Test (SBT) [22] and Geriatric Depression Scale (GDS)[23] respectively; and to the functional status at hospital admission measured by means of the Barthel index (BI) [24] classified as mild (BI 75–90), moderate (BI 50–74), severe (BI 25–49) and total dependence (BI 0–24). The Cumulative Illness rating Scale (CIRS-s and CIRS-c) severity and comorbidity indexes [25], were also included in the gender analysis.

3. Statistical analysis

Prevalence was calculated by sex and percentages for categorical variables and mean (standard deviation) for continuous variables were reported. The comparison between groups was made using the chi squared test for contingency tables and the *t* test for the comparison of proportions. A two-tailed *p* value less than 0.05 was considered statistically significant. Analyses were carried out with JMP Pro 11 (SAS Institute Inc.)

4. Results

Socio-demographic and clinical characteristics of the study population according to gender at hospital admission and discharge are shown in Table 1. Overall, women were older than men, the main age difference was among the oldest old (>85 years). A significantly higher proportion of women was widow and living alone. At hospital admission, the mean number of diagnoses was > 5 in both sexes and a higher percentage of men presented 5 or more diagnoses ($p = 0.002$). At discharge, the number of diagnoses increased in both sexes, and again a higher percentage of men reported 5 or more diagnoses ($p = 0.02$). At admission, the CIRS comorbidity and severity index scores were higher in men ($p < 0.0001$): the first increased in both sexes at discharge, the latter remained almost unchanged. Women were functionally more impaired according to the Barthel index (BI) score in all the classified disability categories. SBT and GDS mean scores were also significantly higher in women ($p < 0.0001$). A previous hospitalization within the past 6 months was more frequent in men ($p = 0.002$).

At admission, the mean number of drugs was >5 in both sexes and higher percentage of men reported the intake of 5 or more drugs ($p = 0.005$). At discharge, the mean number of drugs increased in both sexes contributing to a reduction of the gender gap among those patients taking 5 or more drugs, however a higher percentage of men (+3%) reported 10 or more drugs ($p = 0.04$).

Fig. 1A and B show the mean number of drugs by gender at different age groups, at hospital admission and discharge. In both situations, the mean number of drugs is higher in men for all age groups > 70 years, and in women only for the age class 65–69 years. In the 75–79 and 80–84 ($p = 0.02$) age groups the difference was statistically significant. At discharge, the mean number of drugs increased from admission in both sexes for all age groups.

Fig. 2A and B show the drug distribution according to the 1st ATC level analyzed by gender at hospital admission and discharge. At admission, women used more drugs in the anatomical main groups C (cardiovascular system) although not significantly, in group H (systemic hormonal preparations) ($p < 0.0001$) and group N (nervous system) ($p < 0.0001$). At discharge, H and N group drugs were still more prescribed in women. More specifically, among the drugs in the N group, antidepressants (13% at admission versus 14% at discharge) and anxiolytics (13% at admission versus 15% at discharge) were the most prescribed medications. Either at admission and discharge, men were more prescribed with drugs belonging to the main anatomical group A (alimentary tract and metabolism) ($p < 0.04$), B (blood and blood-forming organs) ($p < 0.004$), G (genito-urinary system and sex hormones) ($p < 0.0001$), J (anti-infectives for systemic use) (not significant), M (muscoloskeletal system) ($p < 0.006$), and R (respiratory system) ($p < 0.0001$).

Table 2 shows the distribution of the most frequent diseases at admission according to gender and Table 3 shows the distribution of the 10 most frequently prescribed drugs at hospital admission and discharge. Pattern of diseases distribution approximately reflects the drugs distribution by gender. Hypertension and diabetes are the most frequent diseases at admission for both sexes, accordingly, drugs for cardiovascular diseases were the most prescribed. Specifically, at hospital admission, antiplatelet drugs, ACE-inhibitors and statins were more prescribed in men. On the other hand beta-blockers, dihydropyridine derivatives and angiotensin II antagonists were more prescribed in women, although the difference was not statistically significant. The medication pattern between sexes did not change at discharge. Overall drug prescription increased at hospital discharge compared with admission, but we failed to find a statistically significant difference within sexes. The most marked increase was for proton pump inhibitors (PPI) in both sexes, mostly in women in whom the number of cases on this therapy is about 30% higher than at admission (+264 women). Similarly, with respect to admission women were more prescribed than men at discharge with sulfonamides (+109 subjects), ACE-inhibitors (+83 subjects), vitamin K antagonists (+45 subjects), dihydropyridine derivatives (+26 subjects) and angiotensin II antagonists (+14 subjects). On the other hand, men were more prescribed with statins (+37 subjects). No differences were found for organic nitrates prescriptions.

Fig. 3A and B show the prevalence of patients according to the number of drugs by gender at hospital admission and discharge. The number of women admitted to hospital taking 1 to 8 drugs is higher than that of men, while at discharge the number of men taking 10 or more drugs is higher.