



Patients' perspectives on management and barriers of regular antiepileptic drug intake

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ABSTRACT

Purpose: The aim of our study was to assess the management of drug intake and potential barriers to adherence reported by two different patient groups.

Methods: The study was performed in cooperation with the Regional Chamber of Pharmacists of Rhineland-Palatinate and three neurologists in private practice specialized in epileptology. In total, 108 patients surveyed in 43 pharmacies (Group P) and 118 patients treated by the specialized neurologists (Group N) completed anonymously a questionnaire on intake of antiepileptic drugs (AEDs). The statistical evaluation was performed using nonparametric tests and logistic regression analyses.

Results: Group N more often used adherence aids, compared with Group P (68.6% vs. 46.3%, $p < 0.01$), and the number of doses per day was significantly lower in Group N (Mann-Whitney test, $p = 0.046$), but the percentage of patients who reported problems with the regular intake of their medication did not differ significantly between groups (Group N vs. P: 47.0% vs. 40.0%). If patients noticed that they missed a dose, 45.3% completely skipped the missed dose (Group N vs. P: 43.0% vs. 48.1%, n.s.). In a multivariate analysis, significant risk factors of problems with regular drug intake were age < 25 yrs. ($p < 0.01$) and patient-reported adverse effect of AED ($p < 0.01$), followed by the number of AED doses per day ($p < 0.05$), while gender, intake habits, usage of adherence aids, and patient-rated efficacy of AEDs were not significant.

Conclusion: Patients treated by neurologists specialized in epileptology did not report less problems with adherence than patients surveyed in pharmacies. Since barriers for a regular intake are diverse, the use of a short questionnaire on management of drug intake may lead to an individually tailored counseling of patients to improve adherence.

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1. Introduction

Since the first international workshop on “Compliance in Epilepsy” 1987 in Salzburg/Austria [1], our knowledge about the magnitude of insufficient adherence, its predictors and its influence on seizure control has increased dramatically. Large studies using medication possession ratio (MPR) to assess adherence, confirmed that approximately one third of the patients with epilepsy treated with antiepileptic drugs (AEDs) show poor adherence (MPR $< 80\%$). Poor AED intake is considered a main cause of breakthrough seizures or insufficient seizure control [2–4] and status epilepticus [5]. Moreover, poor adherence can have serious or even fatal consequences, including increased mortality, emergency department admissions, hospitalizations, motor vehicle accident injuries, fractures, and head injuries [6–8].

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In contrast to a large amount of studies that focus on the proportion of nonadherent patients or risk factors for nonadherence, our study concentrates on how patients deal with their medication in daily practice. We specially try to identify treatment-related barriers as starting points for tailored counseling and education in order to enhance regular intake of medication.

Thus, the aim of our study was to assess patients' perspectives on management of drug intake, including dealing with a missed dose, and to assess risk factors for patients' problems with regular intake of drugs. In addition, we examined whether patients treated by neurologists in private practice specialized in epileptology differ in management of drug intake from patients surveyed in pharmacies.

2. Methods

The study was performed in cooperation with three neurologists in private practice specialized in epileptology and the Regional Chamber

of Pharmacists of Rhineland-Palatinate. The pharmacists had previously participated in a three-hour workshop on adherence of patients with epilepsy held by a pharmacologist and one of the authors (US) and had been informed about the study and about the patient questionnaire. The pharmacists were instructed to hand out the questionnaire only to patients with the diagnosis of epilepsy, in order to exclude patients who were treated with AEDs for disorders other than epilepsy. In total, 43 of 80 pharmacists who had attended the lecture/seminar agreed to participate in the study.

2.1. Patients

Adult patients (≥ 18 yrs.) with epilepsy treated with AEDs and able to answer a short questionnaire were included. In total, 108 patients (Group P) were surveyed in 43 pharmacies and 118 patients (Group N) who were treated by three neurologists in private practice (outside of Rhineland-Palatinate) specialized in epileptology.

2.2. Questionnaire

A questionnaire (see Appendix) was developed to assess patients' management of drug intake and potential barriers of adherence, as part of a counseling tool for patients with epilepsy to enhance AED adherence. The questionnaire comprises 8 items about 1) intake patterns of AED (e.g., at fixed times of the day, related to specific activities like tooth brushing) and the use of adherence aids (e.g., pill boxes), 2) uncertainty about drug intake and dealing with a missed dose, and 3) barriers to adherence of AEDs (e.g., different kinds of drugs). The questionnaire, which can be completed within 10 min, included also open-label questions to allow patients to add aspects which they rated to be important. Furthermore, patients were asked to rate the efficacy and tolerability of their AEDs. The questionnaires were sent back anonymously to the Society for Epilepsy Research (GfE, Bielefeld) for the statistical analysis.

