Thiazide-like Diuretics as First-line Treatment to Improve Blood Pressure Management

Raquel Okubo

School of Nursing: The University of Texas at El Paso

Doctor of Nursing Practice (DNP) Program

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

DNP Quality Improvement Project

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Abstract

Background: Thiazide diuretics are currently the first-line treatment for hypertension (HTN). This class of drugs includes hydrochlorothiazide (HCTZ) and the thiazide-like diuretic, chlorthalidone (CTDN). The quality improvement project began in the fall semester with a 10-day reflective practice log to assess my current practice. A review of the clinical practice log allowed me to evaluate my current practice and identify three opportunities to improve my practice. I developed three potential PICOT questions and selected one for the QI project with the guidance of my Doctor of Nursing Practice (DNP) chairperson. I performed a literature review to gather the best evidence-based intervention to improve my practice. My current practice was to use HCTZ, losartan, or lisinopril as initial treatment for uncontrolled blood pressure (BP). The literature review's new evidence-based intervention was to initiate CTDN 25mg per day as the first line of treatment for HTN in adults 18 to 73 years of age. I presented the QI proposal of the evidence-based intervention to the IRB at The University of Texas at El Paso (UTEP) and my worksite supervisor. Approval from the IRB at UTEP and work supervisor were obtained in letter form before initiation of the QI project. I implemented the evidence-based QI project for six weeks in the Spring semester.

Purpose: This Quality Improvement (QI) project aims to use CTDN as a first-line treatment to achieve effective BP control in patients 18 to 73 years of age within 4 weeks.

Methods: A Plan-Do-Study-Act quality improvement method was used in this QI project. To assess the effectiveness of CTDN treatment, I recorded pre-intervention baseline BP measurements during the initial visit, followed by post-intervention BP measurements two to three weeks after that.

Intervention: Evidence-based CTDN monotherapy was initiated as a first-line treatment for patients 18 to 73 years of age diagnosed with HTN. CTDN was also added as a combination therapy to the drug regimens of known hypertensive patients. Kurt Lewin's three-stage model of change was used as the translational framework for this QI project. This model requires the provider to participate in the steps that include (1) unfreeze (i. e., identifying patients with uncontrolled HTN), (2) change (i. e., beginning treatment with CTDN), and (3) re-freeze (i.e., making the new evidence-base treatment of CTHN permanent).

Results: Twenty-seven patients, eight males, and 19 females, 18 to 73 years of age, were identified for QI improvement. Reductions in SBP (100%) and DBP (81%) were observed in the participants. The average reductions in SBP and DBP were 25 mmHg and 7 mmHg, respectively.

Conclusions: The use of CTDN as a first-line treatment in this patient population reduces both SBP and DBP

Keywords: Diuretic, Thiazides, Essential Hypertension, Hypertension, Potassium-sparing diuretics, Loop diuretics

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Hypertension (HTN) is a global public health concern that affects one billion individuals worldwide. The number of individuals with HTN is projected to increase to 1.56 billion by 2025. Current evidence suggests that efforts to reduce blood pressure (BP) decreases rates of morbidity and premature mortality. High BP has been associated with the risk of sudden death. Early detection and management of BP are essential to reduce the risk of developing CV disease (CVD). Epidemiological associations of BP and CV events have been linked to SBP readings >115 mmHg. In the United States increase in sedentary lifestyle and obesity have contributed to an increase in HTN. Since 2015, HTN has been identified as the leading contributor to premature death, including 10 million deaths and 200 million disability-adjusted life years (Williams et al., 2018). Most clinical treatment guidelines recommend thiazide or thiazide-type diuretics as first-line therapy for the treatment of HTN. According to Cooney et al. (2015) interest in the potent thiazide-like diuretic chlorthalidone (CTDN) has increased after the 2002 publication of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT).

