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Epilepsy & Behavior 117 (2021) 107833

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

The impact of the coronavirus disease (COVID-19) pandemic on outpatient epilepsy care: An analysis of physician practices in Germany

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ARTICLE INFO

Article history:
Received 1 December 2020
Revised 26 January 2021
Accepted 26 January 2021
Available online 19 February 2021

Keywords:
COVID-19
Epilepsy care
Anti-seizure drugs

ABSTRACT

Objective: To gain insight into epilepsy care during coronavirus disease (COVID-19) pandemic, we analyzed prescription data of a large cohort of persons with epilepsy (PWE) during lockdown in Germany.
Methods: Information was obtained from the Disease Analyzer database, which collects anonymous demographic and medical data from practice computer systems of general practitioners (GP) and neurologists (NL) throughout Germany. We retrospectively compared prescription data for anti-seizure medication (ASM) and physicians' notes of "known" and "new" PWE from January 2020 until May 2020 with the corresponding months in the three preceding years 2017–2019. Adherence was estimated by calculating the proportion of patients with follow-up prescriptions within 90 days after initial prescriptions in January or February. We additionally analyzed hospital referrals of PWE. The significance level was set to 0.01 to adjust for multiple comparisons.
Results: A total of 52,844 PWE were included. Anti-seizure medication prescriptions for known PWE increased in March 2020 (GP + 36%, NL + 29%; $P < 0.01$). By contrast, a decrease in prescriptions to known and new PWE was observed in April and significantly in May 2020 ranging from −16% to −29% ($P < 0.01$). The proportion of PWE receiving follow-up prescriptions was slightly higher in 2020 (73.5%) than in 2017–2019 (70.7%, $P = 0.001$). General practitioners and NL referred fewer PWE to hospitals in March 2020 (GP: −30%, $P < 0.01$; NL: −12%), April 2020 (GP: −29%, $P < 0.01$; NL: −37%), and May 2020 (GP: −24%, $P < 0.01$; NL: −16%).
Conclusion: Adherence of known PWE to ASM treatment appeared to remain stable during lockdown in Germany. However, this study revealed findings which point to reduced care for newly diagnosed PWE as well as fewer hospital admissions. These elements may warrant consideration during future lockdown situations.

1. Introduction

The coronavirus (COVID-19) pandemic had an unprecedented impact in recent decades on healthcare systems and social life in many countries including Germany.

Uncertainty regarding the spread and treatment of the disease caused major and rapid changes which culminated in a nationwide lockdown. This included a curfew, shutdown of shops (except for shops necessary for daily needs), and canceling of all cultural events. In addition, major restrictions of social interactions were in place. The nationwide lockdown was put into effect on March 22 and was released in a stepwise fashion from April 20 until the end of May 2020. As hospitals and private practices tried to prepare for COVID-19 emergencies, routine and elective visits and procedures appeared to be reduced to a minimum, with an inevitable impact on health care for patients with chronic diseases such as epilepsy. Hospital-based activities related to epilepsy care were reportedly cut by more than 90% [1]. It is unclear how physicians in private practices and persons with epilepsy (PWE) were able to cope with this chronic disease under these unique circumstances. Moreover, there were concerns regarding a possible drop in medication adherence among PWE during the pandemic, as observed during previous infectious disease outbreaks. During the 2003 severe acute respiratory syndrome (SARS) outbreak in Taiwan, a worsening of seizure control was observed in patients with epilepsy due to ASM withdrawal [2]. Moreover, during the

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https://doi.org/10.1016/j.yebeh.2021.107833
1525-5050/

COVID-19 outbreak in Italy, many PWE reported problems with ASM availability, raising the risk for non-adherence [3].

Non-adherence to anti-seizure medication (ASM) is a common problem in epilepsy treatment and generally applies to about a third of the PWE, in some studies ranging up to 60% of the patients [4–6]. Non-adherent PWE have a substantially higher risk of seizure recurrence as well as increased mortality compared to adherent patients [7,8].

In view of this, we analyzed prescription data in a large German cohort to gain insight into outpatient epilepsy care during lockdown due to the COVID-19 pandemic.

