

**Empagliflozin and/or Metformin: A Combination Approach for Uncontrolled Type 2
Diabetes**

Maria Crespín

School of Nursing, The University of Texas at El Paso

DNP Chair, DNP Quality Improvement Project

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

May 2, 2022

Abstract

Background: Current guidelines recommend metformin as the first-line agent therapy for the management of Type 2 Diabetes (T2D) when diet and exercise are insufficient. When monotherapy with metformin is intolerant or contraindicated, or not sufficiently effective to reach the glycated hemoglobin (HbA1c) target, a second anti-diabetic agent as an alternative or add-therapy to metformin is recommended by all guidelines. The quality improvement project was initiated in the fall semester with a 10-day reflective practice log to assess my current practice. A review of the clinical practice log allowed for evaluation of 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 in search of the best evidence-based intervention to improve my practice. My current practice is metformin 500-1000mg twice daily as a first line treatment for T2DM. The new evidence-based intervention that I found in the literature review was to initiate empagliflozin 10-25mg once daily as the first line treatment or as add-on therapy to metformin in adults 18 to 78 years of age with uncontrolled T2DM. The evidenced based QI proposal was presented to the Internal Review Board (IRB) at The University of Texas at El Paso (UTEP) and my worksite manager. An Approval letter was obtained from the IRB at UTEP and work site manager before initiation of the QI project. The evidence-based QI project was implemented for six weeks in the Spring semester.

Purpose: This Quality Improvement (QI) project aims to use a sodium-glucose cotransporter 2 (SGLT2) inhibitor alone or in combination with other agents to improve glycemic control in patients 18 to 78 years of age with uncontrolled T2DM (HbA1c >7%) within 4 weeks.

Methods: The Plan-Do-Study-Act (PDSA) method of quality improvement was used in this project. Baseline HbA1c levels were recorded at the first visit before initiating the intervention. Post-intervention HbA1c levels were recorded two weeks after initiating the intervention to assess its efficacy and tolerance of the new medication. Blood pressure and weight were recorded on the first visit and after initiating intervention.

Intervention: The SGLT2 inhibitor, empagliflozin was selected as first-line therapy for patients with new-onset T2DM. Empagliflozin was added as a combination treatment to the drug regimens of patients who presented with T2DM that was not adequately controlled by metformin. Inclusion criteria were (1) all patients 18–79 years of age who were (2) newly diagnosed or presenting with uncontrolled T2DM (HbA1c >7%). Kurt Lewin’s three-step model was used as the translational theoretic framework for this project. The steps included (1) Unfreeze (i.e., acknowledging that a change is needed); (2) Change (i.e., initiate treatment with an SGLT2 inhibitor, and (3) Refreeze (i.e., make the change permanent and continue the patient on this drug).

Results: Nineteen patients between the ages of 23–78 years old (18 females and one male) were identified in the QI project. The average reduction in HbA1c levels was 0.21%. Thus, the results of this project suggested an overall trend toward improvement of glycemic control.

Conclusion: Empagliflozin provided as monotherapy or as an add-on to metformin was effective at reducing HbA1c to improve glycemic control. Patients treated with empagliflozin also responded with reduced systolic blood pressure and weight loss.

Keywords: First-line treatment, Type 2 Diabetes, Glycemic control, Monotherapy, Combination therapy, and Sodium-glucose cotransporter-2 inhibitor

Empagliflozin and/or Metformin: A Combination Approach for Uncontrolled Type 2 Diabetes

Increased emphasis has been placed on glycemic management in response to the rising prevalence of type 2 diabetes mellitus (T2DM) in the United States. T2DM is a chronic progressive disease associated with severe complications that include cardiovascular disease, stroke, amputation, end-stage kidney disease, blindness, and premature death (American Diabetes Association, 2020). The United States Centers for Disease Control and Prevention (CDC) estimates that over 34.2 million people are living with diabetes in the United States alone; 90–95% of these individuals have been diagnosed with T2DM (Rowley et al., 2017). With more than 4000 new cases of diabetes are diagnosed each day, the CDC predicts that the number of people living with diabetes may reach ~55 million (Rowley et al., 2017). The resources needed to provide adequate care for all patients with T2DM place a considerable economic burden on healthcare systems that may already be overwhelmed.

