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Mortality, hospitalisation, institutionalisation in community-dwelling oldest old: The impact of medication

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ABSTRACT

Background: High drug use and associated adverse outcomes are common in older adults. This study investigates association of medication use with mortality, hospitalisation, and institutionalisation in a cohort of community-dwelling oldest old (aged 80 and over).
Methods: Baseline data included socio-demographic, clinical, and functional characteristics, and prescribed medications. Medications were coded by the Anatomic Therapeutic Chemical classification. Survival analysis was performed at 18 months after inclusion using Kaplan–Meier, and multivariate analysis with Cox regression to control for covariates.
Results: Patients' ($n = 503$) mean age was 84.4 years (range 80–102), and 61.2% was female. The median medication use was 5 (0–16). The mortality, hospitalisation, and institutionalisation rate were 8.9%, 31.0%, and 6.4% respectively. The mortality and hospitalisation group had a higher level of multimorbidity and weaker functional profile. Adjusted multivariate models showed an 11% increased hospitalisation rate for every additional medication taken. No association was found between high medication use and mortality, nor with institutionalisation. A higher association for mortality was observed among verapamil/diltiazem users, hospitalisation was higher among users of verapamil/diltiazem, loop diuretics and respiratory agents. Institutionalisation was higher among benzodiazepines users.
Conclusion: In the community-dwelling oldest old (aged 80 and over), high medication was clearly associated with hospitalisation, independent of multimorbidity. The association with mortality was clear in univariate, but not in multivariate analysis. No association with institutionalisation was found. The appropriateness of the high medication use should be further studied in relation to mortality, hospitalisation, and institutionalisation for this specific age group.

1. Introduction

The oldest old (defined as individuals aged 80 and over) are characterised by a high level of multimorbidity, resulting in possible high medication intake (Crimmins, 2004; Fulton & Allen, 2002). In this age group, medications are prescribed even though the benefit-risk profile is not always fully understood (Hilmer, McLachlan, & Le Couteur, 2007; Tinetti, Bogardus, & Agostini, 2004). Age related changes in pharmacokinetics and −dynamics alter the sensitivity for the therapeutic effects and often increase the side effects.

High medication use and polypharmacy (defined as the daily intake of five medications or more (Veehof, Stewart, Haaijer-Ruskamp, & Meyboom-de Jong, 2000)), increases the risk of inappropriate prescribing (including overuse, underuse and misuse), drug interactions, and adverse effects in older adults (Hanlon, Schmader, Ruby, & Weinberger, 2001; Manesse, Derkx, De Ridder, Man in't Veld, & van der Cammen, 2000). This can again contribute to drug related problems (DRPs) (Inouye, Studenski, Tinetti, & Kuchel, 2007; Taipale, Hartikainen, & Bell, 2010). DRPs alter the expected bonus of medications on their health into a possible risk. Due to a worsening clinical or functional profile of those aged 80 and more, DRPs will become more prevalent, and potentially impede with the beneficial influence of medications on their health (Best, Gnjidic, Hilmer, Naganathan, & McLachlan, 2013).

Both the beneficial and harmful effects of medication on outcomes have been explored in younger populations (aged 65 and

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over). In this age group, high medication use has been associated with hospitalisation, mortality, and increased health care costs (Meagher, 2001; Stevens, Corso, Finkelstein, & Miller, 2006). In Belgium, medication related hospital admissions account for 20.9% of all hospitalisations in adults aged 65 years and over (Somers et al., 2010).

However, studies exploring the medication use in relation to relevant outcomes in the oldest old (aged 80 and over) are limited, as well as studies exploring the specific role of medications and their effect on outcomes. Studies either failed to disentangle the independent role of medications, due to the strong interrelationship with multimorbidity (Alarcón, Bárcena, González-Montalvo, Penãlosa, & Salgado, 1999; Espino et al., 2006), or studies focussed primarily on the appropriateness of prescribing (Hanlon et al., 2002; Klarin, Wimo, & Fastbom, 2005). Therefore, this study aimed to explore the association of medication use (number of medications, polypharmacy, specific medication groups) in the community-dwelling oldest old (aged 80 and over) with mortality, hospitalisation, and institutionalisation during a follow-up period of 18 months, and taking into account the role of multimorbidity, and demographic, clinical, and functional characteristics.

