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Antiepileptic drugs with mood stabilizing properties and their relation with psychotropic drug use in institutionalized epilepsy patients with intellectual disability

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ABSTRACT

A large number of patients with epilepsy and intellectual disability take medication, amongst which antiepileptic and psychotropic drugs, often simultaneously. Certain antiepileptic drugs have mood-stabilizing properties, e.g. carbamazepine, valproic acid and lamotrigine. The aim of this study was to investigate whether the use of these mood-stabilizers is associated with a different use of psychotropic drugs in a population of institutionalized epilepsy patients with intellectual disability.

We performed a retrospective, cohort study of adults with intellectual disability and epilepsy at the long-stay department of an epilepsy centre in The Netherlands. 246 residents were included.

In patients using lamotrigine we found a statistically significant lower use of antidepressants. We also found significant less prescriptions of anxiolytics in patients using AEDs with mood-stabilizing properties (carbamazepine, valproic acid and lamotrigine). When considering the effect of gender, we found that male patients took significantly more antipsychotics. Most important, we found an inverse relation between the drug load of carbamazepine and/or valproic acid and/or lamotrigine and the use of psychotropic drugs. In a population of institutionalized epilepsy patients with intellectual disability, higher drug loads of mood-stabilizing antiepileptic drugs correspond with less use of psychotropic drugs.

1. Introduction

Epilepsy is a common condition in patients with intellectual disability (ID). The prevalence of epilepsy in mild ID (IQ 50–70) is 6%, for moderate/severe ID (IQ < 50) it is approximately 24% and for profound ID (IQ < 20) 50% (Lhatoo & Sander, 2001). Prevalence rates of epilepsy show an inverse relationship with the level of ID: in people with profound ID there is a high prevalence of epilepsy (53%) and in people with mild ID prevalence is lower (18.9%) (McGrother et al., 2006).

Psychopathology is common in people with epilepsy and also in people with ID. In a population-based study Cooper, Smiley, Morrison, Williamson, and Allan (2007) found that 40% of people with ID suffered "mental ill-health", with problem

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behaviour (22.5%) as the most frequently reported disorder. In a Dutch study, the prevalence of psychopathology in ID is 26.3% for affective symptoms, 21.3% for psychotic symptoms, 52.9% for anxiety symptoms and 43.1% for aggressive symptoms (Stolker, Koedoot, Heerdink, Leufkens, & Nolen, 2002). According to a study of Lott et al. (2004), 40% of the individuals with intellectual disabilities and developmental disorders (IDDD) had a psychiatric disorder. This represented a three/four-fold increase compared to the non-IDDD population.

For patients with epilepsy the reported prevalence of psychiatric disorders differs widely (from 6% to 74%), due to varying definitions of psychopathology (Matsuura et al., 2003). In one review (Gaitatzis, Trimble, & Sander, 2004) about patients with epilepsy in the general population, 6% suffered from a psychiatric disorder. This percentage increases up to 10–20% in populations with temporal lobe and/or refractory epilepsy. Recently, Turky, Felce, Jones, and Kerr (2011) found a seven-fold increased risk for psychiatric disorders in adults with ID and epilepsy, compared to adults with ID, but without epilepsy. The group of adults with ID and epilepsy also showed significantly higher scores on unspecified symptoms and depression symptoms. Not every study reports higher prevalence rates for psychiatric disorders in patients with epilepsy. A European cohort study concluded that for anxiety, a rate of 4.4% was found in the control group vs. 1.8% in the group of patients with epilepsy (van den Broek & Beghi, 2004). Depression was reported in 3% of the epilepsy group vs. 2.9% of the control group. For the total of psychiatric disorders they reported 5.7% in patients with epilepsy and 7.7% in the control group. They also found psychiatric morbidity to be higher in patients with brain dysfunction, uncontrolled epilepsy and multiple drug regimens (Beghi, Cornaggia, & the RESt-1 Group, 2002). Most of the epilepsy patients with ID have one of these three factors. In a recent study by Arshad et al. (2011), two groups of adults with ID were compared, with the presence of epilepsy as varying factor. They report no evidence for increased risk of psychopathology in the ID population with epilepsy. They even found significantly lower scores for rates of mental health problems in the epilepsy group. Their explanation for these findings is not only limited to varying definitions of psychopathology. They also ascribe their findings to the tranquilizing effects of AED on behaviour, and (therefore) fewer need of psychotropic drug use.

Psychopathology can be treated in different ways, drugs are used frequently. Useful drugs are antipsychotics, antidepressants, anxiolytics, lithium, psychostimulants and – remarkably – some antiepileptic drugs (AEDs). The use of psychotropic drugs (not including AEDs) in ID is high, 12–40% in institutions (Singh, Ellis, & Wechsler, 1997). Therefore, it is relevant to explore the relation between the use of certain AEDs and psychotropic drugs. Carbamazepine (CBZ), valproic acid (VPA) and lamotrigine (LTG) are known to have mood-stabilizing, antidepressant and/or anti-manic effects. Other AEDs are reported to have either adverse effects on mood and behaviour (gabapentin, pregabalin, topiramate and levetiracetam) or lack sufficient evidence regarding their effects on mood and behaviour (phenytoin, tiagabine, oxcarbazepine and zonisamide) (Ettinger, 2006). Although, according to a review of Johannessen (2008), AEDs are frequently used in the treatment of psychiatric disorders, effects of AEDs on mood or behaviour in patients with ID and epilepsy are not sufficiently studied. One pilot study was performed to evaluate the effect of LTG in twelve girls with Rett syndrome (Stenbom, Tonnby, & Hagberg, 1998). In four girls, LTG improved happiness, alertness, concentration and ability to make contact. However, in these studies, it may be difficult to distinguish indirect positive effects through control of the epilepsy from direct psychotropic effects of the medication. We found no other studies regarding the effect of AEDs on mood or behaviour in patients with ID and epilepsy.

The aim of this study was to investigate whether use of the AEDs carbamazepine, valproic acid and lamotrigine is associated with a different use of psychotropic drugs in a population of institutionalized epilepsy patients with Intellectual Disability. These AEDs are chosen because of their known positive effect on mood, e.g. their stimulant, anti-depressant or mood-stabilizing properties.

2. Methods

2.1. Patients

In a retrospective cohort study of adults with ID and epilepsy at the long-stay department of an epilepsy centre in The Netherlands, the adults have a 'difficult to treat' condition of epilepsy and therefore a probably large amount of antiepileptic drugs. We included 246 residents. Inclusion criteria were:

(A) A history of epilepsy demonstrated by the active use of AEDs. In absence of AED use, the diagnosis 'epilepsy' was verified in the electronic patient files.
(B) A diagnosis of intellectual disability according to the AAMR definition (AAIDD, 2002).
(C) 18 Years or older.

2.2. Data collection

The data were retrospectively extracted from an Oracle database, containing electronic patient files (EPD), with index date January 15th, 2007. The following items were collected: use of antiepileptic drugs (AEDs), use of psychotropic drugs, the ratio of Prescribed Daily Dose vs. Defined Daily Dose (PDD/DDD ratio) of carbamazepine, valproic acid and lamotrigine. These three drugs are drugs with a known positive effect on mood, in the broadest sense. We investigated the effect on