Effective clinical management of type 2 diabetes mellitus (T2DM) requires an optimized treatment plan to ensure adequate glycemic control and reduce the incidence of diabetic complications. Because of the progressive nature of T2DM, standard first-line treatment with metformin alone is frequently insufficient to achieve glycemic control. In these cases, additional agents are required. The American Association of Clinical Endocrinology Consensus Statement (Garber et al., 2020) recommends the addition of other oral agents to the standard metformin regimen in patients who do not achieve target levels of glycated hemoglobin (HbA1c) after approximately three months of monotherapy or an increase of HbA1c >1.5 %. There are currently many new oral agents available for patients with newly-diagnosed or uncontrolled T2DM. In addition to metformin, which is a biguanide, other non-insulin-based

pharmacotherapies include sodium-glucose cotransporter 2 (SGLT2) inhibitors, dipeptidyl peptidase-4 (DPP4) inhibitors, glucagon-like peptide-1 (GLP1) receptor agonists, thiazolidinediones, (TZD), and sulfonylureas. The antihyperglycemic actions of these drugs are mediated by a variety of distinct molecular mechanisms.

Problem Description

Ben Archer Health Center is a federally qualified health center located in the rural town of Las Cruces, New Mexico that provides primary care to children and adults of all ages. The current practice that was ineffective was Metformin 500-1000mg twice a day as initial treatment for uncontrolled T2DM. The new evidence-based intervention produced by the literature review was to initiate empagliflozin 10-25mg once daily as a first-line treatment or as an add-on therapy to metformin in adults 18 to 78 years of age.

Available Knowledge

The American Diabetes Association (ADA) recommends the management of T2DM with one of six commonly-used antihyperglycemic agents (AHAs), including (1) sulfonylureas; (2) thiazolidinediones; (3) DPP4 inhibitors; (4) SGLT2 inhibitors; (5) GLP1 receptor agonists; or (6) basal insulin analogs. These agents can be provided as add-on therapy when the individualized HbA1c target level is not reached after approximately three months of treatment with metformin alone. The ADA standards of care do not provide any specific recommendations regarding the selection of a drug to be used in a dual-therapy regimen. Instead, their guidelines suggest that drug selection can be based on patient preferences, risk of developing hypoglycemia, side effect profile, and cost, among other patient and disease characteristics (American Diabetes Association, 2020).

The SGLT2 inhibitor, empagliflozin, reduces blood glucose levels in patients with T2DM. Drugs of this class (also known as glucoetics) have a unique mechanism of action and are among the most recently approved AHAs. The insulin-independent antihyperglycemic effects of SGLT2 inhibitors are mediated by their capacity to suppress glucose reabsorption in the renal tubules, thereby facilitating its excretion in urine. In the absence of drug treatment, approximately 90% of the filtered load of glucose is reabsorbed in the proximal convoluted tubule. Thus, SGLT2 inhibitors provide an innovative approach to reducing glycemia.

The United States (US) Food and Drug Association (FDA) has approved three drugs of this class, including canagliflozin, dapagliflozin, and empagliflozin. As a group, SGLT2 inhibitors have excellent safety, efficacy, and tolerability profiles and present no significant risk of hypoglycemia. In addition to improving glycemic control, SGLT2 inhibitors have numerous positive effects on body weight, blood pressure, hyperuricemia, and dyslipidemia, and may prevent fatty liver disease. While SGLT2 inhibitors are typically introduced as second or third-line add-on AHAs for treating T2DM, they can also be used as first-line monotherapy when metformin is contraindicated (Garber et al., 2020).

A systematic review by Scheen et al. (2020) concluded that the addition of an SGLT2 inhibitor to a standard metformin regimen resulted in consistent reductions in HbA1c, fasting blood glucose, body weight, and systolic blood pressure. Of note, no significant differences were observed between Asian and non-Asian patients.

A meta-analysis performed and reported by Chen & Li (2020) compared the efficacy of SGLT2 inhibitors with sulfonylureas as second-line agents in patients who were not adequately controlled on metformin alone. The authors concluded that SGLT2 inhibitors are more effective

over the long term and do not cause hypoglycemia. Secondary outcomes in this study included improvements in body weight and systolic blood pressure.

