



Doctor of Nursing Practice The University of Texas at El Paso

OUCH: OVERCOMING UNCONTROLLED COMPLEX MIGRAINE
HEADACHES

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COHORT X

Angel Pineda, MSN, APRN, AGACNP-BC

- Chairperson: Hector R. Morales, DNP, APRN, PMH-CNS-BC
UTEP | 500 W. UNIVERSITY AVE. EL PASO, TEXAS 79968

OUCH: *Overcoming Uncontrolled Chronic Migraine Headaches*

Angel Pineda

School of Nursing: The University of Texas at El Paso

Doctor of Nursing Practice (DNP) Program

DNP Chair: Dr. Hector Morales, DNP, APRN, PMH/CS-BC

DNP Quality Improvement Project

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Abstract

Migraines are a common type of primary headache that affects over 36 million people in the United States and one billion people worldwide. While oral preventative treatments have been considered first-line therapy for chronic migraines, anti-calcitonin gene-related peptide monoclonal antibodies have recently emerged as an effective treatment option. The purpose of this quality improvement project was to improve the therapy adherence and quality of life outcomes for patients with chronic migraines by facilitating a transition from oral migraine prevention therapy to treatment with an anti-calcitonin gene-related peptide monoclonal antibody agent. This project was developed utilizing the Focus, Analyze, Develop, and Execute QI model. The results of a ten-day reflective practice activity revealed poor patient adherence with oral migraine preventative therapy due to the intolerability of adverse effects. The clinical practice change was implemented with qualifying patients over six weeks utilizing Lewin's change theory as the translational framework. The primary endpoint of this project was an improvement in treatment adherence, reductions in the number of migraine days per month by 50% or more, and improvements in the patients' quality of life with better migraine control and fewer adverse treatment effects.

OUCH: *Overcoming Uncontrolled Chronic Migraine Headaches*

Migraines are a common, often disabling condition with a prevalence of upwards of 15% and an economic impact estimated at \$36 billion each year in the United States (Sacco et al., 2019; Levin et al., 2018). The symptoms associated with acute and chronic migraine include, but are not limited to intense, typically unilateral, pulsating headaches associated with nausea, vomiting, dizziness, photophobia, and/or phonophobia that is frequently exacerbated by movement (Ailani et al., 2021). These symptoms often have a negative impact on an individual's quality of life. Once diagnosed, migraine patients will often begin with a trial of acute abortive treatment. However, when the headache frequency exceeds more than 15 migraine days per month, preventative treatment options are recommended (Frank et al., 2021). The International Headache Society Classification of Headache Disorders (ICHD-3) defines chronic migraine as a condition in which headaches occur more than 15 days per month for more than three months with migraine features on more than eight days per month (Agostoni et al., 2019).

Over the years, several medications have been explored as potential preventative options for migraine, including calcium-channel antagonists, antidepressants, beta-blockers, and antiepileptic medications such as topiramate. The use of each of these agents resulted in a reduction in migraine frequency (Frank et al., 2021; Sacco et al., 2019; Ailani et al., 2021). Although topiramate and other first-line agents have been approved for clinical use, long-term adherence to these oral preventive anti-migraine regimens has been difficult to achieve. Most studies indicate that these treatment strategies are ineffective in 40–50% of patients and that they are overall poorly tolerated because of their adverse effects. Overall, >60% of chronic migraine sufferers abandon treatment after two months (Frank et al., 2021). Additionally, many individuals have only limited access to preventative treatment. Levin et al. (2018) reported that,

of the estimated 38.8% of migraine patients who might benefit from preventative agents, only 5–13% actually receive treatment.