2. Methods

2.1. Data source

The data analyzed for this study are derived from the IMS® Disease Analyzer Database (IQVIA), which collects information on drug prescriptions and diagnoses as well as demographic and medical patient characteristics from practice computers throughout Germany. The annual official summary statistics of all physicians in private practice in Germany (German Medical Association; http://www.baek.de) form the basis for the data sampling of private practices. Several epidemiological studies have previously used this system [9–12]. The database has been evaluated and found to be valid and representative of the German population with respect to epidemiological and pharmaeconomic features [11,13]. For this study, a total of 812 general practitioners (GP) and 86 neurologists (NL) all over Germany were analyzed.

The Disease Analyzer database includes information on physician specialty and office region (West or East Germany) as well as the following patient data: age, gender, place of residence, health insurance coverage (private [PI] or statutory health insurance [SHI]), diagnosis (International Classification of Diseases, 10th edition [ICD10]), visit date, and medication with daily dosage and prescriptions of medication down to package level. The physicians' notes for each visit are also available. However, no personal information can be obtained from any of the data in the database, and data were collected anonymously (in accordance with Section 3(6) German Federal Data Protection Act (Bundesdatenschutzgesetz)).

2.2. Standard protocol approvals, registrations, and patient consent

The local ethics committee of the Friedrich-Alexander-Universität Erlangen-Nuremberg has confirmed that there was no need for formal approval of this study using completely anonymized data. This is in line with German law (Section15 German Medical Association professional Code of Conduct/BOÄ). As the data were anonymized, the identification of individuals was impossible. Consequently, informed consent could not be sought and was not required.

2.3. Patients and ASM

Using the aforementioned database, adult persons with epilepsy (PWE, ≥18 years) were identified by their ICD-10 codes for epilepsy and enrolled in the study. The diagnosis "epilepsy" is indicated by the ICD-10 codes G40.X.

The COVID-19 pandemic led to a lockdown in Germany, which started in March 2020 and was gradually eased until it was eventually lifted in May 2020. Therefore, we included prescription data for ASM and physicians' notes from January 2020 until May 2020 and during the corresponding months in the three preceding years 2017, 2018, and 2019. Prescriptions of all drugs licensed and marketed for the treatment of epilepsy in Germany during the study period were included. This comprised all drugs listed under the Anatomical Therapeutic Chemical (ATC) code N03 "Antiepileptics" that were available in Germany during the study period. In addition, we analyzed hospital referrals of PWE by GP and NL during the study periods.

We differentiated "known" from "new" PWE. We defined known PWE as patients having received at least one epilepsy diagnosis ≥90 days before the respective study periods in 2017–2020 and new PWE as patients who received their first epilepsy diagnosis during the respective observation periods.

2.4. Statistical analysis

We compared the prescription data pertaining to ASM for known and new PWE separately from January 2020 until May 2020 with prescriptions of ASM during the corresponding months in the years 2017–2019. We used two-sided *t*-tests to test for differences in 2020 compared to the mean of 2017–2019. Due to the amount of comparisons (age- and sex-stratified), the significance level of $p < 0.01$ was considered statistically significant in these explorative analyses.

We estimated the medication adherence of known PWE during the lockdown by calculating the proportion of patients with a follow-up prescription during the 90 days after their prescription was issued in January or February 2017–2020. Anti-seizure medication prescriptions in Germany are usually for a supply of medication that will last for about 90 days.

3. Results

A total of 52,844 patients were included in the study (2017–2019: 32,955 patients; 2020: 19,889 patients; Table 1).

3.1. Prescription data

For known PWE, there was a significant increase in ASM prescriptions in March 2020 compared to March 2017–2019 (Fig. 1). This was true for patients seen by both GP and NL (GP +36%, NL + 29%; $p < 0.01$). By contrast, there was a decrease in prescriptions in April 2020 and May 2020 in both physician groups (Fig. 1). These effects were more pronounced in May 2020 (April 2020: GP −6%; NL −4%; May 2020: GP −16%, $p < 0.01$, NL −21%, $p < 0.01$) and were similar in all age groups (18 years – >80 years; Supplementary Table S1) as well as in men and women. There was a great variance in the number of PWE seen by specific practices which resulted in large standard deviations (Fig. 1, Fig. 2).

