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Original article

Treatment patterns and costs in patients with generalised anxiety disorder: One-year retrospective analysis of data from national registers in Sweden

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ABSTRACT

Purpose. – To investigate medication use, direct healthcare costs and comorbidities in patients with generalised anxiety disorder (GAD) within specialised care in Sweden 2006–2007.
Methods. – A retrospective study was conducted using data from the National Patient Register and the Swedish Prescribed Drug Register. All patients with a primary GAD (ICD-10) diagnosis in 2006 were followed for 12 months to study medication use and health care consumption. Resource use was evaluated from the number of hospitalisation episodes, number of visits to outpatient care and medication dispensed. Costs were calculated by multiplying the number of visits and hospitalisation episodes with the corresponding unit costs. Descriptive statistics were used for all analyses.
Results. – Three thousand seven hundred and one patients with a primary GAD diagnosis were included in the study. Thirty-four percent of the patients ($n = 1246$) had at least one secondary comorbid diagnosis. SSRIs/SNRIs were the most commonly dispensed medications, followed by benzodiazepine-anxiolytics, hypnotics and antihistamines. The mean number of treatment days for all medications prescribed and dispensed was highest (1144 days) for elderly women aged 65 years or more (treatment days per patient could exceed 365 days due to multiple concomitant medication use). Elderly patients were frequently prescribed benzodiazepine-anxiolytics ($n = 92/117$ men [79%]; $n = 238/284$ women [84%]) and hypnotics ($n = 70$ men [60%]; $n = 178$ women [63%]) compared to the overall study population ($n = 612/1303$ men [47%] and $n = 935/2398$ women [39%], respectively). GAD-related direct costs accounted for 96% of all direct costs. Mean number of hospitalisation days and corresponding costs were high (19 days; SEK 92,156; $n = 358$ [9.7%]) in relation to medication (SEK 5520; $n = 3352$ [91%]) and outpatient costs (SEK 7698; $n = 3461$ [94%]).
Conclusions. – The high rate of polypharmacy, significant psychiatric comorbidity and widespread use of benzodiazepine-anxiolytics and medications not indicated for GAD suggest that the disease burden is high. Total direct costs associated with the disease were high but still likely to be underestimated.

1. Introduction

Generalised anxiety disorder (GAD) is a chronic anxiety disorder defined as excessive and uncontrollable worry about everyday life situations. GAD is one of the most common anxiety disorders seen by primary care physicians, although it is frequently under-recognised and often misdiagnosed [36,46]. European epidemiological data suggest that around 2% of all adults are affected over a 12-month period and that women are two to three times more likely to suffer from GAD as men [25]. Lifetime estimates of the prevalence of GAD vary, but are generally within the range of 2–6% among the adult general population worldwide [24,25,47]. Prevalence rates are particularly high in midlife and in the elderly [46]. In one study, GAD was the most frequently reported anxiety disorder among Dutch patients aged 55 to 85 years [7], and around half of elderly individuals with GAD in a US sample reported late-onset GAD [13]. In Scandinavia, GAD and/or depression prevalence is high and up to one-half of the cases were identified by general practitioners in one study [29].

The human and economic burden of GAD is high. GAD adversely affects work performance and psychosocial functioning, increases disability and has a significant impact on health-related quality of life, particularly later in life [33,34]. Patients with GAD also experience a high degree of comorbidity. Around 90% present with at least one additional lifetime psychiatric disorder [47], and lifetime comorbidity with depression is approximately 60% [22]. Somatic conditions such as chronic pain, gastrointestinal disorders, diabetes and cardiac symptoms are also frequently reported

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[10,14,18]. Consequently, GAD is associated with considerable economic costs as a result of lost work productivity and high levels of medical resource utilisation [19].

Treatment strategies for GAD have changed considerably over the past 10 years. Current evidence-based guidelines recommend initial treatment with an antidepressant, either a selective serotonin reuptake inhibitor (SSRI) such as sertraline, paroxetine or escitalopram, or a serotonin noradrenaline reuptake inhibitor (SNRI), either duloxetine or venlafaxine [5,6]. The calcium channel modulator pregabalin was also approved for GAD in 2006 and is recommended as a first-line treatment by the World Federation of Societies of Biological Psychiatry (WFSBP) [6]. Benzodiazepine-anxiolytics are indicated as a short-term strategy to obtain immediate symptomatic relief, but their use is not generally recommended for more than a few weeks. Treatment guidelines are useful tools for assisting physicians in clinical decision-making. However, recommendations are largely based on the results of controlled trials in highly selected symptomatic patients and do not necessarily mirror real-life situations for the prescription of medication in GAD patients with multiple comorbid conditions [1]. A recent evidence-based review on the pharmacotherapy of GAD was published in January 2011 [5]. The authors concluded that there have been few investigations of the management of patients who have not responded to first-line treatment, despite the fact that switching to another evidence-based treatment or use of augmentation strategies may be beneficial.

