Original Work

Pharmacist-led Anti-seizure Medication Management: Delegation Protocol Implementation and Impact Analysis

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Abstract

Background: Anti-seizure medication (ASM) management is complicated and time-consuming; delegating management to pharmacists could minimize the burden. Data suggests improved outcomes with pharmacist medication management. Without data in ambulatory settings, there is a need to identify the impact of delegating ASM management to pharmacists.

Methods: A pharmacist delegation protocol was developed, implemented, and analyzed to evaluate the impact of pharmacist-led ASM management in an epilepsy clinic. This delegation protocol allowed pharmacists to titrate and taper ASMs, sign prescription orders, and enter laboratory orders. A chart review was conducted before and after implementation of the protocol to determine the time to initiation of ASMs and workflow efficiency.

Results: The pre-implementation cohort included 47 patients; 24 (51%) were male, and the average age was 42 years (SD 18.0). The post-implementation cohort included 50 patients; 24 (48%) were male, and the average age was 45 years (SD 15.8).

The average time to initiation of ASMs was 32.3 hours (SD 31.6) and 35.2 hours (SD 44.5) in the pre- and post-implementation groups, respectively. The average number of electronic medical record (EMR) messages sent between the care team was 4 (SD 1.9) and 0.3 (SD 0.6), respectively.

The number of messages sent by the following groups was reduced after the implementation of the delegation protocol: care team (-3.7; $P < 0.001$), providers (-1.2; $P < 0.001$), pharmacists (-1; $P < 0.001$).

Conclusion: Implementation of a pharmacist-driven ASM management delegation protocol increases the efficiency of caring for patients with epilepsy without sacrificing the timely initiation of ASM medications.

In the United States, more than three million adults and children live with epilepsy.[1] Approximately 50% of newly diagnosed patients will not respond to an initial anti-seizure medication (ASM) trialed.[2] The standard of care for epilepsy treatment includes a trial of ASM monotherapy; if the patient fails two or three ASMs as monotherapy, polytherapy is commonly started.[3] Guidelines for initial and subsequent ASM selection do not exist. Many factors influence ASM choice for patients, including unique pharmacokinetic properties of the drug, adverse effects, seizure type, adherence, dosage form, and insurance status. In relation to pharmacokinetics, many ASMs have significant dependence on hepatic isoenzymes to metabolize the compounds; several also inhibit or induce isoenzymes themselves, which can alter the metabolism of other medications. Notably, the side effect profiles of ASMs vary greatly. However, many have both systemic and neurologic side effects, such as fatigue, somnolence, ataxia, tremor, dizziness, and nausea. Additionally, the various mechanisms by which ASMs act have differing effects on certain seizure types, which, in turn, adds another layer of complication to the selection and maintenance of these medications. These factors, combined with reduced patient response to ASMs, lead to frequent medication changes.

Transitional polytherapy is a technique that is used to make ASM changes while reducing breakthrough seizure risk. This involves gradually titrating the new ASM to a target dose. Once the target is achieved, the baseline ASM is gradually withdrawn.[4,5] The Study by a Panel of Experts: Considerations in Replacement in Antiepileptics (SPECTRA) provides recommendations on best practices for titration and taper of various ASMs.[4]

Transitional polytherapy can be time consuming for epilepsy providers, and there could be benefits for delegating this responsibility to pharmacists. Studies have demonstrated improved clinical outcomes with pharmacist-driven management of medications with a narrow therapeutic index.[6,7] Specific to epilepsy, a multi-center study using national pharmacy services databases evaluated the outcomes

of pharmacist ASM management in hospitalized Medicare patients. Both the death rate and length of stay were significantly lower in hospitals with this service.[8] Despite these positive findings, the generalizability is limited due to the age and inpatient nature of the study population. There is no data on the impact of pharmacist ASM management in ambulatory care.