For new PWE, there also was a decrease in issued prescriptions in April 2020 and even more pronounced in May 2020 as compared to the corresponding months in 2017–2019 (Fig. 1). This was noticed in practices of GP and NL alike (April: 2020 GP: −13%, NL −11%; May 2020: GP −22%, $p < 0.01$, NL −29%, $p < 0.01$). There were no significant increases in ASM prescriptions issued to new PWE in March 2020 as seen for known PWE (Fig. 1). These effects were similar in all age groups (18 years–>80 years, Supplementary Table s2) and in men and in women.

The proportion of PWE who received a follow-up prescription after their prescription in January or February as a measure for adherence increased slightly in 2020 compared to 2017–2019 (2020: 73.5%, 2017–2019: 70.7%; $p = 0.001$; Table 2).

3.2. Hospital referrals

General practitioners and NL referred fewer PWE to hospitals in March 2020 (GP: −30%, NL: −12%), April 2020 (GP: −29% NL:

Table 1
Patient characteristics.

	General practitioners		Neurologists	
	2017–2019	2020	2017–2019	2020
Known PWE	11,489	7876	11,989	9183
Age (Mean, SD)	59.2 (19.4)	60.3 (19.2)	55.2 (18.8)	56.0 (18.4)
Female (%)	48.5	48.1	50.5	50.5
New PWE	5833	1703	3644	1127
Age (Mean, SD)	58.2 (21.1)	59.3 (20.7)	55.8 (21.1)	55.2 (21.5)
Female (%)	48.8	48.8	50.1	50.0

PWE = Person with epilepsy, SD = Standard deviation; no difference was significant.

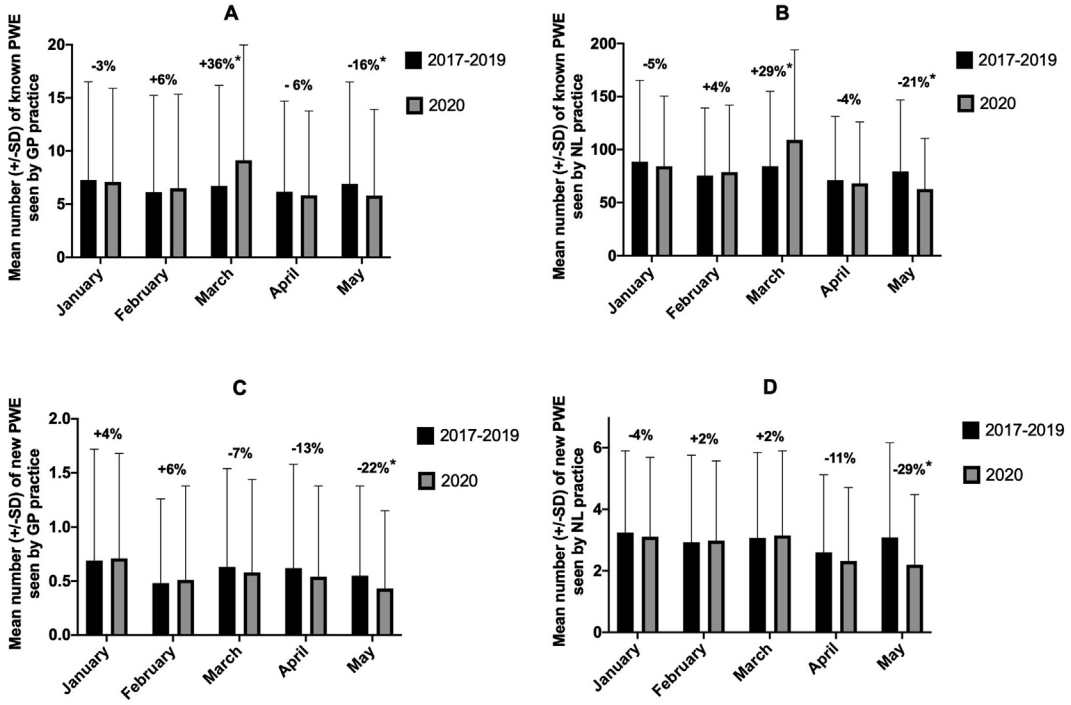

Fig. 1. Prescriptions to known and new PWE in January–May 2020 versus January–May 2017–2019 by practice specialty: (A) Known PWE seen by general practitioner (GP); (B) known PWE seen by neurologist (NL). (C) New PWE seen by general practitioner (GP); (D) New PWE seen by neurologist (NL). Numbers above columns indicate the percentile differences 2020 vs. 2017–2019 for each month. *: $p < 0.01$; PWE = Person with epilepsy, SD = Standard deviation.