A systematic review by Fuchigami et al. (2020) compared the cardiovascular benefits of drug regimens that included SGLT2 inhibitors *versus* those of the DPP4 class. The results of the study suggested that SGLT2 inhibitors were superior to DPP4 inhibitors for achieving goals that included reductions in body weight, serum aspartate transaminase (AST) and alanine aminotransferase (ALT), fasting plasma glucose, and fasting plasma insulin levels. Consistent with previous reports, the results of this study also suggest that the use of SGLT2 inhibitors may improve hepatic steatosis.

A meta-analysis by Zou et al. (2020) evaluated the cardiovascular outcomes in patients treated with SGLT2 inhibitors compared to controls. They concluded that SGLT2 inhibitors decreased the cardiovascular risk associated with T2DM and led to a reduction in the incidence of major adverse cardiovascular events. Usman et al. (2018) also reported that treatment with SGLT2 inhibitors significantly reduced the incidence of major adverse cardiac events, including non-fatal myocardial infarction, heart failure, and premature mortality in patients diagnosed with T2DM. All three available SGLT2 inhibitors appear to have similar cardioprotective effects.

A consensus statement from the American Association of Clinical Endocrinology (2020) confirmed that empagliflozin (Jardiance®) was associated with significantly reduced rates of all-cause and cardiovascular death and reduced the risk of hospitalization for heart failure in patients enrolled in the EMPA-REG OUTCOME (Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes) trial.

Lautch et al. (2020) compared the results of monotherapy and dual initiation therapy with numerous agents. The results of their meta-analysis revealed that dual initiation therapy led to

significantly better outcomes than were achieved with most of the monotherapy regimens with respect to reductions in HbA1c, body weight, and SBP over 24–26 weeks of follow-up of T2DM patients who were poorly controlled on metformin alone.

A systematic review and meta-analysis by Donnan et al. (2019) aimed to examine any harmful post-market sequelae of SGLT2 inhibitors that were identified by drug regulatory agencies. The authors concluded SGLT2 inhibitors were associated with no increased risk of harm compared to placebo or active comparators, specifically with respect to acute kidney injury, diabetic ketoacidosis, urinary tract infections, or fractures.

A randomized placebo-controlled trial conducted by Babar and Aktar (2021) compared the outcomes of 240 obese T2DM patients with inadequate glycemic control while on both metformin and sitagliptin (HbA1c >7%). In this 24-week study, patients in group B were provided with add-on treatment with empagliflozin (10 mg twice a day), while patients in group A were provided with a placebo. Patients treated with empagliflozin lost more weight than those provided with a placebo (6.9 ± 2.4 kg *versus* 3.1 ± 0.8 kg, respectively).

Hussain et al. (2021) reported the results of a randomized controlled trial designed to compare empagliflozin and dapagliflozin in patients with T2DM with inadequate glycemic control while on conventional first-line treatment. After 12 weeks, both groups exhibited weight loss from baseline values. Patients treated with empagliflozin exhibited a greater reduction in body mass index (BMI) compared to the patients treated with dapagliflozin. Both drugs were well-tolerated with no major adverse effects. Urinary tract infections were more prevalent in the patients on dapagliflozin (9.3%) than in those treated with empagliflozin.

A randomized controlled trial performed by Hadjadj et al. (2016) compared the safety and efficacy of combination treatment (metformin and empagliflozin together) to monotherapy

with either metformin or empagliflozin alone in patients with T2DM. The combination of empagliflozin and metformin was well-tolerated and resulted in significant reductions in HbA1c compared to empagliflozin (once daily) or metformin (twice daily) alone, with no increase in the incidence of hypoglycemia. Combination therapy also resulted in significantly greater reductions in HbA1c than were achieved with monotherapy with either of the two drugs. The combination regimen also resulted in a more significant weight loss at 24 weeks compared to metformin or empagliflozin alone.