Thiazide diuretics reduce fluid retention and treat salt-sensitive HTN in most adults, including African Americans, the elderly, and those diagnosed with metabolic syndrome (Roush et al., 2015). Over the years, many researchers have argued that HCTZ and CTND can be used interchangeably (Cooney et al., 2015). Both drugs target the sodium chloride symporter in the distal convoluted tubule of the kidney. However, while the half-life of HCTZ is 6.5 to 9 hours, the half-life of CTDN is 25 to 55 hours (Liang et al., 2017). Thus, CTDN is a superior diuretic as the first line of treatment for HTN.

Problem Description

Providence Medical Partners is an ambulatory clinic on the west side of El Paso, Texas that provides primary medical care for ambulatory adults and the local geriatric population. The current practice that was not effective was to use HCTZ, losartan, or lisinopril as initial treatment for uncontrolled blood pressure (BP). The new evidence base intervention produced by the literature review was to initiate CTDN 25mg per day as the first line of treatment in adults 18 to 73 years of age.

Available Knowledge

Clinical practice guidelines (CPGs) aid in the effective management of HTN (Philip et al., 2021). Major CPGs reviewed for this QI project included JNC 8 Guidelines for the Management of Hypertension in Adults (Armstrong, 2014); the publication entitled "Systematic Review of the 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults" (Reboussin et al., 2018); the 2017 ACC/AHA clinical practice guideline for high BP in adults (Whelton et al., 2018); the 2018 European Society of Cardiology (ESC)/European Society of Hypertension (ESH) Guidelines for the management of arterial hypertension (Williams et al., 2018); and the 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children from Hypertension Canada (Nerenberg et al., 2018). All five CPGs recommend thiazide diuretics as first-line treatments for HTN.

In a meta-analysis conducted by Dineva et al. (2020) the authors concluded that CTDN was superior to HCTZ in controlling both SBP and DBP. The results of this study were based on outcomes from 1289 sources, including 37 randomized control trials (RCTs). Of note, the authors identified no significant difference in the safety profiles of HCTZ *versus* CTDN.

The goal of the ALLHAT study (Johnson et al., 2019) was to quantify the impact of lisinopril, amlodipine, doxazosin, and CTDN on heart failure secondary to HTN. Participants in the ALLHAT trial were randomized to lisinopril, amlodipine, and doxazosin treatment groups, then compared to outcomes from groups treated with CTDN. The results of this study revealed that CTDN was more effective at reducing BP and preventing heart failure.

A Cochrane systematic review published by Xue et al. (2015) compared the use of renin-angiotensin system (RAS) inhibitors with other drugs used to treat HTN. Among their results, the authors of this study found that the incidence of heart failure and stroke in patients treated with RAS inhibitors was higher than in those treated with a first-line thiazide drug. The authors concluded that thiazide diuretics were superior to RAS in preventing CV complications.

Chen et al. (2018) published an updated version of the 2015 review that evaluated the risks and benefits of RAS inhibitors compared to other first-line antihypertensive drugs in patients diagnosed with HTN. The study included 45 randomized, double-blind, parallel design RCTs that included 66,625 participants. The authors concluded that all-cause mortality was similar among those treated with first-line RAS inhibitors, CCBs, thiazides, and beta-blockers. However, first-line treatment with a thiazide diuretic resulted in a reduced incidence of heart failure and stroke when compared to outcomes using first-line RAS inhibitors.

Another Cochrane systematic review by Musini et al. (2019) specifically addressed the use of pharmacotherapy to treat HTN in adults 60 years of age or older. The primary aim of this study was to quantify the effects of antihypertensive drug treatment compared with placebo or no therapy on mortality due to all causes. Most of the studies reviewed in this work featured thiazide diuretics as first-line treatment. Among the important findings, the result revealed that

pharmacotherapy to reduce BP in hypertensive patients ≥60 years of age reduced the incidence of stroke, heart attack, and premature death.