At the tertiary academic medical center where this study took place, pharmacists are embedded within the epilepsy clinic and provide medication support at the request of providers. At the time of this study's initiation, the adult epilepsy clinic at this site followed approximately 2,100 patients. Four epilepsy-trained pharmacists fulfilled 1.0 pharmacist full-time equivalent position that supported seven epilepsy providers and multiple other neurological practitioners. To be considered an epilepsy-trained pharmacist, individuals demonstrated competency by accurate completion of a select group of ASM titrations and tapers of varying difficulty with direct oversight from a previously trained epilepsy pharmacist. Prior to this study, pharmacists developed ASM titration, taper, and cross-titration regimens for patients using the transitional polytherapy method, assessed adverse drug reactions and monitored for drug-drug interactions at the request of providers. Each regimen created one or more pharmacotherapy recommendations that required provider approval. The approval was most commonly obtained through electronic medical record (EMR) messaging, which required action from the provider and led to workflow inefficiencies and delayed ASM initiation. The recommendations were approved by providers with minimal or no changes. Given the limited evidence of the benefits of pharmacist-driven ASM management in an ambulatory care setting and the potential impact of workflow efficiencies on patient care at this site, there is a need to explore the utility of pharmacists in the role of ASM management. The purpose of this study was to assess the impact of a pharmacist-driven ASM management delegation protocol on the workflow efficiency and time to ASM initiation when implemented in an adult epilepsy clinic. To our knowledge, this study is the first to describe the impact of pharmacist ASM management in ambulatory care.

Methods

Development and Implementation of Protocol

An interdisciplinary workgroup of epilepsy providers and pharmacists reviewed SPECTRA recommendations[4] and other expert opinions from the literature, professional experience, and ASM package inserts to develop a pharmacist-driven ASM management protocol which delineated pharmacist scope of practice. Subsequent to a provider selecting the ASM, goal dose, and titration type, the protocol delegated the creation of ASM titration, taper, and cross-titration regimens to a single pharmacist. It allowed the pharmacist to determine the rate and duration of ASM titrations, tapers, or cross-titrations to reach the goal dose. Providers activated the protocol by specifying the ASM(s) to be changed, goal dose(s), rationale for medication change, and whether the