A systematic review published by Molugulu et al. (2017) reported that combined therapy with an SGLT2 inhibitor together with metformin was more effective at promoting reductions in body weight and HbA1c levels compared to monotherapy with metformin alone. A comparison of the outcomes from each of the three currently-available SGLT2 inhibitors revealed no substantial differences in weight reduction. However, empagliflozin (25 mg per day) was the most effective at reducing HbA1c levels. SGLT2 inhibitors used in combination regimens to treat patients with T2DM with poorly-controlled blood glucose levels were more effective at reducing HbaA1c and body weight compared to monotherapy with metformin alone.

The final study that I reviewed was a meta-analysis that compared the effects of glucose-lowering drugs on body weight and blood pressure in adults with T2DM. Metformin had a significant impact on both body weight and systolic blood pressure. However, diastolic blood pressure was reduced in patients treated with SGLT2 inhibitors, pioglitazone, exenatide (twice daily), or semaglutide. In subgroup analyses of trials that lasted 52 weeks or more, semaglutide and SGLT2 inhibitors were found to be effective at reducing both body weight and systolic blood pressure (Tsapas et al., 2021).

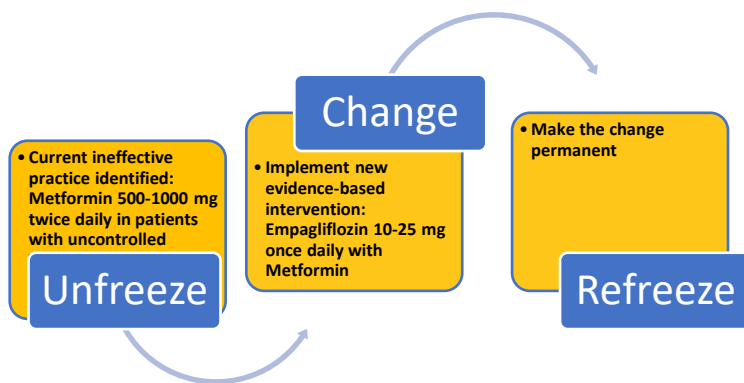
Rationale

This quality improvement (QI) project is designed to implement change in the management of T2DM in the primary care setting using Kurt Lewin's change model (Lewin, 1958) as shown in Figure 1. This model postulated that individuals and groups are influenced by driving forces that can hinder, foster, or maintain change. Lewin's theory of change comprises three stages: Unfreezing, Change, and Refreezing. 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 phase of the change process includes efforts to "unfreeze" the current situation by increasing the driving forces or decreasing the restraining forces that modulate change. This step often elicits a change in the behavior of the provider. It requires an acknowledgment/awareness that the current practice needs to be changed or abandoned. For example, Burnes (2004) stated that feelings of discomfort, apprehension, and distress might be experienced during this period. Educating individuals regarding the motives for change can enhance the strength of driving forces and facilitate the transition from the first to the second stage of Lewin's model. "Change" (moving) is the second phase of this model. During this period, the provider moves toward a new equilibrium of driving and restraining forces. The provider can transition to a state of disequilibrium to change current practice treatment for T2DM, which includes the new evidence-based treatment. The final phase is "refreezing" which is a process that must occur after the change is implemented to sustain the new equilibrium (Burnes & Bargal, 2017). In this stage, the provider has observed the benefits of the evidence-based treatment with empagliflozin and can refreeze and make the change permanent for patients in the future.

Figure 1

Kurt Lewin's Change Theory for T2DM



Specific Aims

The specific aim of this evidence-based project was to change the current ineffective treatment for T2DM of metformin to improve my clinical practice. The evidence-based QI intervention is the initiation of empagliflozin treatment (10–25 mg once daily) alone or as combination therapy with metformin. The inclusion criteria were patients with uncontrolled T2DM (HbA1c >7%) between the ages of 18-76.

Methods

Context

This evidence-based QI project was carried out at the Ben Archer Health Center, an FQHC located in rural Las Cruces, New Mexico. There are approximately 12 clinics included within this organization that are distributed throughout the southwest region of the state. The project The QI project started on September 5, 2021, with CITI training for IRB human research, HIPPA, research populations, ethical considerations, and regulations.