Musini et al. (2017) also published a Cochrane review focused on pharmacotherapy for hypertension in adults ages 18 to 59 years. The primary aim of this study was to quantify the impact of antihypertensive drugs on mortality due to all causes in adults. As part of this review, the authors evaluated patients on thiazide treatment divided into high-dose and low-dose cohorts. The authors concluded that low-dose thiazide was beneficial in reducing the incidence of mortality due to all causes and total CV events, including coronary heart disease and stroke.

The 2018 guidelines provided by Hypertension Canada for evidence-based diagnosis, risk assessment, prevention, and treatment of HTN suggest that adult patients might start with monotherapy or single-pill combination therapy. Recommended choices for monotherapy include long-acting diuretics, such as thiazide or thiazide-like diuretics (Nerenberg et al., 2018).

More recently, Filipova et al. (2020) published a study entitled "Combining angiotensin receptor blockers with CTDN or HCTZ–which is the better alternative? A meta-analysis" that was designed to investigate the impact of the combination of an ARB with CTDN or HCTZ on SBP and DBP measurements in patients diagnosed with HTN. The results suggested a small but statistically significant improvement in BP control among patients treated with CTDN *versus* HCTZ.

Finally, an editorial by Kjeldsen et al. (2020) criticized the decision made by the International Society of Hypertension (ISH) to move thiazide or thiazide-like diuretics from first-line therapy to Step 3 for the treatment of HTN. This decision was based on findings from the ACCOMPLISH trial, which concluded that CV events among patients with systolic HTN might be avoided via the use of combination therapy. Kjeldsen et al. (2020) argued that this decision

was not supported by the results of numerous outcome trials that revealed the benefit of thiazide or thiazide-type diuretics in preventing CV disorders, including stroke, heart failure, MI, left ventricular hypertrophy, and aortic aneurysm.

Rationale

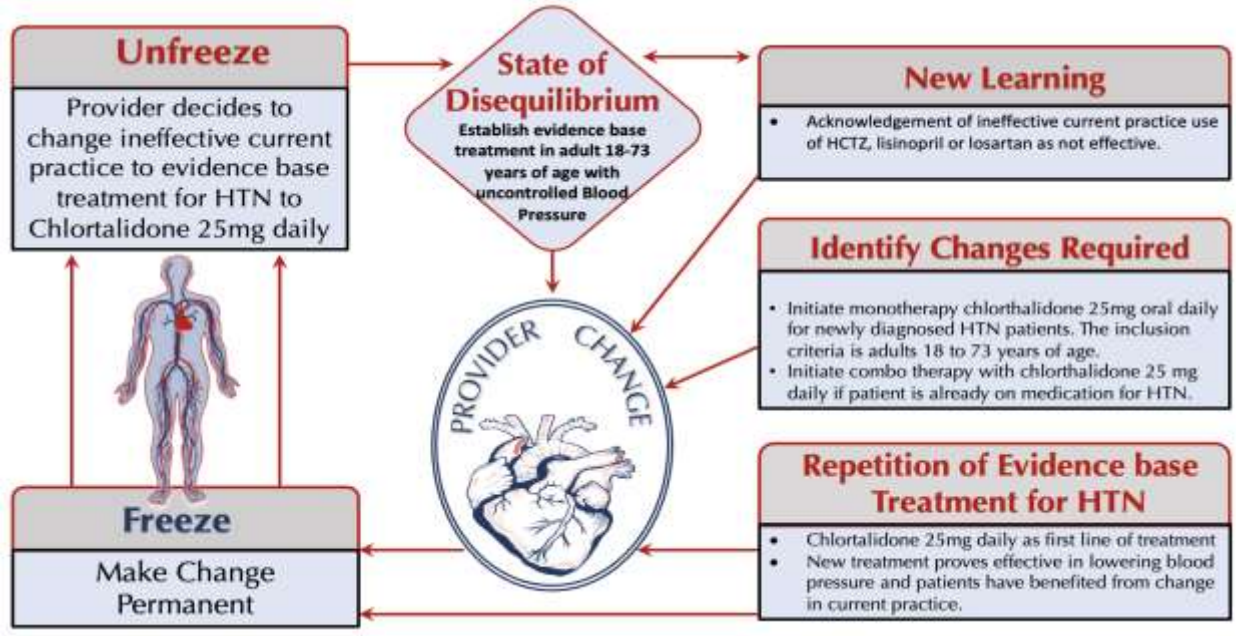
Kurt Lewin's model of change supports this quality improvement project that was first described in 1958. The model focuses on stages of change/transition that were identified as unfreezing, change or transition, and freezing/refreezing (Doolin et al., 2010). The theory explains how an intervention or set of interventions can lead to change and allows one to promote change based on causal analysis and best evidence.