FIGURE 1. Flowchart of Patient Inclusion and Exclusion

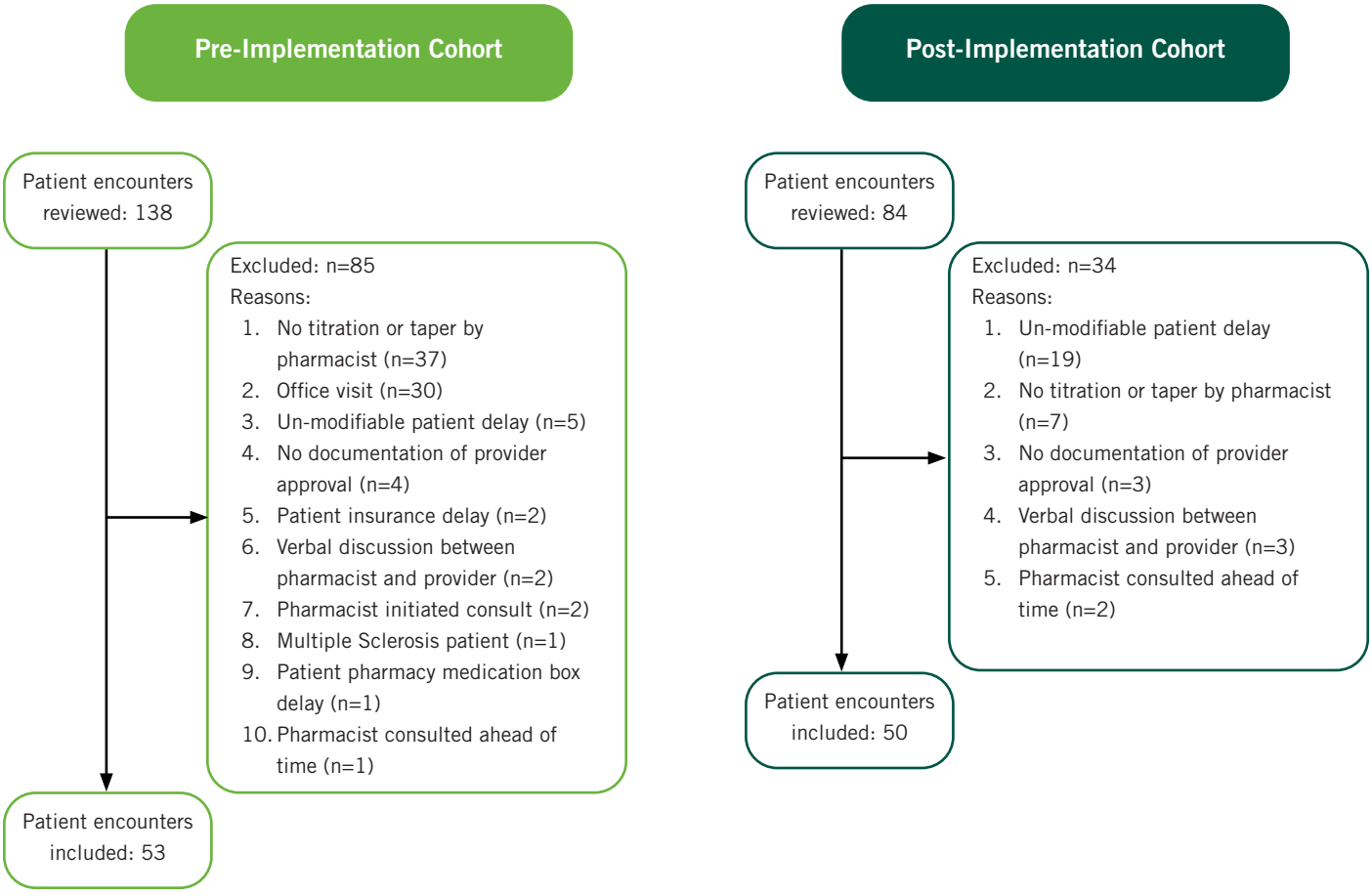

TABLE 1. Results of statistical analysis for each titration method comparing values before and after the implementation of pharmacist-led anti-seizure medication (ASM) management delegation protocol. Results reported as mean (standard deviation)

Method	*Variable*	*Pre-implementation*	*Post-implementation*	*P-value**
All Methods	Time to ASM Initiation – hours	32.3 (31.6)	35.2 (44.5)	0.629
	Care Team Messages	4.0 (1.9)	0.3 (0.6)	< 0.001
	Provider Messages	2.2 (1.0)	1.0 (0.6)	< 0.001
	Pharmacist Messages	1.6 (0.9)	0.6 (0.7)	< 0.001
Concurrent Cross-titration	Time to ASM Initiation – hours	21.9 (28.9)	39.9 (53.3)	0.485
	Care Team Messages	3.6 (1.7)	0.4 (0.7)	< 0.001
	Provider Messages	2.1 (0.9)	1.2 (0.6)	0.004
	Pharmacist Messages	1.4 (0.8)	0.7 (0.9)	0.018
Sequential Cross-titration	Time to ASM Initiation – hours	45.3 (34.9)	27.3 (29.9)	0.139
	Care Team Messages	4.7 (2.5)	0.2 (0.4)	< 0.001
	Provider Messages	2.5 (1.2)	0.8 (0.6)	< 0.001
	Pharmacist Messages	1.9 (1.2)	0.6 (0.5)	< 0.001
Taper only	Time to ASM Initiation – hours	17.5 (16.3)	29.0 (25.9)	0.335
	Care Team Messages	3.4 (1.7)	0.2 (0.4)	< 0.001
	Provider Messages	1.9 (0.8)	1.0 (0.0)	0.02
	Pharmacist Messages	1.4 (1.1)	0.3 (0.5)	0.008
Titration only	Time to ASM Initiation – hours	36.5 (32.8)	45.3 (60.7)	0.881
	Care Team Messages	4.1 (1.5)	0.5 (0.5)	< 0.001
	Provider Messages	2.4 (0.9)	0.8 (0.4)	< 0.001
	Pharmacist Messages	1.6 (0.7)	0.7 (0.8)	0.006

**p-value from t-test of log-transformed data*

pharmacist should titrate only, taper only, cross-titrate concurrently, or cross-titrate sequentially when designing the ASM regimen. Following protocol activation, the pharmacist devised a titration, taper, or cross-titration regimen based on patient-specific factors and information from the provider. Once a regimen was created, the pharmacist counseled and followed up with the patient until successful completion of the medication transition or until provider consultation was required.