Recent research focused on the vasodilatory properties of calcitonin gene-related peptide (CGRP) has revealed its key role in the pathophysiology of migraine headaches (Huang et al., 2019). This led to the development of therapeutic anti-CGRP monoclonal antibodies (mAbs). At this time, there are four different injectable mAb formulations available for use as a novel approach to migraine prevention (Sacco et al., 2019). Several randomized clinical control studies, meta-analyses, and systematic reviews have been performed which have demonstrated the efficacy of these novel drugs. Administration of anti-CGRP mAbs results in the same, if not greater reduction in the frequency of migraine headaches compared to oral preventative agents (Overeem et al., 2021). These new treatment options also have higher tolerance profiles which have led to improved treatment adherence over that observed using conventional treatment with topiramate or other oral therapies (Frank et al., 2021). The availability of treatment options with fewer adverse effects improves the likelihood of therapy adherence; this may lead to a reduction in overall disability associated with migraines and improvements in quality of life.

Background Knowledge

The pathophysiology of migraines is both complex and dynamic; the most widely accepted theory centers on the concept of cortical spreading depression (CSD). CSD is a wave of neuronal hyperexcitation followed by depression involving multiple regions of the vasculature (Chan et al., 2020; Mathew & Klein, 2019). Activated trigeminal nerves release CGRP, vasoactive peptides, and neurotransmitters (e. g., serotonin), which induce the release of proinflammatory mediators (Levin et al., 2018). The proinflammatory mediators then promote the synthesis of additional CGRP, which is released over hours to days, corresponding to the four

to 72-hour duration of a typical migraine episode (Levin et al., 2018; Chan et al., 2020; Mathew & Klein, 2019).

CGRP is a 37-amino acid peptide with two isoforms known as α and β . CGRP α is detected primarily in the central and peripheral nervous system, while CGRP β is found primarily in enteric sensory neurons (Levin et al., 2018; Hargreaves & Olesen, 2019; Schou et al., 2017; Agostoni et al., 2019; Shi et al., 2020; Scuteri et al., 2021). Recent studies involving external jugular vein sampling during migraine attacks revealed elevated serum levels of CGRP that responded to the administration of sumatriptan, thus providing additional support for the role of CGRP in this pathologic process (Taylor, 2018; Mathew & Klein, 2019; Hargreaves & Olesen, 2019; Tepper, 2019). The link between CGRP and migraine prompted scientists to explore targeted treatment options, which ultimately led to the development of mAbs designed to block CGRP signaling. Anti-CGRP ligand and anti-CGRP receptor mAbs are large molecules that bind to their respective targets with high specificity. These agents interact minimally with the immune system and thus have few to no potential adverse effects (Levin et al., 2018; Hargreaves & Olesen, 2019; Schou et al., 2017; Agostoni et al., 2019; Tepper, 2019). An additional advantage of these mAb preparations is their long half-lives in plasma and lack of active toxic metabolites. These agents are not metabolized in the liver but instead are ultimately broken down into their constituent amino acids (Hargreaves & Oleson, 2019; Mathew & Klein, 2019).

At this time, there are four United States Food and Drug Administration (FDA)-approved mAbs that can be used to block CGRP signaling. Erenumab is a human mAb that binds to the CGRP receptor, while galcanezumab, fremanezumab, and eptinezumab are humanized monoclonal antibodies that potently and selectively bind to the CGRP peptide ligand (Hargreaves & Oleson, 2019; Mathew & Klein, 2019). Several randomized clinical trials, most

comparing CGRP mAb treatment to conventional oral therapies, revealed that nearly half of patients treated with CGRP mAbs experience reduced headache frequency (typically ~50%) with additional benefits that include reductions in the intensity of headache pain, the need for analgesics, and headache-related disability, leading to an overall improved quality of life (Torres-Ferrus et al., 2021; Overeem et al., 2021; Kuruppu et al., 2021; Masoud et al., 2020; Deng et al., 2020). Most of these trials used the metric, monthly migraine days (MMDs), to analyze and evaluate month to month efficacy; a reduction in MMDs of >50% was established as a common goal for migraine prevention (Torres-Ferrus et al., 2021; Overeem et al., 2021; Kuruppu et al., 2021; Tepper et al., 2021).

Intended Improvement

This project aimed to improve patient outcomes by initiating preventative migraine treatment with CGRP mAbs. These agents have been proven to be equally or more effective at reducing migraine frequency and providing symptom relief with superior tolerability, which may lead to improved adherence to therapy.

