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Psychopharmacological treatment in children and adolescents with autism spectrum disorders in Germany

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ABSTRACT

Data on psychopharmacological treatment of individuals with autism spectrum disorder (ASD) are scarce, especially for European countries. This study evaluated psychopharmacotherapy utilisation in children and adolescents with a diagnosis of ASD in Germany. Data of a large statutory health insurance company were analysed and outpatients aged 0–24 years with a diagnosis of ASD during a 1-year-period (2009) were identified. For this cohort, the prescription of psychopharmacotherapy was evaluated. Additionally, we analysed time trends in prescriptions from 2004 to 2009. One thousand one hundred twenty-four patients (75.4% male; mean age: 11.1 years) matched the inclusion criteria. The prevalence of ASD was 0.37% in males and 0.12% in females, respectively. Of all ASD patients, 33.0% were prescribed psychotropic drugs in 2009. 12.5% of ASD patients were treated with stimulants or atomoxetine, 11.7% with antipsychotics, 9.1% with antiepileptics, 6.8% with benzodiazepines, and 3.8% with antidepressants/SSRI. Regarding substances, methylphenidate (24.4% of all psychotropic prescriptions), risperidone (13.3%) and valproate (9.1%) were most frequently prescribed. Psychopharmacologic treatment prevalence was age-related and increased from 16.3% in individuals aged 0–4 years to 55.1% in 20–24 year olds. From 2004 to 2009, the proportion of ASD patients treated with psychotropic drugs rose from 25.9% to 33.0%. This naturalistic study furnishes evidence that the proportion of ASD patients treated with psychotropic drugs has grown considerably in Germany over the least years, with methylphenidate and risperidone being the most frequently prescribed substances. Compared with data from the USA, the proportion of ASD patients with psychopharmacological treatment is noticeably lower in Germany.

1. Introduction

The term "autism spectrum disorders" (ASD) summarises a range of pervasive developmental disorders, including (amongst others) the diagnostic categories of DSM-IV "autistic disorder", "Asperger disorder/syndrome" and "pervasive developmental disorder, not otherwise specified" (Wing, Gould, & Gillberg, 2011) and the ICD-10 diagnoses "childhood

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autism" (ICD-10 code: F84.0), "atypical autism" (ICD-10 code: F84.1), "Asperger's syndrome" (ICD-10 code: F84.5), "other pervasive developmental disorders" (ICD-10 code: F84.8) and "pervasive developmental disorder, unspecified" (ICD-10 code: F84.9). Core features of ASD are social interaction deficits, impaired communication and language skills and stereotyped or repetitive behaviours and interests; about 50% of ASD patients have mild up to severe intellectual disabilities (Charman et al., 2011).

In a systematic review of thirty-two surveys from the years 1966–2001, the prevalence of ASD was 0.7–72.6 per 10,000 individuals, with a median prevalence (calculated from studies published between 1992 and 2001) of 12.7 per 10,000 (Williams, Higgins, & Brayne, 2006). ASD show a marked male preponderance, with the male-to-female ratio ranging from about 4:1 in ASD to 10:1 in high-functioning autism or Asperger's syndrome (Fombonne, 2009). Up to 70% of patients with ASD exhibit psychiatric comorbidities, e.g. ADHD, anxiety disorders, conduct disorder, schizophrenia or depression, which are persistent from childhood to adolescence (Simonoff et al., 2008; Simonoff et al., 2013). Sleep disorders and epilepsies are also more frequent in individuals with ASD (Bolton et al., 2011; Souders et al., 2009).

Despite large efforts to identify effective pharmacological substances for the treatment of the core symptoms of ASD (e.g. Hampson, Gholizadeh, & Pacey, 2012), to date no pharmacological treatment for these symptoms is available. However, for the aforementioned comorbidities, psychopharmacological treatment is recommended in current guidelines (e.g. DGKJP, 2007; for an overview of current treatment strategies: McPheeters et al., 2011). Nevertheless, the level of evidence for the majority of those treatments is only moderate (Hurwitz, Blackmore, Hazell, Williams, & Woolfenden, 2012; McPheeters et al., 2011; Williams, Wheeler, Silove, &Hazell, 2010). This can be attributed to different factors, e.g. scarcity of well-designed clinical studies in this population (Reichow, 2012) or non-effectiveness of substances that are effective in non-ASD patients (e.g. King et al., 2009; Williams et al., 2010). Besides, a significant proportion of ASD patients receive also complimentary or alternative medication (Anagnostou & Hansen, 2011).

In Germany, no medication is approved especially for treatment of autistic children; in the USA, the FDA has approved risperidone for the treatment of irritability in autistic children and adolescents (FDA, 2006).

Regarding the pharmacoepidemiology of ASD, there exists a small, but growing body of literature: starting with the study of Aman, van Bourgondien, Wolford, and Sarphare (1995), there is now a variety of studies that have been performed in difference settings (inpatient, outpatient and both) and that are based on different information sources (e.g. internet surveys or healthcare insurance data sets) and differing samples with respect to age ranges, diagnoses and sample sizes (see Table 1). The to date largest study (Mandell et al., 2008) found in a nationally representative sample of sixty thousand six hundred forty-one US-American Medicaid patients with ASD a prevalence of psychotropic medication of 56% during a 1-year period (2001). In that study, the substance group most frequently prescribed was antipsychotics (31%), followed by antidepressants (25%) and stimulants (22%). With only few exceptions (Baghdadli, Gonnier, Valancogne, & Aussilloux, 2005; Memari, Ziaee, Beygi, Moshayedi, & Mirfazeli, 2012), the vast majority of studies on psychopharmacology use in ASD have been conducted in the USA, so there is a significant lack of data for European countries. This lack of data is regrettable, especially as prescription patterns in child and adolescent psychiatry tend to show quite significant differences between Europe and the USA (Zito et al., 2008). Also, there is a scarcity of studies reporting longitudinal trends in ASD pharmacoepidemiology.

The main objective of this study was therefore to assess cross-sectionally psychopharmacological medication in child and adolescent outpatients with diagnosed ASD with respect to age and sex. The second goal was to evaluate time trends in medication patterns in this patient group.

2. Experimental procedures

2.1. Database and identification

We conducted a cross-sectional study using claims data of the statutory health insurance company Gmünder ErsatzKasse (GEK) for the year 2009. In the corresponding year, the GEK insured 1.8 million persons living in all regions of Germany.

We included all individuals aged up to 24 years that were insured at least one day in all four quarters of 2009. Due to this criterion, the vast majority of our population at risk was continuously insured throughout the whole year.

Subsequently, we identified outpatients with ASD who received at least one of the following diagnoses in the corresponding year coded according to the German modification of the International Classification of Diseases (ICD-10 GM):

- Childhood autism (ICD-10 code: F84.0)
- Atypical autism (ICD-10 code: F84.1)
- Asperger's syndrome (ICD-10 code: F84.5)
- Other pervasive developmental disorders (ICD-10 code: F84.8)
- Pervasive developmental disorder, unspecified (ICD-10 code: F84.9)

Within this cohort, we calculated the annual prevalence of psychopharmacological treatment to be comparable with published studies. To evaluate time trends, this procedure was also computed for the years 2004–2008.

We selected all psychotropic substances according to the anatomical therapeutic chemical (ATC) code "N" (nervous system) but excluded anaesthetics (ATC-code: N01) and analgesics (ATC-code: N02). Furthermore, the following groups were analysed separately: antidepressants (ATC-code: N06A), antipsychotics (ATC-code: N05A), anxiolytics/tranquiliser