Contributions of Pharmacists in the Treatment of Epilepsy: A Systematic Review

Tiago M Reis, MD; Marília SA Campos, BSc; Michelly M Nagai, MD; Leonardo RL Pereira, PhD

Epilepsy is a chronic neurological disorder characterized by recurrent seizures affecting approximately 50 million individuals worldwide. Its treatment is complex and may involve the use of antiepileptic drugs (AEDs), a special diet, immunotherapy, and neurostimulation. Pharmacotherapy is the primary choice for the treatment of epileptic disorders, and AEDs, either alone or combined with other antiepileptics, are used for the chronic form of the disease. Although polytherapy is often required to keep patients seizure-free, it is often cited as a cause of undesirable quality-of-life effects, such as adverse reactions and drug interactions.

In this context, pharmacists are important health professionals in counseling and monitoring patients with epilepsy (PWE) because they are easily accessible and know about pharmacotherapy, health education, and management of chronic diseases. Moreover, through pharmacotherapeutic monitoring, the pharmacist can detect the emergence of health problems and can help prevent the progression of comorbidities. Considering the complexity of treating epilepsy and the lack of information about pharmacists’ contributions to epilepsy management, this study aimed to identify studies on clinical services performed by pharmacists for PWE and the services’ impact on the health of these patients.

METHODS

We performed a systematic review of studies listed in PubMed, Scopus, and Lilacs. To search articles, the mesh terms “pharmacist,” “pharmaceutical care,” and “pharmaceutical services” were combined separately with “epilepsy” and “anticonvulsants.” Each of these descriptors was entered in a Boolean combination using the connector “AND.” Searches were also carried out using the translations of the descriptors and terms in Portuguese and Spanish. The authors included articles published up to March 3, 2015. When necessary, the descriptors were adapted according to the database.

A 2-stage method was used to screen and analyze the studies identified in the search results. In the first stage, 2
reviewers (TMR and MSAC) independently searched articles in the databases and excluded duplicated articles. In the second stage, reviewers screened the titles followed by a reading of the abstracts (or the full text when there was insufficient information in the abstract) to select publications. The criteria of inclusion were: studies describing clinical services performed by pharmacists for PWE; original article; published in English, Portuguese, or Spanish; and full text available. Studies eligible for inclusion could be observational or experimental. Disagreements between reviewers in relation to inclusion of the articles in the review were resolved through discussion and consensus by all researchers (TMR, MSAC, MMN, and LRLP).

The selected articles underwent full reading for the extraction of the following information: authors and year of publication, origin of the study, study objective, place of performance data collection, inclusion and exclusion criteria for subjects, pharmacists’ contributions, indicators of evaluation of the intervention, outcomes, main conclusion, evaluation tools, and funding. The collection of data was performed simultaneously and independently by 3 researchers (TMR, MSAC, and MMN) who discussed and resolved any interpretation conflicts.

The quality of the studies included in the review was evaluated using the Downs and Black checklist, a tool developed to assess the quality of reporting, external and internal validity, and clinical and statistical power of studies. Scores below 50% were considered weak, and those between 50% and 69%, 70% and 79%, and 80% and 100% were considered fair, good, and very good, respectively. At the end of the study, the results were organized in accordance with the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

**RESULTS**

After matching descriptors, 4463 studies were identified and 5 were in accordance with inclusion criteria (Figure).

These studies were conducted in nursing homes, primary care clinics, pediatric outpatient clinics, children’s hospitals, and epilepsy clinics. The pharmacists’ contributions identified in the articles were registration of information related to the patient, health education, and counseling. The average quality score of study reporting was 49% (SD = 17%), which was considered weak. In addition, the average scores by domain were: reporting 66% (11%), external validity 53% (30%), internal validity—bias 71% (29%), internal validity—confounding 30% (30%), and power 20% (45%). The use of validated or standardized evaluation tools such as Beers Criteria, SF-36, Behave-AD, MARS, QOLIE-10, and GHQ-12 seemed to improve the Downs and Black score.