The first step of the three-stage model, known as “unfreezing,” requires the abandonment of prior treatment interventions by the provider. Once “unfrozen,” the provider can transition to a state of disequilibrium to change current practice treatment for HTN via acts that include new evidence-based treatment for HTN. Once the provider observes the benefit of the evidence-based treatment of chlorthalidone, these changes can be “refrozen” and incorporated for future patients to benefit from the new evidence-based treatment. This model is largely cyclical in nature and permits an appropriate response once disequilibrium develops in a current state or practice. An individual may move between all three stages and return to the beginning to introduce new information. The process also involves the critical motivation needed to institute change to become permanent (Hussain et al., 2018).

Change requires adding force that disrupts a perceived equilibrium and/or removing barriers to destabilization of current behavior. Figure 1 provides a visual representation of Lewin's model of change and the steps I applied to implement changes in current practice using evidence-based CTDN as the first line for treatment of HTN in adults 18-73 years of age.

Figure 1

Change Theory (Lewin, 1958): a Visual Interpretation for Treatment Hypertension.



Specific Aims

The primary aim of the evidence-based QI project was to change ineffective current treatment for HTN of HCTZ, lisinopril, or losartan to improve my clinical practice. The evidence-based QI intervention is to start patients with monotherapy or combination therapy of CTDN 25mg daily. The inclusion criteria were hypertensive adults ages 18-73 years of age with uncontrolled HTN.

Methods

Context

The QI project aims to lower BP using evidence-based treatment with CTDN 25mg as first-line treatment. The QI project was implemented at Providence Medical Partners in an ambulatory clinic on the west side of El Paso, Texas, that provides primary medical care to

adults and the local geriatric population. The QI project commenced on September 3, 2021, with CITI training for IRB human research, HIPPA, research populations, ethical considerations, and regulations.

Detailed Description of Intervention(s)

Needs assessment. On September 7, 2021, I conducted a needs assessment using a 10-day reflective practice log to identify three opportunities to improve my current practice at Providence Medical Partners Clinic (Resler location, El Paso, Texas). Data collected in the needs assessment included the age and gender of each patient, chief complaint, diagnosis, assessment tools, Current Procedural Terminology (CPT) codes, International Classification of Disease (ICD)-10 codes, interventions, and documentation of the need for follow-up visits. The inclusion criteria were adult patients 18 to 73 years of age.

Review of patients. Ninety-three patient visits were recorded in the 10-day reflective practice log. Thirty-two percent (32%) of these encounters involved a diagnosis of HTN. Patients were categorized based on demographic data, diagnosis, treatment, and tools used for each patient visit.

Insight gained. After reviewing my 10-day reflective practice, I identified three protentional opportunities to improve the care that I presently provide my patients. Three potential PICOT questions were developed. I met with my Doctor of Nursing Practice (DNP) chairperson, and one PICOT question was selected for the quality improvement project and began my literature review.

PICOT question. This DNP QI Project aims to use evidence-based data to improve BP control among adults 18–73 years of age seen at Providence Medical Partners ambulatory primary care clinic.

Population: Patients 18 to 73 years with uncontrolled BP.

Intervention: Therapy with CTDN (25mg per day by mouth) was initiated.

Current practice: HCTZ, Losartan, or Lisinopril.

Outcomes: Controlled blood pressure.