Methods

Context

This QI project was conducted at Texas Tech University Health Sciences Center El Paso (TTUHSC EP) Department of Neurology outpatient clinic. This is the largest neurology practice in West Texas and the only academic practice located within a 500-mile range. The clinic provides service to the borderland community encompassing El Paso County, Texas, Ciudad Juarez, Mexico, and Southern New Mexico (Texas Tech, n. d.). The practice specializes in general neurology, epileptology, movement disorders, interventional neurology, and critical care neurology. The practice team includes seven neurologists, four interventional neurologists, eight

nurse practitioners, ten neurology residents, six medical assistants, and one social worker. The Department of Neurology is affiliated with the University Medical Center of El Paso (UMC), El Paso Sleep Center, the El Paso Psychiatric Center, and Sierra Medical Center. These facilities work collaboratively to meet the needs of patients requiring neurologic care (Texas Tech, n.d.). The population served in this community is predominantly Hispanic and Spanish-speaking, with unique barriers that limit their access to care, including economic, communication, and educational factors. As the clinic is part of a teaching institution, there was an exceptional amount of support and resources available to ensure the successful implementation of this Quality Improvement (QI) project.

Planning the Intervention

The QI project utilized Kurt Lewin's change theory model (Lewin, 1958) as the translational framework to guide the implantation of the proposed practice change. This change management theory was selected in part as it has demonstrated broad applicability in the area of healthcare and has contributed to the success of numerous QI projects (Wojciechowski et al., 2016). Effective use of this model requires investigators to evaluate and take into account the entire environment as the change evolves through three stages: unfreeze, change and refreeze (Woody, 2020; Shirey, 2013). The first step of the process, known as "unfreezing", involved preparing for the change by conducting a ten-day reflective practice which, in this case, focused on identifying the need for improvement in preventative migraine treatment. The Focus, Analyze, Develop and Execute (FADE) QI model (see Figure 1) was then utilized to explore the identified practice issue and develop a practical alternative to the status quo (Nursing Assignment Acers, 2021). A literature review utilizing EMBASE, MEDLINE, CINAHL, Academic Source Complete, Health Source, and COCHRANE databases was conducted.

Information collected from this review confirmed that limited adherence to preventative migraine therapy is a known phenomenon and proposed the use of CGRP mAbs as an effective treatment alternative. This collection of evidence-based literature was then utilized to develop the QI project proposal. The highest level of evidence gathered from the literature review was incorporated together with the PICOT question that was developed specifically for this project.

The proposed PICOT question focused on:

Population: Patients 18–65 years of age diagnosed with migraine headaches

Intervention: Administration of a CGRP mAb

Current Treatment: Weekly titration of oral topiramate to the goal of 100 mg per day

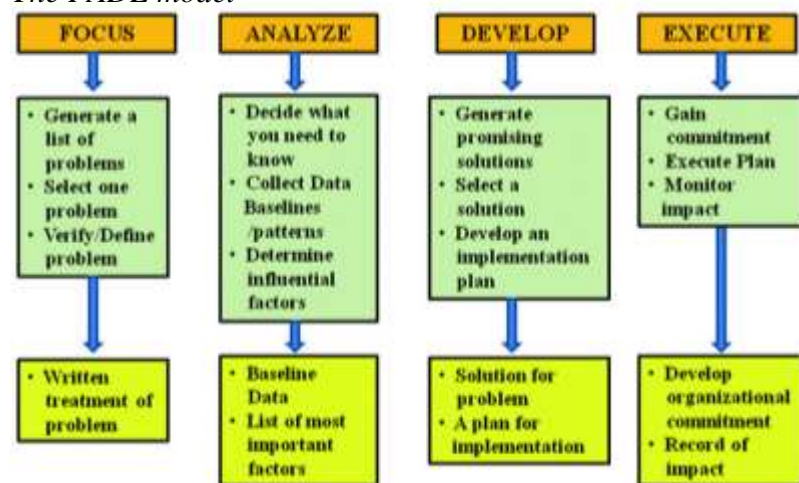
Outcome: Reduced migraine frequency and increased compliance with therapy

Time: Over a period of 4 weeks.