**DISCUSSION**

Studies have shown that the participation of pharmacists in a multidisciplinary team can improve the health of patients with chronic diseases, such as cardiovascular disease, hypertension, diabetes, asthma, dyslipidemia, and renal disease. However, this review found little evidence in the scientific literature about the availability of pharmacist services to PWE (Figure). Despite the low number of articles highlighting pharmacists’ involvement in the management of epilepsy (Figure) and the weakness of these studies (according to their Downs and Black classification), the results did show the positive

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**PRACTICAL IMPLICATIONS**

The treatment of epilepsy is complex; it can cause drug-related problems and hamper patient quality of life. Clinical services performed by pharmacists may optimize the pharmacotherapy and avoid or mitigate these problems. To our knowledge, no previous systematic review has shown how pharmacists have contributed to the treatment of epilepsy, which clinical services have been performed, and what impact these contributions have made. These study results can guide the reorientation of pharmacists’ contributions in the care of epilepsy, demonstrate the benefits that pharmacists’ professional treatment management provide, and encourage the provision of pharmacist-led clinical services to patients with epilepsy.

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**Figure. Selection of Articles for Review**

<table>
<thead>
<tr>
<th>Articles identified (n = 4463)</th>
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<tbody>
<tr>
<td>- 61.3% PubMed</td>
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<tr>
<td>- 24.5% Scopus</td>
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<tr>
<td>- 14.2% Lilacs</td>
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</tbody>
</table>

| Duplicates removed (n = 2516) |

<table>
<thead>
<tr>
<th>Articles assessed for eligibility (n = 1947)</th>
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<tbody>
<tr>
<td>- 98.3% were not original articles studying pharmacists’ interventions in PWE</td>
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<tr>
<td>- 0.9% were not published in English, Spanish, or Portuguese languages</td>
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<tr>
<td>- 0.8% did not have full text available</td>
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| Studies included in the review (n = 5) |

PWE indicates patients with epilepsy.
impact of the pharmacists’ contributions. In these studies, the pharmacists’ interventions were essential to improving the health of the PWE they served. Pharmacists’ interventions were able to prevent problems related to the use of medicines. The results included improvements in patient knowledge about epilepsy and their quality of life, agility in daily activities, and medication adherence (Table). Furthermore, pharmacists’ contributions were also vital in the success of pharmacotherapy in children, which usually requires closer professional care and the guidance of caregivers. More studies are needed to highlight the positive impacts of pharmaceutical services on the health of PWE of all ages and needs.

In the study by Midlov et al (Table), pharmacists evaluated medication use, identified therapeutic problems, and proposed changes in prescriptions to a health team, when the pharmacotherapy was not appropriate. Thus, pharmacists performed pharmaceutical counseling and pharmacotherapeutic follow-up, as well as systematic measurement and evaluation of results. In the study by Lertsinudom et al (Table), pharmacists provided guidance to ensure the adequacy of the pharmacotherapy through therapeutic drug monitoring. Likewise, Murphy et al (Table) demonstrated that pharmacists involved in the review of prescriptions were able to prevent errors in dose and frequency of administration of AEDs. In turn, Fogg et al and Chen et al developed studies in which a pharmaceutical counseling session was provided to patients and caregivers. The pharmacists provided a medication review, discussed the rationale for the pharmacotherapy components, provided patient medication education, and increased the patient’s health education.
(Table). All of these successful scenarios demonstrate that including pharmacists in care staffs produces effective results for the success of the collaborative therapy and the quality of life of PWE.