2.3. Ethics

The ethics committee of the University of Muenster in Germany approved the study protocol.

2.4. Statistical evaluation

Nonparametric test (Fisher's exact Test, Mann–Whitney Test) and logistic regression analyses were used for statistical analysis. Stepwise multivariate logistic regression analyses were performed to identify potential risk factors for problems with regular intake of the medication. Statistical significance was set at $p < 0.05$ (two-sided, if not mentioned otherwise). For statistical analyses IBM SPSS for Windows 23.0 was used.

3. Results

3.1. Demographic and clinical data

The demographic and clinical data of the included patients are summarized in Table 1. Patients surveyed in pharmacies (Group P) were significantly older than patients treated by neurologists specialized in epileptology (Group N) (37.0 ± 15.0 yrs. vs. 48.1 ± 15.0 yrs., $p < 0.01$). Correspondingly, occupation significantly differed between groups ($p < 0.01$), i.e., the rate of retired persons (28.3% vs. 14.4%) and housewife/-man (16.0% vs. 8.5%) was higher, and the rate of pupils/students and employed persons was lower (3.8% vs. 12.7%) in Group P. Overall, Group P rated the efficacy of AED better compared to Group N ($p < 0.01$) and patients of Group P were more often seizure-free (72.9% vs. 53.0%, $p < 0.01$). This is not surprising, because patients with difficult-to-treat epilepsies are more frequently referred to specialized neurologists. The groups differed only slightly and not significantly with regard to tolerability of AEDs. The majority of patients rated the tolerability of AED as very good (42.5%) or good (36.2%).

3.2. Intake pattern of antiepileptic drugs and use of adherence aids

The intake pattern of AEDs and the use of adherence aids are shown in Table 2. The vast majority of patients (82.3%) took their AED twice daily, 5.8% once daily and 11.9% three times daily or four times daily. The number of doses per day was significantly lower in Group N compared to Group P ($p = 0.046$). Most patients took their AEDs at a fixed time of the day (64.6%) or related to specific activities, e.g., tooth brushing, (45.6%) (no significant group differences). In total, almost all patients (98.2%) reported to take their AEDs at fixed time of the day or related to specific activities. Patients treated by specialized neurologists

Table 1
Demographic and epilepsy related data by patient group.

Demographic data of patients	Group N n = 118	Group P n = 108	p	Total n = 226
Gender (% female)	56.8%	61.1%	n.s. ^a	58.8%
Age in years, mean \pm SD (range)	37.0 \pm 15.0 (16–81)	48.1 \pm 15.0 (17–85)	0.001 ^b	42.3 \pm 16.0 (16–85)
Occupation, n (%)				
Employed	64 (54.2%)	51 (48.1%)	0.001 ^a	115 (51.3%)
Unemployed	4 (3.4%)	4 (3.8%)		8 (3.6%)
Pupil/student	15 (12.7%)	4 (3.8%)		19 (8.5%)
Housewife/man	10 (8.5%)	17 (16.0%)		27 (12.1%)
Pensioner	17 (14.4%)	30 (28.3%)		47 (21.0%)
Other	8 (6.8%)	0 (0.0%)		8 (3.6%)
Patient-rated efficacy of AEDs, n (%)				
Very good: no more seizures	62 (53.0%)	78 (72.9%)	0.001 ^b	140 (62.5%)
Good: markedly less or less severe seizures	36 (30.8%)	22 (20.6%)		58 (25.9%)
Satisfactory: somewhat less or less severe seizures	14 (12.0%)	6 (5.6%)		20 (8.9%)
Unsatisfactory: seizures unchanged or deteriorated	5 (4.3%)	1 (0.9%)		6 (2.7%)
Patient-rated tolerability of AEDs, n (%)			n.s. ^b	
Very good: no adverse effects	46 (68.7%)	58 (77.3%)		94 (42.5%)
Good: only minor adverse effects	16 (23.9%)	10 (13.3%)		80 (36.2%)
Satisfactory: adverse effects present, but tolerable	4 (6.0%)	4 (5.3%)		45 (20.4%)
Unsatisfactory: adverse effects, barely tolerable	1 (1.5%)	3 (4.0%)		2 (0.9%)

Group N, patients treated by specialized neurologists; Group P, patients surveyed in pharmacies.

^a Fisher's exact Test.

^b Mann–Whitney Test.

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