The proposal was then shared with providers within the practice including the Department Chair to garner support for this initiative. Ultimately, the proposed practice change was accepted and supported by all the Neurology attending physicians within the practice.

Figure 1

The FADE model



The next step, known as “change”, required planning focused on the implementation of this practice change. Working collaboratively with the medical assistant staff, resources and information for patient assistance were compiled. These resources included migraine/headache log forms and patient educational materials. New and established migraine patients were evaluated during the initial four weeks of the project with an emphasis on patients suffering from chronic migraine. Patients who met the appropriate diagnostic and treatment criteria were initially assessed with a Migraine Disability Assessment (MIDAS) test and were offered CGRP mAbs as a therapy option along with other treatment options that included onabotulinumtoxin A and conventional oral therapy. Patients who chose to initiate CGRP mAb therapy were educated on the proper administration of this medication and treatment expectations. These patients were then followed up within a month (during the fifth and sixth week of the project timeline) to evaluate their migraine frequency and therapy adherence. All patients participating in the project were educated on the maintenance of a headache log to track symptom frequency and patterns.

The final step, “refreeze”, takes place after the project timeline once the patients who began CGRP mAb therapy had completed their one-month follow-up. During these follow-up visits, quantitative and qualitative data were collected regarding the patients’ overall experience with the change in therapy. The results of the intervention were shared with clinic staff and the Department Chair. During a “refreezing meeting session,” plans were developed with the Department Chair that were directed at ensuring the sustainability and expansion of this QI project for the benefit of future chronic migraine patients.

Study of the Interventions

The QI project identified patients 18–65 years of age who were diagnosed with chronic migraine as eligible for inclusion. Patients were educated on CGRP mAb therapy as well as other

preventative treatment options, including oral therapies and onabotulinumtoxin A therapy. Those who elected to start CGRP mAb therapy were treated with either (1) galcanezumab (240 mg single subcutaneous injection as a loading dose followed by 120 mg monthly) or erenumab (70 mg subcutaneous injection once monthly). These two CGRP mAb therapies were selected based on their overall availability, results demonstrated in clinical trials, affordability, and availability of a patient assistance program (Kuruppu et al., 2021; Overeem et al., 2021; Torres-Ferrus et al., 2021). Patient education was provided that addressed the administration of subcutaneous injections, common side effects, and treatment expectations in both English and Spanish. Patients were also provided with printed educational materials regarding treatment and a sample migraine log to document symptoms.

Evaluation Methods

Patients meeting criteria for treatment with CGRP mAb therapy were screened utilizing the MIDAS tool which provided us with an understanding of the impact of their migraines on their quality of life over the previous three months. This information was evaluated together with patient-reported MMDs and any adverse events or adherence issues associated with previous migraine prevention regimens. This information was utilized as a baseline measure for ongoing evaluation. All patients were provided with a sample log and asked to maintain a record of their MMDs. The patients who elected to start treatment with a CGRP mAb were then re-evaluated four weeks after their first injection. At this follow-up visit, patients were asked to provide their migraine log and asked about any adverse effects they may have experienced in response to the new therapy. Patients were also asked to describe their quality of life during the previous month with a particular focus on how their migraines interfered with their ability to complete their activities of daily living, participate in recreational activities, and maintain productivity at work

and at home. They were also asked to indicate their overall satisfaction with their new treatment. All data were collected and documented in the electronic health record and in a de-identified Excel spreadsheet to facilitate further analysis.

Analysis

MIDAS scores provided a quantitative baseline assessment of the impact of migraines on quality of life. Additionally, MMD data obtained pre- and post-intervention were gathered to determine whether the intervention resulted in a reduction in migraine frequency. Qualitative data gathered at follow-up visits provided us with insight into therapy adherence and quality of life complications associated with treatment and/or migraine frequency.

