Increased use of antidepressants at the end of life: population-based study among people aged 65 years and above

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Abstract

Background: the new antidepressants are generally effective and safe for older people, but may have serious side-effects. The use has been rapidly increasing, but focus on upper age groups has been limited. The pattern of antidepressant use as death approaches has never been analysed.

Objective: to analyse the use of antidepressants among individuals aged 65 years and above with respect to time trends, age and proximity to death.

Design: population-based prescription study.

Setting: the County of Funen, Denmark, 1992–2004 (∼470,000 inhabitants).

Results: the 1-year prevalence of antidepressants increases steadily over time in all age groups. Among the 65+ year-olds it also increases with age and differs substantially between the youngest and the oldest. Very high prevalences are observed: 26.8% among females 85–89 years old and 17.5% among males 85 years and above in 2004. In all age groups the use of antidepressants increases substantially with proximity to death in the last 3 years of life. In the last phase of life the use is independent of whether the patient dies at age 65 or 90 about 33% of females and 25% of males receive antidepressants in the last 6 months.

Conclusions: the use of antidepressants among 65+ year-olds increases with age and proximity to death to very high levels. Future studies may clarify the problems and diagnoses giving rise to the use of antidepressants for such a large proportion of older people, and especially the problems giving rise to treatment as death approaches.

Keywords: antidepressive agents, drug prescriptions, aged, death, pharmacoepidemiology, elderly

Introduction

The consumption of antidepressants has increased dramatically over the years. This is particularly due to the selective serotonin reuptake inhibitors (SSRIs) introduced in the late 1980s and a few newer agents/substances. The indications for these drugs have gradually changed, and in addition to major depression, include mild depression, neuropathic pain, panic disorders, most anxiety disorders, eating disorders and treatment of agitation in patients with dementia. Major depression and depressive symptoms are, however, suggested to be the major indication [1]. The SSRIs are considered safer than the tricyclic antidepressants. Side-effects particularly serious for older people have, however, been described, e.g. hyponatraemia [2], upper gastrointestinal bleeding [3], and falls [4]. The high prescribing rates have been of great clinical and public health importance and an
Evidence from psychiatric morbidity surveys suggests that the current level of major depression in the general population is about 5%, but higher in older age groups. European studies have reported point prevalences of 15–20% for people aged 80+ years [5]. For all age groups, many depressed people go undiagnosed and among those diagnosed antidepressants are often not initiated [3–7]. The use of antidepressants for treatment of depression is thus expected to be lower than the prevalence of depression. Drug utilisation studies based on antidepressant prescription data have been carried out in many countries including Denmark [8, 9]. Details about prescribing levels for older age groups have, however, been limited. Upper age groups have been very wide (e.g. 65+ [10], 75+ [11]) and the number of persons very small.

Patient characteristics including comorbidity and prognosis affect prescribing decisions, even for conditions unrelated to a patient’s main medical problem [12]. Prescribing of antidepressants may change as life expectancy shortens. Specific prescribing patterns at the end of life may influence prevalence figures and particularly those for older age groups with high mortality. No previous study has analysed the use of antidepressants in relation to proximity to death despite the fact that it may bring important knowledge to our understanding of the use of these drugs among older people.

Based on pharmacy data covering a population of ∼470,000 people during 1992–2004, the aim of this paper was to analyse the use of antidepressants among individuals aged 65 years and above with respect to time trends, age, and proximity to death.

Methods

The study was based on prescription data and demographic information about all inhabitants in the County of Funen (∼470,000). All data were retrieved from Odense University Pharmacoepidemiologic Database (OPED).

Data

Demographic data containing gender, birth, date of migration and death for all persons living in the county were retrieved for 1992–2004 and linked to individual records on all antidepressants redeemed at all pharmacies in the county. Pharmacy records included date of redemption, patient identification, date of birth, gender, and drug ATC-code1). Of the 1,420,934 prescriptions, the 4.2% redeemed by persons living outside the county at the time of redemption were excluded. The antidepressants were classified into: (i) Tricyclic antidepressants (TCAs), (ii) SSRI, and (iii) other antidepressants. No information on indication or dosing was available.