2. Methods

This study used data of the Belfrail-cohort (Vaes et al., 2010), a prospective, observational population-based cohort study. In summary, eligible patients were adults aged 80 years and older, without known dementia, and not in acute or palliative care. Inclusion of patients was done by general practitioners (Vaes et al., 2010). For this study, all community-dwelling patients with medication records available were selected, yielding the Belfrail-MED cohort ($n = 503$).

2.1. Baseline data

General practitioners and clinical research assistants collected the data (structured questionnaire, clinical examination, and standardised tests). Baseline data collection consisted of socio-demographic, clinical, and functional data described in the baseline study of the Belfrail-MED cohort (Wauters et al., 2016).

Socio-demographic data included age, gender, level of education, whether they lived alone, or received nursing care at home.

Clinical characteristics were collected from the standardised medical history and the list of current medical problems. Multimorbidity was operationalised using the Cumulative Illness Rating Scale (CIRS) (Miller, Rifai, Parrdis, Wouck, & Stack, 1992). The CIRS measures the chronic medical illness burden whiletaking into consideration the severity of chronic diseases. The CIRS counts thenumber of 14 body systems affected with moderate disability, morbidity orextremely severe disease (severity score at least 3) (Hudon, Fortin, & Soubhi, 2007) (possible range: 0–14) (Boeckxstaens et al., 2014).

Functional characteristics included Activities of Daily Living (ADL, derived from the KATZ scale), physical activity (LASA Physical Activity Questionnaire, LAPAQ), cognitive status (Mini Mental State Examination, MMSE, adjusted for age and level of education) (Crum, 1993), and fall risk (Tinetti).

Medication data included all chronic medications at baseline. The brand name, active substance, and the prescribed daily dose were recorded by the general practitioners.

2.2. Follow-up data

Follow-up data was collected using standardised questionnaires, filled in by the general practitioners. The original follow-up period was 5 years. For this study, we defined a cut-off at 18 months, because in longer follow-up periods, associations with baseline characteristics are expected to fade away. Patients who died, who were institutionalised, or were hospitalised during the 18 months follow-up period were considered as 'events'.

The data on mortality included date and cause of death. Data on hospitalisation (defined as unplanned hospital stays lasting longer than 1 day) included the date of the first hospital stay. Institutionalisation was defined as entering the nursing home for permanent stay. The date of entering a nursing home was recorded.

2.3. Medication handling

All drugs were recorded by brand or compound name. They were entered into a data program based on the official register of medications on the Belgian market (source: https://www.ehealth.fgov.be). The medication was translated into the Anatomical Therapeutic Chemical classification (WHO ATC/DDD 2013) ("WHO | The Anatomical Therapeutic Chemical Classification System with Defined Daily Doses (ATC/DDD)," (WHO, 2016)).

For the analysis of the medication use in association with the outcomes, we used three models: the number of medications, polypharmacy, and medication subclasses. Polypharmacy was defined as the chronic intake of $\geq$5 medications [2]. For the medication subclasses, we analysed the first (main anatomical groups) and second ATC level (therapeutical main groups). Subsequently, we analysed medications at the third ATC level (therapeutic subgroup) or lower for medications or medication groups that are specifically mentioned in Potential Inappropriate Medication (PIM) lists (BEERS, STOPP/START) (O'Mahony et al., 2014; The American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012). Additionally, we created a dichotomous variable including all medications with anticholinergic properties, according to the study of Durán, Azermai, and Vander Stichele (2013).

2.4. Functional data handling

The KATZ ADL-scale and the LAPAQ scores were divided into smaller groups to determine those with the highest care dependency, and those with the lowest physical activity respectively.

The KATZ ADL-scale (range 6–30) has six domains (bathing, clothing, toileting, transferring, continence, and feeding), and a higher domain or overall score signifies being more care dependent. We identified those care independent (KATZ ADL score 6, scoring 1 at all six domains), the somewhat care dependent (KATZ ADL scores 7–12), and those most care dependent (scoring 13 and more).

The raw LAPAQ scores (range 0–∞) were divided into quartiles. The lowest quartile was identified as those with the lowest physical activity.

Finally, the MMSE was used for identification of cognitive impairment, with a cut-off adapted to the age and level of education of the respondents (Crum, 1993).

2.5. Statistical analysis

SPSS 21.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

For descriptive statistics means, medians or proportions were used. Comparison of continuous data was done using *t*-tests or non-parametric tests in case of skewed data. Analysis of categorical variables was done using Chi-square tests.

The Kaplan–Meier method was used to estimate survival. For the assessment for the difference of survival between the groups