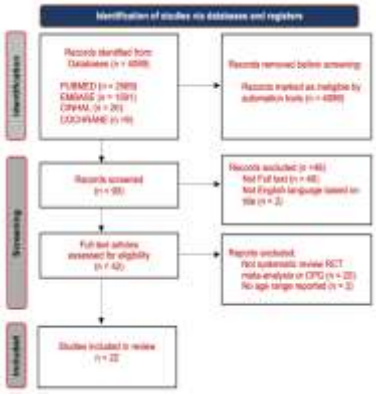
Time: Within four weeks.

Literature review. The literature review for the project was guided by the question: What is the best effective evidence-based first-line treatment for HTN in adults 18-73 years of age.

I searched the following databases for RCTs published between 2016 – 2021: Medline, CINAHL, PubMed, Embase, and the Cochrane databases with key terms: diuretics, thiazides, essential hypertension, hypertension, potassium-sparing diuretics, and loop diuretics. The literature search focused on studies that provided the highest level of evidence, including level 12, systematic reviews of randomized controlled trials (RCTs) and meta-analyses; level 11, meta-analyses of experimental RCTs and quasi-experimental studies; and level 10, integrative reviews of experimental RCTs and quasi-experimental studies (Figure 2).

Figure 2

Study diagram of research articles published from 2016 to 2021.



Note: Twenty-two studies (i.e., "First-line drugs for hypertension" as shown below) met the inclusion criteria for quantitative synthesis focused on 18-73- year-old participants.

DNP QI proposal. The Plan-Do-Study-Act (PDSA) cycle guided the QI project. According to the IHI (2020), the PDSA cycle is used in the QI project to test the change (i. e., Plan), carry out the test (i. e., Do), observe the consequences and learn from them (i. e., Study), and determine what modifications if any should be made (i. e., Act).

The QI project focused on using CTDN 25mg daily as a first-line treatment for hypertensive patients who receive care at the Providence Medical Partners/Resler clinic. The following is an outline of the different components of the PDSA cycle:

Plan: I Identified uncontrolled hypertensive patients ages 18-73 years of age.

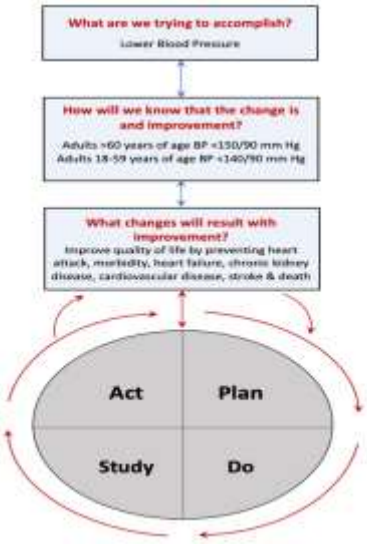
Do: I documented a baseline BP on the initial visit before initiating CTDN 25mg daily. I then scheduled patients for follow-up 2-3 weeks after to record a post-intervention BP.

Study: I compared BP measurements taken before and after evidence-based treatment for each patient.

Act: Based on an analysis of the BP results, I determined the evidence base efficacy of CTDN for reducing BP in 18–73-year-old adults at my clinic (Figure 3).

Figure 3

PDSA: QI for hypertension (IHI, 2020)



IRB application and work supervisor letter approval. The QI project used evidence-based literature and methodologies and complied fully with the federal regulations and requirements regarding the rights and welfare of the human participants. These requirements included:

1) A work letter from my work site supervisor providing approval to perform a QI project.

2) Submission of QI project proposal and application to the University of Texas at El Paso Institutional Review Board (IRB).

On November 8, 2021, UTEP IRB letter of approval was obtained for this QI project entitled "Thiazide Diuretic as First-line Treatment for Effective Blood Pressure Management" [QI ref. 1811282-1]. The IRB determined this project did not meet the definition of human subject research under the purview of the IRB according to federal regulations.