Ethical Issues

This QI project received institutional and departmental support from TTUHSC El Paso. The UTEP IRB approved this study as a QI project and not a research study requiring IRB oversight. Patient confidentiality was maintained throughout in accordance with the standards set by the Health Insurance Portability and Accountability Act (HIPAA) and TTUHSC departmental and institutional policies. No patients were forced to participate or coerced to select a particular treatment option. Patient encounters included discussions of all available treatment options with no bias towards any therapy or product. These discussions also included information on adverse effects, expected outcomes, patient-specific considerations, and the costs of each therapeutic option.

Results

Outcomes

Thirty-two patients ranging in age from 18-65 years met the inclusion criteria and were evaluated during the six-week timeframe. The original patient cohort included 28 females and

four males; 24 of the patients were Hispanic, seven were Caucasian, and one was African American. Of this group, 10 patients elected to initiate CGRP mAb therapy; all were females between the ages of 18–60 years and included seven Hispanic, two Caucasian, and one African American patient. Four of the participants were new to the clinic; the other six were established patients. Among the patients who agreed to participate, eight had reported adverse effects or adherence problems while on other preventative therapies during the past six months. Among the remaining 22 patients who declined to participate, eight cited trypanophobia as the reason for declining treatment, two were actively planning to become pregnant, nine elected to pursue onabotulinumtoxin A therapy for migraine management, and 13 chose to remain on their current oral regimen or begin treatment with an alternative oral agent.

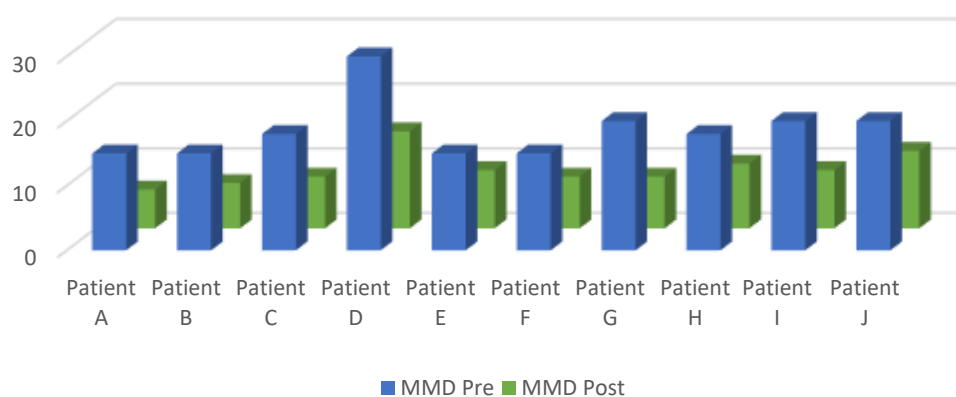
All 10 patients who elected to receive treatment with CGRP mAbs completed the recommended follow-up at four weeks following their initial monthly injection. The average MIDAS score for these patients before treatment was between two and three, which indicated mild to moderate disability from migraines. Those electing CGRP mAb therapy reported an average of 18.6 MMDs before this new intervention. Interestingly, these patients reported an average of 9.2 migraine days in the first month following the initiation of CGRP mAb therapy (see Figure 2).

A MIDAS score at the four-week follow-up visit would not have been an accurate representation of the impact of the new treatment regimen as this tool is designed to evaluate a three-month migraine history. For this reason, qualitative data were gathered at follow-up patient encounters. Nearly all the patients expressed satisfaction with CGRP mAb therapy. Patients reported that they preferred a standard dose of treatment with CGRP mAb therapy as opposed to the dose titration that was required when using oral treatments. Another positive benefit was the

improved functionality that accompanied decreased migraine frequency. Four of the patients expressed mild discomfort upon administration of the subcutaneous injection, though no injection site reactions were reported during the initial month of therapy. One patient who elected to initiate therapy with galcanezumab misunderstood the prescribing instructions and only administered one injection (120 mg) during the initial month of therapy. This patient was advised to continue with recommended once-a-month injection instead of completing the loading dose.