1Anatomical classification by WHO (10) giving a code for each specific pharmacological substance.

Statistical analysis

The 1-year prevalence of antidepressant drug use was defined as the number of subjects with at least one prescription during a calendar year per 100 inhabitants. Age-specific prevalences were defined with respect to the population at 1 January each year. Due to high mortality in older age groups many subjects do not survive a calendar year. Naive prevalence estimates counting the number of subjects with at least one prescription during a calendar year tend to underestimate the prevalence among age groups with high mortality and comparison across age groups becomes questionable. To overcome this problem, we calculated the prevalence of prescribing as 1 minus the probability of remaining drug free during the year by use of the Kaplan–Meier method. Death and migration were handled as censoring events.

To analyse if the observed age relationship in the general use of antidepressants could be attributable to specific prescribing patterns close to death, we repeated the computations of the 1-year prevalence excluding individuals 1 and 2 years prior to death.

To analyse the effect of proximity to death, we used a retrospective cohort design including people who died in 2001–04. We constructed six observational 6-month windows backwards in time, beginning with patients’ dates of death and ending 3 years prior to death. The proportion of users in each interval was computed. This analysis was restricted to people living in the county during the last 3 years of life. Finally, it was repeated for people who died 1995–98.

All analyses were conducted for males and females separately using age group classification of 20–64, 65–69, . . . , 90–94, and above 95 years. The age group below 65 years was included for comparison. Due to small numbers some upper age groups were pooled for specific analyses. A 95% confidence level was used in constructing confidence intervals (CI).

Results

As illustrated in Figure 1, the 1-year prevalence of antidepressant use increased steadily from 1992 to 2004 in all age groups. A clear age relationship was observed, and the 1-year prevalence peaked at 26.8% among females 85–89 years old and 17.5% among males 85 years and above. The absolute increase was most pronounced among females, and among older compared with younger age groups.

Exclusion of individuals 1 or 2 years prior to death decreased the prevalence estimates up to 2 percentage points, but time trends and the age relationship were not changed (data not shown).

In all age groups the use of antidepressants increased with proximity to death in the last 3 years of life (Table 1). This increase was most pronounced among males. Below the age of 95 years, about 33% of females and 25% of males had received antidepressants in the last 6 months of life. The
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same pattern of use was observed among people who died in earlier years (1995–98), but the levels were lower (data not shown).

The change in the 1-year prevalence of SSRIs and TCAs in the different age groups is shown in Figure 2. In 1992, the TCAs dominated. For all age groups, however, the use of TCAs declined over time. The increase in the SSRIs has been most pronounced among the oldest age groups. In 2004, the 1-year prevalence was highest among older age groups whereas the opposite was true for the TCAs. The pattern shown in Figure 1 is mainly attributable to the increased use of SSRIs over the years.

![Figure 1. Annual prevalence of antidepressant users among inhabitants in the County of Funen, Denmark, 1992–2004 (no. of users per 100 inhabitants per year). The estimated prevalence for the year 2004 is shown with 95% confidence intervals (CI). The number of subjects in each age group refers to 1 January 2004.](image)

![Table 1. The proportion of people who received antidepressants during successive 6-month periods prior to date of death, among inhabitants dying in the period 2001–04](image)
Discussion

This study provides an updated picture of the continuously increasing use of antidepressants among older people in routine clinical practice. The 1-year prevalence of antidepressants increases with age up to very high levels. As death approaches, the use of antidepressants increases regardless of age.

When evaluating the results, a number of issues need to be considered. Indications may differ with age, gender and calendar time and, furthermore, with physical health and comorbidity. Information on disease status or indication for the antidepressant treatment was unavailable as clinical outcome. It is a strength that the analysis is based on 13 years of prescriptions for a large unselected population. We used individual data from a pharmacy database covering all sales of antidepressants for all non-hospitalised persons in the county (considered representative of the Danish population) [13]. The validity and the completeness of the database are very high, and the population well defined by demographic data. Antidepressants purchased outside the county may result in underestimation of the prevalence estimates. Based on the percentage of antidepressants bought in the Funen County by people living in other areas (less than 5%) and the assumption that younger age groups are more mobile than older age groups we have, however, no reason to believe it invalidates our study. The present data allowed us to use the Kaplan–Meier method to estimate annual prevalences. Hence comparison across age groups was reliable despite high, age-related mortality rates. Time trend analyses may have been disturbed by change in official prescribing or redemption rules, but no significant changes occurred.

