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Treatment consumption and treatment re-enrollment in GHB-dependent patients in The Netherlands

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ABSTRACT

Background: The objective of this study was to assess treatment consumption and re-enrollment in treatment in patients with gamma-hydroxybutyrate (GHB)-dependence in Dutch Addiction Treatment Centers (ATCs) in comparison with other addictions.

Methods: A cohort-study using nationwide administrative data from regular Dutch ATCs associated with the Dutch National Alcohol and Drugs Information System (LADIS), covering an estimated 95% of ATCs. We selected in- and out-patients with alcohol, drug and/or behavioral addictions with a first treatment episode in 2008–2011 and consecutive treatments until 2013 (n = 71,679). Patients still in treatment at that date (n = 3686; 5.1%), forensic patients (n = 1949; 2.7%) and deceased patients (n = 570; 0.8%) were excluded, leaving 65,474 patients (91.3%). Of those, 596 (0.9%) patients had GHB dependence. We analyzed number of treatment contacts, treatment duration, admissions and admission duration of the first treatment episode, and re-enrollment (defined as having started a second treatment episode in the study period).

Results: GHB-dependent patients showed the highest number of treatment contacts, duration of treatment and chance of being admitted. Re-enrollment rates were 2–5 times higher in GHB-dependent patients than other patients with adjusted HR of other addictions ranging from 0.18 (95% confidence interval [CI]: 0.15–0.21) to 0.53 (95% CI: 0.47–0.61).

Conclusions: This study demonstrates high levels of treatment consumption and high rates of treatment re-enrollment in GHB-dependent patients. These findings highlight the urgency of developing effective relapse prevention interventions for GHB-dependent patients.

1. Introduction

Gamma-hydroxybutyrate (GHB) and its precursor gamma-butyrolactone (GBL) are popular drugs of abuse in several countries including the Netherlands. Although originally developed as an anesthetic, due to unpredictable side effects like vomiting, medical use is nowadays limited. As sodium oxybate, GHB is registered for treatment of narcolepsy and, in some countries, for treatment of alcohol withdrawal as well (Brunt et al., 2013a; Snead and Gibson, 2005). The well-reported euphoric and sexually stimulating effects of GHB have facilitated its development as a party-drug. Prevalence estimates of current GHB use in Australia, the United Kingdom and the Netherlands range from 0.1% to 0.4% in the adult population, whereas rates among regular nightclub attenders are considerably higher with a reported current use prevalence of up to 10.5% (Corkery et al., 2015; van Amsterdam et al., 2012; Van Laar et al., 2012).

Over the last decade, medical complications as a result of GHB abuse have increased. In the Netherlands, Emergency Department (ED) presentations have increased from 300 in 2004–1200 in 2009 (Brunt et al., 2013a; Van Laar et al., 2012). Intoxications with GHB frequently occur, because of its narrow therapeutic window and short plasma half-life (van Amsterdam et al., 2012; Wood et al., 2011). Intoxications usually result in coma and may even be fatal, especially in the case of co-abuse of other sedative substances like alcohol (Corkery et al., 2015; Knudsen et al., 2008; Zvosec et al., 2011).

The high addictive potential of GHB has been recognized only since a decade (Snead and Gibson, 2005; van Amsterdam et al., 2012). In accordance, since 2007 a marked increase in GHB-related treatment

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seeking has been noticed in Dutch addiction treatment centers (ATCs; van Amsterdam et al., 2012). GHB users frequently report withdrawal symptoms upon cessation of daily use of GHB. Regular GHB use may result in tolerance and dependence in weeks, and many GHB-dependent users report an 'around the clock' dosing pattern in which they need to take doses every one or two hours as well as several nightly doses to prevent withdrawal symptoms (McDonough et al., 2004; Tarabar and Nelson, 2004; van Noorden et al., 2009). Abrupt decrease or discontinuation of heavy GHB use may result in a severe and life-threatening withdrawal syndrome characterized by autonomic instability, delirium and aggression (McDonough et al., 2004; Snead and Gibson, 2005; Tarabar and Nelson, 2004; van Noorden et al., 2009).

To date, studies that compare course and characteristics of GHB dependence with other addictions are lacking. Treatment of GHB dependence has neither been systematically investigated. Hence, no international guidelines exist (de Jong et al., 2013). Nevertheless, treatment of GHB dependence usually starts with inpatient detoxification due to the high level of physical dependence. Detoxification with benzodiazepines, the recommended treatment in most case reports and reviews, often appears problematic due to benzodiazepine-resistance (de Jong et al., 2012; McDonough et al., 2004; Sivilotti et al., 2001; van Noorden et al., 2014; Wojtowicz et al., 2008).

For several years, in Dutch ATCs detoxification with titration and tapering using pharmaceutical GHB is common. Results in terms of feasibility, effectiveness and safety are promising (de Jong et al., 2012; de Weert-van Oene et al., 2013; Dijkstra et al., 2016). However, reported relapse-rates appear to be high: after 3 months of follow-up, 65% of patients had relapsed in GHB abuse (Dijkstra et al., 2016).