Figure 2

Monthly Migraine Days



Note. Monthly migraine days reported by patients prior to therapy initiation (blue) compared to one month following therapy initiation (green).

Several of the educational components developed for use as part of the QI project provided patients with additional knowledge that empowered them to take more control of their health and influenced their healthcare decisions. For example, once they were enrolled in patient assistance programs to defray the costs of CGRP mAb therapies, many patients used this opportunity to investigate the availability of patient assistance programs for other prescription drugs. Thus, the QI project has provided our patients with both information and motivation to reduce their overall health care costs. Furthermore, educational materials focused on the use of a

migraine log have provided patients with the opportunity to identify previously unrecognized triggers and patterns associated with their migraine condition.

Discussion

Summary

This QI project began with the intention of evaluating the reduction in MMDs and adherence to preventative therapy as primary endpoints. All ten patients who elected to start CGRP mAb therapy completed their initial one-month drug trial and indicated their intent to continue with the recommended monthly injections. The reduction in the average MMDs reported by this QI project was consistent with the results of larger randomized clinical trials that tracked the number of patients who achieved a 50% reduction in MMDs (Kuruppu et al., 2021; Overrem et al., 2021; Mavridis et al., 2021). Only mild discomfort was reported secondary to the administration of subcutaneous injections. This might be compared to reports of confusion, mental fog, dizziness, drowsiness, nausea, and other adverse effects that were historically reported by patients taking preventative oral therapies.

Implications

The results of this QI project support the data obtained from the literature review, indicating favorable results for patients with chronic migraine. Data from the literature suggest that the use of CGRP mAbs may result in a 50% reduction in MMDs and a favorable side effect profile compared to conventional treatment with oral therapies such as topiramate (Sacco et al, 2019). My results suggest that CGRP mAb therapy might be considered for use in chronic migraine sufferers who are treatment naïve as well as in those who have not responded to conventional oral treatment options. Significant emphasis should be placed on patient education

with a focus on reasonable treatment expectations because none of the currently-available options are likely to result in 100% migraine prevention.

Limitations

Among the limitations of this QI project, was the small sample size of patients electing treatment as well as the single center focus of the project. The results from the patients treated with CGRP mAbs were not compared to those from patients who elected another treatment option. These findings might be evaluated in a longitudinal and multisite study that would provide time for optimal effectiveness of all therapies, notably for CGRP mAbs and onabotulinumtoxin A. Additionally, this QI project was focused solely on the utilization of CGRP mAb for the treatment of patients diagnosed with chronic migraines. While some of these treatment options can also be used to treat episodic migraines, patients with this diagnosis were not included in this project. Furthermore, patients who elected to start treatment were offered only two of the four available treatment options; thus, no direct comparisons of all available anti-CGRP mAb preparations could be achieved. Likewise, as previously discussed, one of the patients did not fully understand the prescribing instructions; this may require some additional attention when designing future studies. Finally, the development of other CGRP-targeted therapies is an exciting new aspect of migraine medicine that was not considered or evaluated within the scope of this QI project.

Conclusion

Migraines are a highly debilitating condition with the third-highest prevalence among all known medical conditions (Mavridis et al., 2021). The development of effective, disease-specific, and cost-effective treatment options that improve the quality of life for migraine sufferers is thus a medical imperative. CGRP mAbs are novel therapies with demonstrated

effectiveness in migraine prevention; their integration into clinical practice has been supported by the American Headache Society and the American Academy of Neurology (Mavridis et al., 2021). The results of this QI study suggest that treatment selection should be individualized. While conventional oral therapies that remain effective in individual patients do not need to be replaced by newer therapies, the latter should be considered as part of the growing arsenal of available treatment strategies. Further work will be necessary to ensure CGRP mAb therapy and future treatment options are cost-effective and available to all patients who suffer from uncontrolled migraines. Overall, CGRP mAbs are an innovative therapeutic strategy for migraine sufferers and address the need for effective and well-tolerated preventive treatment options (Levin et al., 2018).

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