Two EMR tools were developed to support consistent protocol use and documentation among users. An electronic referral order was used by providers to initiate the protocol and specify the required elements. The second tool was a standard documentation template that incorporated all required protocol elements, allowing for consistent pharmacist documentation. The template was formatted in situation, background, assessment, and recommendation (SBAR) format with explicit follow-up plans.

Following organizational approvals of the protocol and EMR tools, epilepsy-trained pharmacists received verbal education highlighting the use of EMR tools, provider consultation requirements, and laboratory orders they were approved to order. Epilepsy providers were notified of the delegation protocol and virtually trained on the appropriate use of the electronic referral order.

Study Design

To evaluate the impact of the pharmacist-driven ASM management protocol, time to initiation of ASM therapy and workflow efficiency were evaluated pre- and post-implementation of the pharmacist ASM management protocol. Time to initiation of ASM therapy was defined as the time elapsed between provider consult and prescription signature by the provider. Workflow efficiency was quantified as the quantity of messages sent through the EMR between members of the care team. Messages were stratified into groups: those sent by a provider, a pharmacist, and the care team. The number of messages sent by the care team is the summation of messages sent by a provider, pharmacist, registered nurse, or medical assistant. A message was counted if its purpose was to clarify goal dose(s) of ASM, method of ASM change, or the intent of ASM change. All EMR messages included in the analysis were sent during the time of initiation of ASM therapy, as defined previously. Message quantity did not include those sent to a patient. Data was further stratified based on method of ASM medication change. Four methods may be requested based on patient factors and include: cross-titration concurrently, cross-titration sequentially, titration only, or taper only. Patients 18 years and older were included if a provider requested pharmacist assistance in the creation of an ASM regimen. Patients were excluded if the provider referral occurred at an in-person clinic visit where the consult time was unmeasurable; if the patient had unmodifiable delays in therapy greater than five days (e.g., some patients did not want to immediately start therapy); and other reasons as outlined in Figure 1. This study was granted exemption by the University of Wisconsin-Madison Institutional Review Board.

Statistical Methods

Data were summarized by pre/post

implementation by mean (SD). All outcome variables were non-normally distributed and skewed right. Normality assumptions were met after a log(x+1) transformation. Comparison of outcomes between pre/post implementation for all processes and for each process individually utilized a t-test on the transformed data. Due to the small number of repeated subjects, their data were treated as independent samples. Significance level was set at 5% and all analyses were conducted in R version 4.0.

Results

Pre-Implementation

The patient demographics of each group were similar. The average age of those included was 42 (SD 18.0), and 24 patients (51%) were male. Pre-implementation data was collected retrospectively from January 2017 to December 2019, identifying 138 patient encounters with 130 unique patients that were reviewed for exclusions. The final analysis included 53 patient encounters for 47 unique patients.

Of the pre-implementation group, 14 encounters were concurrent cross-titration regimens (26.4%), 15 were sequential cross-titration regimens (28.3%), 16 were titration-only regimens (30.2%), and 8 were taper-only regimens (15.1%). In all, the average time to initiation of ASM therapy was 32.3 hours (SD 31.6). The average number of EMR messages sent among the care team was 4 (SD 1.9).

Post-Implementation

Post-implementation data was collected retrospectively from April 2020 to March 2021. In this group, 84 patient encounters were reviewed for exclusions. The final analysis included 50 patient encounters with 50 unique patients. The average age of those included was 45 (SD 15.8), and 24 patients (48%) were male.

Of the post-implementation group, 22 encounters were concurrent cross-titration regimens (44%), 15 were sequential cross-titration regimens (30%), 5 were titration-only regimens (10%), and 6 were taper-only regimens (12%). In all, the average time to initiation of ASM therapy was 35.2 hours (SD 44.5). The average number of EMR messages sent among the care team was 0.3 (SD 0.6).