−37%), and May 2020 (GP: −24%, NL: −16%; Fig. 2). This decrease was statistically significant for GP in March 2020 through May 2020 ($p < 0.01$, Fig. 2). Again, this pattern was similar in all age groups and in women as well as in men (Supplementary Table s3).

4. Discussion

The COVID-19 pandemic caused rapid and extensive changes in the healthcare systems of many countries including Germany and finally led to a limited nationwide lockdown. This study analyzed the impact of these actions on outpatient care for nearly 20,000 PWE as provided by GP and NL. Both groups of physicians care for the majority of adult PWE in Germany [14].

In the current study, the proportion of PWE who received a follow-up prescription after their prescription in January or February 2020 increased slightly during the lockdown from March 2020 until May 2020 compared to the corresponding months in 2017–2019. This was due to a significant increase in ASM prescriptions for known PWE in advance of the approaching lockdown in March 2020. A significant decrease in prescriptions followed in April 2020 and May 2020.

Known PWE appeared to act responsibly and stocked up on ASM in March 2020 before complete lockdown, which allowed them to have a sufficient supply during it. This is in line with the recommendations of many medical societies [15]. Consequently, the estimated adherence of known PWE to their ASM treatment did not decrease during lockdown. In fact, it increased slightly compared to the corresponding months in 2017–2019. Adherence remained within the expected adherence range of approx. 65% that was reported for adult PWE in Germany in a previous study [6].

Increases in German prescription numbers in March 2020 have already been reported for cardiovascular and diabetes medication [16]. Kostev et al. also reported a significant increase in the prescription of psychotropic drugs in the week prior to the beginning of the lockdown, referring to possible panic buying on the part of patients [17].

During the SARS outbreak in Taiwan 2003, seizure diaries were studied. The authors described a loss of contact to medical care providers that led to increased non-adherence and reduced seizure control [2]. The stable adherence in our study may indicate a more proactive and stable relationship between PWE and the treating physicians within our cohort.

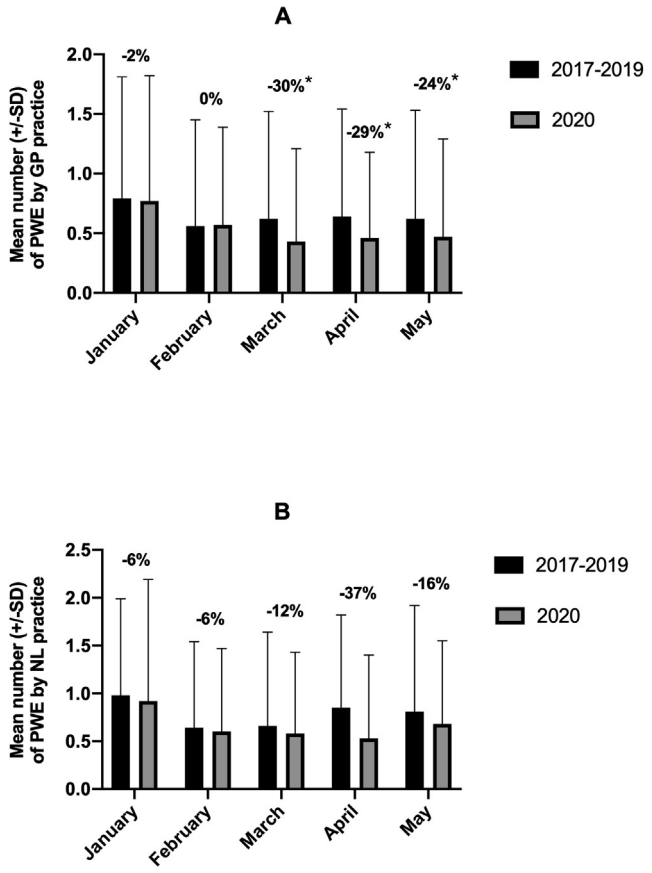

Fig. 2. Differences in the number of hospital referrals per practice in January–May 2020 versus January–May 2017–2019 by practice specialty. (A) PWE seen by general practitioner (GP); (B) PWE seen by neurologist (NL). Numbers above columns indicate the percentile differences 2020 vs. 2017–2019 for each month. *: $p < 0.01$; PWE = Person with epilepsy, SD = Standard deviation.