Several studies have investigated healthcare costs associated with GAD [9,19], but few studies have been conducted anywhere on treatment patterns and resource utilisation in patients in specialised care. Moreover, the economic burden of GAD in Sweden is currently unknown. Therefore, the aim of this study was to investigate medication use, direct healthcare costs and comorbidities in patients with a primary ICD-10 GAD diagnosis within specialised outpatient and inpatient care in Sweden between 2006 to 2007.

2. Methods

2.1. Study population

This was a retrospective study that combined data from the National Patient Register and Swedish Prescribed Drug Register [44]. The study was approved by the Regional Research Ethics Review Board (Stockholm, Sweden). Source data are the property of the National Board of Health and Welfare, Sweden. Data were made anonymous prior to analysis. All patients who were recorded with an ICD-10 diagnosis of GAD F41.1 in specialised care in Sweden during 2006 were eligible. Patients were identified from the National Patient Register, which covers all inpatient care episodes and most specialised outpatient care visits, and records both primary and secondary diagnosis codes. A primary diagnosis is defined as the main diagnosis for which the patient is treated at a given visit; a secondary diagnosis is any other diagnosis registered by the physician that is not the main reason for treatment. A total of 5284 patients with primary/secondary GAD were recorded. However, in order to reduce sample heterogeneity, only data for patients with a primary GAD diagnosis were included in the final analysis population.

2.2. Data and statistical methods

Patients were monitored in the registers for 12 months after the first inpatient or outpatient visit with GAD as a primary diagnosis during 2006, which were the study inclusion criteria. The primary study outcomes were medication treatment patterns and resource use. Data on medication use were obtained from the Swedish Prescribed Drug Register, which stores records of the date and amount of prescription drugs dispensed by pharmacies to individuals. These data were linked to data from the National Patient Register via personal identification numbers. Medications were grouped into pharmacological categories (Table 1) and treatment patterns studied using descriptive statistics. Only psychoactive medications were included in the analyses, i.e. substances that act primarily on the central nervous system to alter brain function, resulting in changes in perception, mood, consciousness, or behaviour [38]. Dispensed prescriptions were recorded with the dose schedule, number of packages and number of tablets per package; from this, the number of treatment days for each patient was calculated by medication and pharmacological category. The sum of treatment days per patient could exceed 365 days when medications were used in parallel, or if prescriptions were allocated for a longer duration than our study period of 12 months.

Resource use was evaluated from the number of hospitalisation episodes and number of visits to outpatient care. Records for hospital admissions and outpatient visits were obtained from the National Patient Register. An inpatient care record covered one inpatient episode and its duration (in days), starting from the point of inpatient admission and ending with inpatient discharge. An outpatient visit was defined as an occasion where a patient was seen by a specialist in public outpatient care. Outpatient visits and inpatient episodes were categorised as either GAD- or non-GAD-related; visits/episodes recorded with a primary diagnosis other than GAD were classified as non-GAD-related. Outpatient and inpatient costs were calculated for the 12-month period following the date in 2006 of the first recorded primary GAD diagnosis. Outpatient costs were calculated by multiplying the number of visits with the corresponding unit cost. Inpatient costs were calculated by multiplying the number of inpatient days with the corresponding cost per bed-day [39,41]. The length and number of

Table 1
Medication categories.

Drug category	
SSRIs	Escitalopram, paroxetine, sertraline, citalopram, fluoxetine, fluvoxamine
SNRIs[a]	Venlafaxine, duloxetine, mirtazapine, mianserin
Antiepileptics	Pregabalin, gabapentin, lamotrigine
TCAs	Clomipramine, nortriptyline, amitriptyline, trimipramine
Phenothiazines	Chlorpromazine, haloperidol, flufenazine, levomepromazine, perfenazine, prochlorperazine, flupentixol, chlorprotixene, zuclopentixol
Antipsychotics	Quetiapine, olanzapine, risperidone, ziprasidone, aripiprazole, sertindole, clozapine
BZD-anxiolytics	Diazepam, oxazepam, alprazolam, lorazepam
Hypnotics	Flunitrazepam, nitrazepam, triazolam, zaleplon, zopiclone, zolpidem
Antihistamines	Propiomazine, alimemazine, promethazine, hydroxizine
Other	Buspirone

SSRIs: selective serotonin reuptake inhibitors; SNRIs: selective noradrenaline reuptake inhibitors; TCAs: tricyclic antidepressants; BZD: benzodiazepine.
[a] Includes mirtazapine and mianserin (act by modulating synaptic turnover of noradrenaline and serotonin).