Since GHB dependence is a relatively new phenomenon, very little is known about the course of GHB dependence, treatment effectiveness, and use of treatment facilities in addiction care. The high relapse rates reported by clinicians indicate a possible under-treatment compared to other addictions, that might be due to the complexity of GHB dependence, like the high physical dependence, the narrow therapeutic window and short plasma half-life, and the potentially life-threatening withdrawal syndromes.

We used nationwide administrative data to investigate treatment characteristics and separate treatment episodes in individual patients and compared GHB-dependent patients with other drugs of abuse and behavioral addictions. Under the assumption that re-enrollment in treatment after a terminated treatment episode would be indicative of a relapse in abuse, we studied re-enrollment in treatment: having started a second treatment episode in the study period. We hypothesized that, as compared with patients with other dependencies, treatment-intensity in GHB-dependent patients would be higher since the frequent need of inpatient detoxification of these patients will likely result in more treatment contacts and more ATC admissions. In addition, we hypothesized that because of the high relapse rates GHB-dependent patients more often had multiple treatment episodes than patients dependent on other common drugs of abuse or behavioral addictions.

2. Material and methods

2.1. Design and setting

We used administrative data of the Dutch National Alcohol and Drugs Information System (LADIS). The LADIS has been founded in 1986 and includes outpatient and inpatient clinical treatment data of 11 large ATCs in the Netherlands, covering an estimated 95% of all addiction treatments in the country (EMCCDA, 2015). Since 1994, all patients entering regular Dutch addiction care receive an identification number in LADIS, allowing to identify first and subsequent treatment episodes of every individual patient. Since 2007, the LADIS identification number is based on the Citizen Service Number, a unique personal number for everyone who is registered in Municipal Personal Records Database in The Netherlands, minimizing the chance of duplicates in the database. A preliminary report on the GHB treatment data of 2007–2010 has been previously published in a Dutch addiction journal (Mol et al., 2014).

2.2. Participants

From 2008 to 2012 all 71,679 patients who initiated and completed a first treatment episode in regular Dutch ATCs associated with LADIS were selected, according to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) definition of 'first treatment' (EMCDDA, 2012). Patients were followed until December 31st, 2013. Patients who had not ended treatment by that time were excluded (n = 3686; 5.1%). Since GHB was not registered as separate drug-class in forensic addiction care (n = 1949; 2.7%), these patients were excluded from analyses. In addition, we excluded patients who had deceased during the first treatment episode (n = 570; 0.8%). In total 65,474 patients with a first treatment episode in the study period were included for analyses (91.3%). The following categories of primary addiction for which treatment was initiated were considered and used in analyses: GHB, cocaine, opioids, amphetamines, alcohol, cannabis, ecstasy, medication, gambling and a rest-category consisting of other substances as well as behavioral addictions like sexual addiction and game addiction ('other'). In addition, information on co-abuse was available in LADIS, as well as the number of treatment contacts, number of ATC admissions, duration of admission (length of hospitalization in ATC) and duration of treatment. Available sociodemographic data included gender, age, and ethnic background.

2.3. Re-enrollment definition

Re-enrollment in treatment was defined as having started a second treatment episode in the study period. A second treatment episode was considered valid if the initiation date was after the recorded termination date of the first treatment episode. If a recorded termination date of the first treatment episode was lacking, initiation of a second treatment episode was defined if the new date was at least 6 months after the previous treatment contact. This is according to the international standard of EMCDDA (EMCDDA, 2012). If a second treatment episode had not started by December 31st, 2013, a single treatment episode was recorded for this patient.

2.4. Statistical analyses

Using descriptive statistics, we summarized the sociodemographic and clinical characteristics of primarily GHB-dependent patients and patients with other addictions. We used the median and interquartile range (IQR) in tables in case of skewed distributions. We used ANOVA to compare number of treatment contacts, duration of treatment, being admitted, and duration of admission between GHB and the other drugs of abuse and behavioral addictions. With regard to re-enrollment, we calculated several parameters. First, we calculated the proportion of patients that re-enrolled in the study period: the re-enrollment proportion. This proportion was the percentage of patients with more than one treatment episode, in which the time factor was not taken into account. The second parameter was the re-enrollment rate: after the first treatment episode, patients were followed until a next treatment episode, or until the end of the study period. The re-enrollment rate takes time at risk or person years (product of the number of patients and follow-up time) into account, but not the fact that patients could get lost to follow-up. The re-enrollment rate was calculated as follows: number of patients with a second treatment episode × 100/sum of person years, and can be interpreted as the number of patients per 100 that had started a second treatment episode within one year after completing the first treatment episode. Third, we calculated the Hazard Ratios (HR) of re-enrollment with Cox regression models, by using the time at risk. In a