Table 2
Follow-up ASM prescriptions.

	2017–2019 (mean+/−SD)	2020	*P* value
Patients with ASM prescription in January or February (*N*)	11,266 +/− 526	12,407	
Patients with next ASM prescription within 90 days (*N*, %)	7955 +/− 369 (70.7 +/− 1.1 %)	9124 (73.5 %)	0.001

ASM = antiseizure medication, *N* = number of patients, SD = Standard deviation.

Nevertheless, the present study indicated a reduction in care for PWE during the lockdown in Germany.

There was a significant decrease in ASM prescriptions issued to new PWE in April 2020 and May 2020 which implies that fewer new PWE were seen by NL and GP. This may support the hypothesis that patients with newly diagnosed epilepsy in particular were underdiagnosed and undertreated during the time of the lockdown.

In addition, both GP and NL referred fewer patients to hospitals for further diagnostics and/or treatment in March 2020, April 2020, and May 2020. It remains unclear whether the physicians were hesitant to do so or had difficulties finding a hospital that was willing and able to electively admit PWE during lockdown. Neither can be excluded that PWE themselves were more reluctant to hospital referrals.

This study did not find any major differences in the behavior of GP and NL.

In addition, the analysis of the different subgroups of PWE revealed similar findings in men and in women as well as in all age groups. This is of note since there were concerns that older patients may have been especially at risk of restricted access to patient care during the lockdown. In the current cohort however, the care of older PWE in terms of prescriptions and hospital referrals was no worse than that provided to younger patients.

This study was subject to several limitations.

It is a retrospective analysis of anonymous data of adult patients with epilepsy who were identified by ICD-10 codes and also included physicians' notes. Although ICD coding by physicians has been shown to be reliable for identifying PWE [18], the possibility of misdiagnosis in individual cases cannot be excluded. The same applies to the physicians' notes.

Although the majority of adult PWE in Germany are cared for by GP and NL in private practices [14], another limitation is that data from patients treated in hospitals or emergency rooms and other hospital outpatient departments are missing. In addition, 'new PWE' as defined in this study might include patients who have longstanding epilepsy, but are new to a specific practice.

The main drawback of the study is the lack of data regarding seizure frequency and severity in patients during lockdown. Recent work has shown that during a lockdown situation, there are various factors that could possibly contribute to a higher risk of increased seizure frequency, such as insomnia or economic difficulties [19]. Moreover, during public health outbreaks, PWE are at particular risk of severe psychological distress, and treatment should not only focus on seizure control but also address mental health problems [20].

By contrast, this study relied primarily on prescription data and utilization of outpatient health care as indirect markers of treatment quality.

The results of our study contribute to the identification and analysis of possible problems in the management of chronic diseases such as epilepsy during a lockdown situation [21,22]. On this basis, structured recommendations regarding the allocation of resources and prioritization of healthcare issues may be developed and improved [23]. Innovative strategies including digital health tools may assist in addressing possible shortcomings [24].

5. Conclusion

Adherence of known PWE to ASM treatment appeared to remain stable during lockdown in Germany from March 2020 to May 2020. However, our findings point to reduced care for PWE during lockdown, which mainly concerned patients with newly diagnosed epilepsy and hospital referrals. These findings may warrant consideration with regard to the care of patients with chronic diseases such as epilepsy during any future crises that may arise and impact healthcare systems similarly.

Conflicts of interest

K. Kostev is an employee of IQVIA, a company that focuses primarily on analyses for pharmaceutical companies and runs the database used in this analysis. This study was not part of any business project, however.

S. Gollwitzer received personal fees from Desitin, Eisai, UCB, but these outside the submitted work.

J.D. Lang served on the speakers' bureau of Eisai and UCB.

H.M. Hamer has served on the scientific advisory boards of Arvelle, Bial, Desitin, Eisai, facetoface, GW, Novartis, Sandoz and UCB Pharma. He has served on the speakers' bureaus of or received unrestricted grants from Amgen, Ad-Tech, Bial, Bracco, Desitin, Eisai, GW, Nihon Kohden, Novartis, Pfizer, and UCB Pharma.

The remaining authors have no conflicts of interest.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2021.107833.

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