Comparison of Pre and Post-Implementation Results

Table 1 shows the results for time to initiation of ASM therapy and workflow efficiency pre- and post-implementation of the pharmacist-led ASM management delegation protocol. There were no statistically significant differences in time to initiation of ASM therapy for any of the titration methods between the pre- and post- implementation groups. The number of messages from all groups significantly reduced following the implementation of the pharmacist-driven ASM management delegation protocol.

Discussion

The goal of our study was to assess the impact of a pharmacist-driven ASM management delegation protocol on the workflow efficiency and time to ASM initiation when implemented in an adult epilepsy clinic.

The analysis of this study shows that workflow efficiency is significantly improved for all methods of ASM change as defined by reduced EMR messages exchanged between the care team. Reducing the amount of time that these healthcare professionals are required to efficiently initiate their patients' ASM therapy allows them to shift their energy to alternative workflows or expand their ability to care for additional patients.

The results show that the implementation of a pharmacist-driven ASM management delegation protocol does not significantly change the time to ASM initiation. These results suggest that institutions can shift ASM management workflows from exclusively physician-driven to pharmacist-led management without increasing the amount of time to initiation of ASM therapy. This ability for pharmacists to play a larger role in the care for patients taking ASM medications provides financial benefit to institutions by using pharmacists in this role without requiring extensive time from physicians. Additionally, these results show that institutions can provide increased access to care for patients by allowing the redistribution of physician time to other needed responsibilities or additional care opportunities.

Limitations

Subjective management of patients prior to protocol implementation could have led to inconsistencies in the therapeutic decisions made. Additionally, a small sample size for this study lowers its power to expose statistical differences. Furthermore, it is difficult to evaluate clinical outcomes without standard objective measures for this population. Considering the measure of time to initiation, several factors have an impact on this value that are beyond control of the pharmacists; however, this may be the reality in many healthcare environments.

Conclusion

The implementation of a pharmacist-driven ASM management delegation protocol increases the workflow efficiency of caring for patients with epilepsy without sacrificing the timely initiation of ASM medications.

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Christine A. Garmoe, PharmD had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

References

1. Centers for Disease Control and Prevention. Epilepsy data and statistics. Updated September 30, 2020. Accessed January 18, 2022. www.cdc.gov/epilepsy/data/index.html
2. Kwan P, Brodie MJ. Phenobarbital for the treatment of epilepsy in the 21st century: a critical review. *Epilepsia.* 2004;45(9):1141-1149. doi:10.1111/j.0013-9580.2004.12704.x
3. Kwan P, Brodie MJ. Effectiveness of first antiepileptic drug. *Epilepsia.* 2001;42(10):1255-1260. doi:10.1046/j.1528-1157.2001.04501.x
4. St Louis EK, Gidal BE, Henry TR, et al. Conversions between monotherapies in epilepsy: expert consensus. *Epilepsy Behav.* 2007;11(2):222-

234. doi:10.1016/j.yebeh.2007.04.007
5. Garnett WR, St Louis EK, Henry TR, Bramley T. Transitional polytherapy: tricks of the trade for monotherapy to monotherapy AED conversions. *Curr Neuropharmacol.* 2009;7(2):83-95. doi:10.2174/157015909788848884
6. Downing A, Mortimer M, Hiers J. Impact of a pharmacist-driven warfarin management protocol on achieving therapeutic International Normalized Ratios. *Am J Health Syst Pharm.* 2016;73(5 Suppl 1):S69-S73. doi:10.2146/sp150039
7. Smith AP, Millares-Sipin CA, James M, Cohen H. Impact of a Pharmacist-Initiated Vancomycin Monitoring Program. *Consult Pharm.* 2016;31(9):505-510. doi:10.4140/TCP.n.2016.505
8. Bond CA, Raehl CL. Clinical and economic outcomes of pharmacist-managed antiepileptic drug therapy. Pharmacotherapy. 2006;26(10):1369-1378. doi:10.1592/phco.26.10.1369