On October 29, 2021, I was granted permission by the worksite supervisor at Providence Medical Partners to conduct the QI project titled "Thiazide-like Diuretic as First-line Treatment to Improve Blood Pressure Management."

Study of Interventions

I implemented the QI project over a six-week timeline on January 18, 2022. I performed BP measurements using a manual BP cuff to confirm uncontrolled HTN after patients were permitted to wait alone in the examination room for 15 minutes. The criteria for enrollment in the QI project included patients 18–59 years of age with a BP ≥140/90 mmHg and patients ≥60 years of age with BP ≥150/90 mmHg. Monotherapy (CTDN; 25mg mg daily) was initiated in newly diagnosed hypertensive patients. The same dose (CTDN; 25mg mg per day) was provided to patients who remained hypertensive on a pre-existing antihypertensive medication regimen.

Patients who accepted new medication were instructed to keep a home diary and bring it to the clinic on the next patient visit. I recorded a baseline BP at the first and follow-up visit. The QI project intervention incorporated the PDSA cycle consistent with its goal.

Kurt Lewin's Model of Change (Lewin, 1958) provided the theoretical framework that guided this QI project. This model included a three-step process (i. e., unfreezing, changing, and refreezing). The theory explains the three-step interventions the provider must accomplish to establish and to make the new evidence base treatment permanent

Measures

My completed DNP QI project demonstrated the benefit of the change in evidence-based treatment of CTDN. The impact on BP improvement is supported by comparing pre and post BP measurements.

Analysis

Quantitative patterns in pre-intervention and post-intervention BP measurements were measured by averaging SBP and DBP to calculate pre- and post-intervention BPs. Evaluation of data is presented on two separate line graphs for SBP and DBP (figure 1). Twenty-seven patients (eight males and 19 females) met the criteria for the QI project. Seventeen patients were < 60 years of age and 10 were ≥60 years of age.

Ethical considerations

Patient inclusion. Inclusion criteria for the QI project required hypertensive adults 18-73 years of age with uncontrolled BP. Patients who qualified for the QI project were consulted regarding the decision to initiate new treatment. Side effects as listed by the drug manufacturer, goal of treatment, and evidence-based treatment for HTN were discussed with the patient. Patients were allowed to make an informed decision regarding the new treatment. All patients

were provided with an opportunity to refuse treatment and were provided with an alternative treatment strategy as necessary.

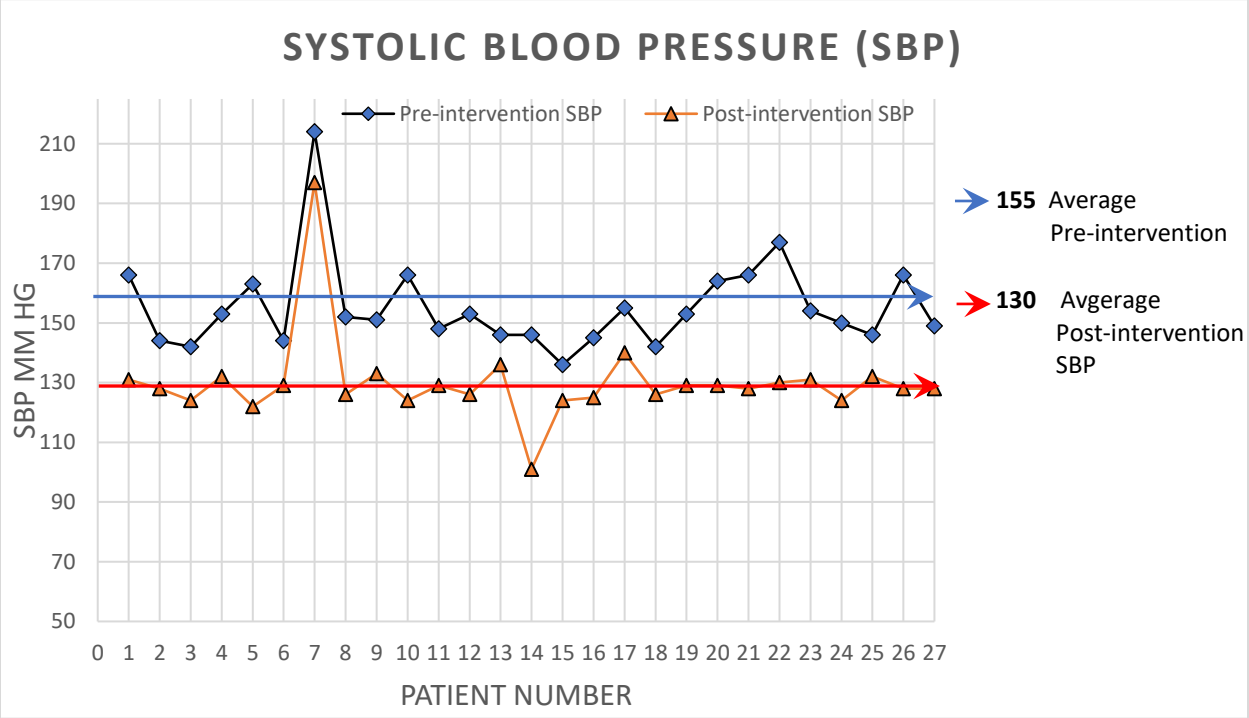
Clinical data. I collected, managed, and analyzed all patient data. The patient data remained in the electronic health record throughout the study. Only non-identifying data were collected together with initial (pre-intervention baseline) and follow-up (post-intervention) BP measurements.