Nevertheless, according to Fogg and colleagues, it is difficult to find pharmacists to work with pharmacist-led epilepsy consultations. On one hand, in most nations, clinical services provided by pharmacists are not reimbursed, which discourages pharmacists from taking on this role. On the other, the authors suggest this situation also may reflect pharmacists’ knowledge gaps that would inhibit them from performing clinical services. In a study centered in Aracaju, one of northwestern Brazil’s largest cities, almost 80% of pharmacists working in community pharmacies were found to have insufficient knowledge to perform clinical services such as dispensing drugs. This shows that a large number of Brazilian pharmacists do not seem to be properly prepared for the act of guidance and provision of medicines as observed in some American studies over the past decade.

As such, one can infer that the same problem exists with the dispensing of AEDs in Brazil, as well as for pharmacists working in other types of health establishments or in the management of the pharmacotherapy of individuals with other chronic diseases. This reinforces the need for better qualification of professional pharmacists prior to graduation and for their constant efforts to update their own scientific knowledge base—this is necessary to improve patient care, especially where the pharmacist-led consultation is in the implementation phase.

This assumed gap in professional knowledge can also explain why in the 5 studies reviewed, pharmacists were
found to not be performing the pharmaceutical care. The importance of this clinical practice has been demonstrated to promote success of pharmacotherapy in PWE in nursing homes and clinics (eg, places where the cited studies were developed). Moreover, lack of information and understanding among physicians, other health professionals, and patients about how pharmacists can contribute to seizure control and quality of life of PWE can also hamper the deployment and implementation of pharmaceutical care services.

For this scenario to change, pharmacists must be trained on epilepsy, pharmacotherapy, and the skills needed to perform the care process.\textsuperscript{55-35} In addition, the development of instruments to guide the care of PWE, such as algorithms and protocols, could assist with the implementation of relevant and effective methods of patient assessment and would also encourage the pharmacotherapeutic monitoring of PWE through pharmaceutical care.

Another point deserves to be discussed: no study about the role of pharmacists in epilepsy was found in Lilacs, which is responsible for disseminating studies conducted predominantly in Latin American and Caribbean countries. This may be evidence of the possible limited contributions of countries from this geographical region to research focused on pharmacists’ role in the care of PWE. Furthermore, it is possible to verify the importance of properly planning the research methods of future studies, mainly if their subject involves the impact of clinical services performed by pharmacists. The selected studies that used validated or standardized evaluation tools (eg, Beers criteria, SF-36, Behave-AD, MARS, QOLIE-10, and GHQ-12) had higher score in the Downs and Black scale. The use of these types of tools avoid bias in results, thereby improving the quality of the study.\textsuperscript{56}

**Limitations**

Because we searched for evidence of studies solely in academic databases, we may have underestimated the real-world participation of pharmacists in the management of PWE. Possibly, pharmacists are helping to manage the pharmaceutical care of PWE, but they are not disclosing it in scientific articles. The disclosure of these unpublished services could encourage the implementation of pharmaceutical care in epilepsy management.

**CONCLUSIONS**

Our review indicates that pharmacists are involved in the following clinical activities for the care of PWE: therapeutic drug monitoring, medication review, pharmacotherapeutic follow-up, pharmaceutical counseling, and systematic measurement and evaluation of health results from the drug treatment. The findings suggest that clinical services performed by pharmacists can improve the treatment outcomes and the epilepsy-related health of PWE. However, a limited number of articles are available in the scientific literature that highlight these contributions. Further study is warranted to evaluate the impact of clinical services performed by pharmacists in the management of epilepsy.

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**Authorship Information:**

TMR, MD, pharmacist, has expertise with pharmaceutical services in community pharmacies and rational use of drugs. He was responsible for collection, management, analysis, and interpretation of data; for writing of the manuscript; and for the decision to submit the manuscript for publication.

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MMN, MD, pharmacist, has expertise in the rational use of drugs. She was responsible for collection, management, analysis, and interpretation of data; for writing of the manuscript; and for the decision to submit the manuscript for publication.

LRLP, PhD, pharmacist, professor of the University of São Paulo, has experience in pharmaceutical services. He was the supervisor of the study and participated in all of its steps.

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**REFERENCES**