The positive age relationship observed is consistent with Canadian observations covering 1993–1997 [14], and cross-sectional data from Italy (2001) [15] and Finland (2002) [16]. These studies reported prevalence estimates based on the naïve approach and, thus, to some extent underestimated the prevalence in upper age groups. This study indicates that the use of antidepressants among older age groups has reached a level possibly higher than what may be
expected from our knowledge of depression and treatment rates. The prevalence and age relationship of indications other than depression (anxiety and pain management for example) are uncertain. The indications may co-exist and are not always treatment requiring [17]. The positive age relationship observed was not attributable to the specific pattern of use at the end of life and has to be explained mainly by other mechanisms. Chronic disease, physical health problems and related disability may contribute to the age-related effects on prescribing rates [18, 19]. General practitioners have described late-life depression as part of a spectrum including loneliness, lack of social network, and reduction in functioning [20]. Antidepressants may be tried for relief of sadness and loneliness. Patients unlikely to benefit from the drugs are exposed to side-effects and the potential for interactions with other medications. In some cases, antidepressants may be prescribed instead of a more supportive intervention.

Generally little is known about depression during the last years of life other than it is associated with a host of prevalent medical conditions. Specific groups of patients have been studied, e.g. patients with congestive heart failure. Their depression scores have been shown to increase during the last months of life [21]. In palliative care settings the point prevalence of depression has been estimated at 15–30% [22]. Neither the patient nor the caregivers may be aware that death approaches, and remaining lifetime is relatively unpredictable for most older people. For terminally ill cancer patients clinicians’ survival predictions have, however, been shown to be correlated with actual survival [23]. Our findings suggest that antidepressants are used for treatment of problems associated with end of life. Whether antidepressants are the appropriate treatment is still to be proved. The use of antidepressants in the last phase of life seemed independent of whether the patient dies at age 65 or 85 years which is consistent with a study showing that the number of days spent in hospital during the last years of life is independent of age [24]. What may explain the somewhat lower use of antidepressants among the 95+ year-olds during last years of life has to be investigated in further studies.

The 1-year prevalence of antidepressant prescribing differed substantially between people below and above 65 years, and specifically between the younger and the older of the 65+ year-olds. This study underlines the importance of focusing on older people in drug utilisation studies. Important knowledge may otherwise be lost [25]. Interpretation of prescribing patterns in inhomogeneous populations defined by wide age groups should be made cautiously. We furthermore conclude that by taking into account proximity to death one may gain new and clinically relevant insight into the use of specific drugs among older people.

The use of antidepressants for older people may be substantially different in healthcare systems other than the Danish. The consumption of antidepressants is, however, generally high in many countries and the levels in Denmark are not unique [14, 26]. This is the first population-based study aiming to analyse the use of antidepressants as death approaches, and the results deserve to be replicated in other contexts. The findings presented have important implications for society, clinicians and policy makers. The prescribing rates for older people are shown to be very high particularly close to death. Future studies may clarify the problems and diagnoses giving rise to the frequent prescribing for the old and especially as death approaches.

**Key points**

- Focus on older people has been lacking in most antidepressant drug utilisation studies and the use when death is approaching has never been analysed
- The use of antidepressants continues to increase in all age groups
- Among the 65+ year-olds, the use of antidepressants increases with age to levels much higher than what may be expected
- The use of antidepressants increases during the last 3 years of life irrespective of age: 33% of females and 25% of males had antidepressants during their last 6 months of life
- It is important to explore the reasons for prescribing antidepressants for so many older people, and especially the problems giving rise to treatment as death approaches.

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**Conflict of interest**

None.

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