Results

Twenty-seven patients (age 18-73) met the inclusion criteria of the evidence-base QI project and were treated with CTDN. Of these, 27 patients (100%) responded with a reduction in SBP; 22 of the 27 (81%) exhibited reductions in DBP. The average pre-intervention SBP was 155 mmHg, and the post-intervention average was 130 mmHg (figure 4). The average DBP pre-intervention was 85 mmHg and 78 mmHg post-intervention (figure 5). I performed all the measurements included in this study to maintain the reliability of the data.

Figure 4

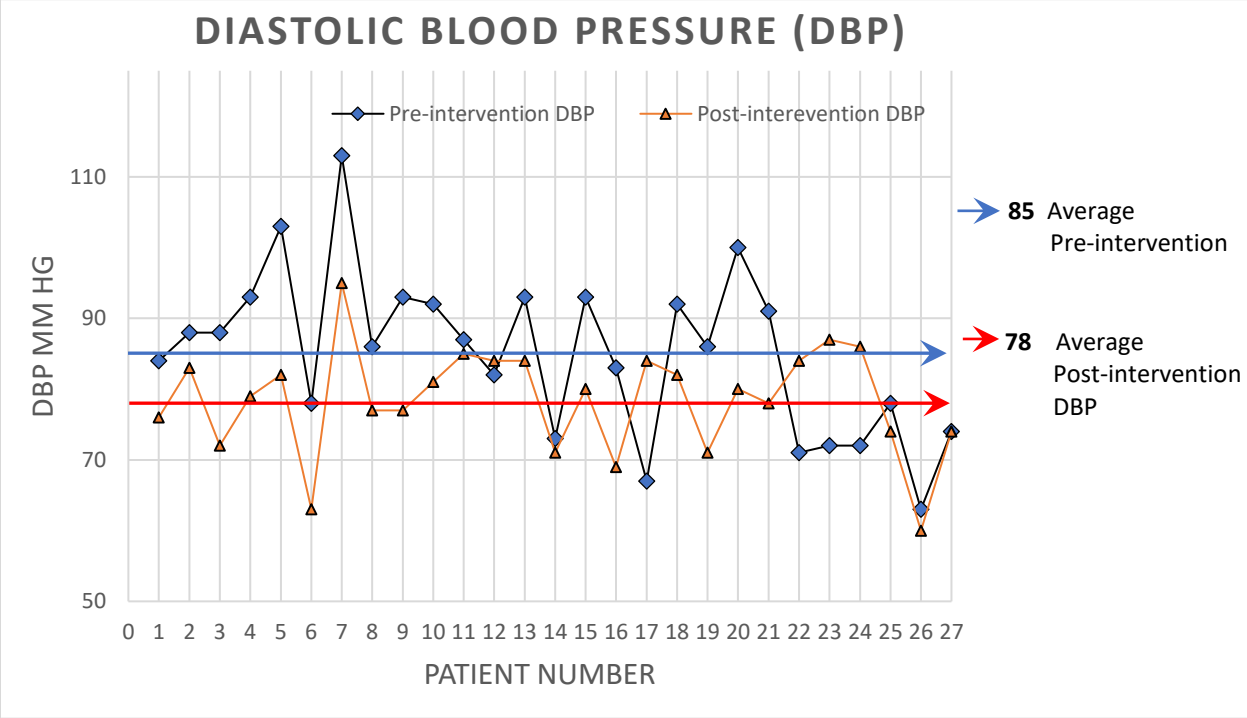
SBP at Baseline (pre-intervention) and Follow-up (post-intervention)



Note: Shown are pre-intervention (black line) and post-intervention SBPs (orange line) for each patient (1–27). Average values for the entire cohort are indicated by the blue (pre-intervention SBP at 155 mmHg) and the red line (post-intervention SBP at 130 mmHg).

Figure 5

Diastolic BP at Baseline (pre-intervention) and Follow-up (post-intervention)



Note: Shown are pre-intervention (black line) and post-intervention SBPs (orange line) for each patient (1-27). Average values for the entire cohort are as indicated by the blue (pre-intervention DBP at 85 mmHg) and the red line (post-intervention DBP at 78 mmHg).

The PDSA QI model cycles and Lewin's Model of Change provided awareness of the phases of the QI project. The PDSA cycles provided immediate feedback to the patients as they monitored their BP and witnessed the reduction of BP. Provider analysis of data provided data to support the benefit of using CTDN as a first-line treatment to control HTN.

The QI project enrolled 27 participants. Of the initial 27, all patients participated in a follow-up post-intervention visit (one patient did not comply with the CTDN regimen and admitted to never taking medication).

Discussion

Summary

The QI project has documented the efficacy of CTDN as mono- or combination CTDN to reduce BP. The results of the QI project support the evidence-based CTDN as a first-line pharmacologic treatment for HTN and have been proven to lower BP and prevent CVD outcomes and premature death. This QI project further supports the literature on the benefits of preventing stroke, heart failure, MI, left ventricular hypertrophy, aortic aneurysm, and HTN-related conditions, including obesity, diabetes, and impaired renal function.

Interpretation

After completing the QI project, patients taking CTDN to reduce BP took an active role in monitoring their BP. Patients brought their BP diary to follow-up visits and reported that they were more involved in their healthcare. Patients reported making healthful changes to their diet, engaging in exercise, having fewer headaches, and finding it easier to breathe. Patients benefited from less leg edema and lost weight due to the diuretic effect of this drug. Overall the patients were satisfied with the results of the new evidence base treatment regimen.

Limitations

I implemented the QI project in an ambulatory primary care patient clinic over the course of six weeks. While the simplicity of this project facilitates its use in other settings, its sustainability will depend on its specific application of the QI project by other providers at different locations. My evidence-based QI project findings at Providence Medical Partners clinic prove that first-line treatment with a thiazide-like diuretic CTDN will effectively reduce BP.

Conclusions

The QI project aimed to improve BP control in our primary care patients with evidence base first line treatment CTDN 25mg mg daily. The evidence-based QI project demonstrated the effectiveness of CTDN as an antihypertensive agent that can be used to reduce BP. CTDN can be found among the preferred evidence-based first-line antihypertensive drugs because of its unsurpassed efficacy in reducing BP combined with its prolonged half-life.

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