Intervention

Needs assessment. On September 7, 2021, I conducted a needs assessment using a 10-day reflective practice log (RPL) to identify opportunities to improve my current practice at Ben Archer Health Center. The data that was collected in the RPL included demographics such as age, gender, the reason for the visit, diagnosis and assessment tools used, intervention, and the need for follow up visits. Diagnosis codes (ICD-10) and Current procedural codes (CPT) were also included in the RPL.

Review of Patients. One-hundred-thirteen patients were recorded in the RPL. Thirty-four different diagnoses were identified. Eleven percent were diagnosed with T2DM. Each diagnosis was color coordinated.

Insights gained. After reviewing my ten-day RPL, I identified three potential opportunities to improve the care that I presently provide for my patients. Three potential PICOT questions were developed. I met with my Doctor of Nursing Practice (DNP) chairperson and selected one PICOT question for the QI project. Once the chairperson approved my project, I performed a literature review.

PICOT Question. This DNP QI Project aims to use evidence-based research validated intervention to improve glycemic control in patients with uncontrolled T2DM at Ben Archer Health Center in Las Cruces, NM.

Population: Patients 18-79 with uncontrolled T2DM (HbA1c >7%)

Intervention: Empagliflozin 10-25 mg once daily

Current practice: Metformin 500-1000 mg twice daily

Outcomes: Improved glycemic control

Time: Within 2-weeks

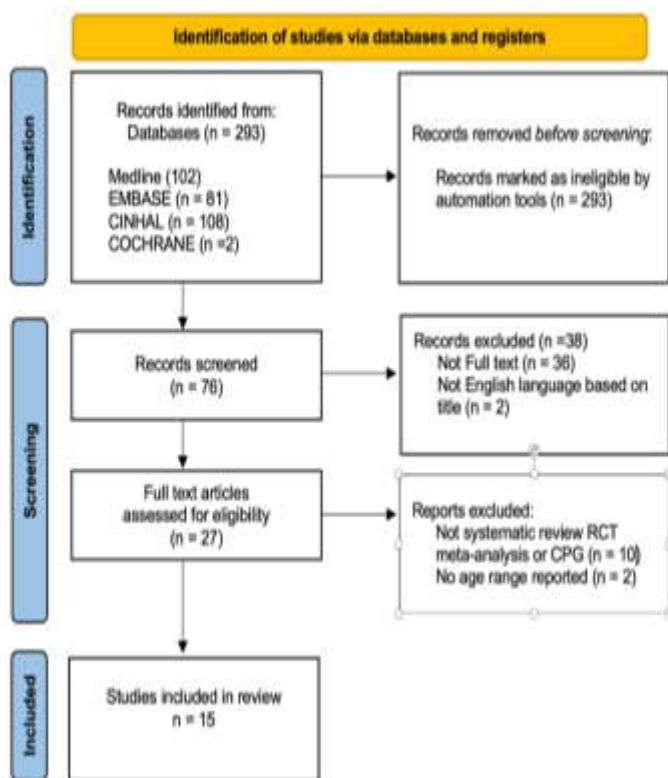
Literature Review

The following question was used to guide the literature review (Figure 2):

What is the best effective evidence-based treatment for uncontrolled T2DM in adults 18-78 years of age? I searched the literature using the CINAHL, PubMed, Embase, and Cochrane databases for randomized-controlled trials (RCTs), clinical practice guidelines, meta-analyses, and systematic reviews that were published in 2016 through 2021. The following keywords were used: Type 2 Diabetes, Monotherapy, Combination therapy, Sodium-glucose cotransporter-2 inhibitor (SGLT2), and Glycemic control

Figure 2

Study Flow Diagram



Note. PRISMA 2020 flow diagram for new systematic reviews that include searches of databases and registers only (Page et al., 2021).

DNP QI Proposal. The Plan-Do-Study-Act (PDSA) model guided the DNP QI project (Figure 3). This tool involves a circular motion and multiple interactions in an improvement cycle. Plan involves planning the change. Study includes analyzing results. Do is carrying out the change. Study involves analyzing results to determine what went wrong or was learned.

Plan: Identify patients between the ages of 18–79 years with new-onset T2DM or previously-diagnosed T2DM that remained uncontrolled on metformin (i.e., HbA1c >7%). Initiate empagliflozin as monotherapy or as a combination treatment for patients already taking metformin.

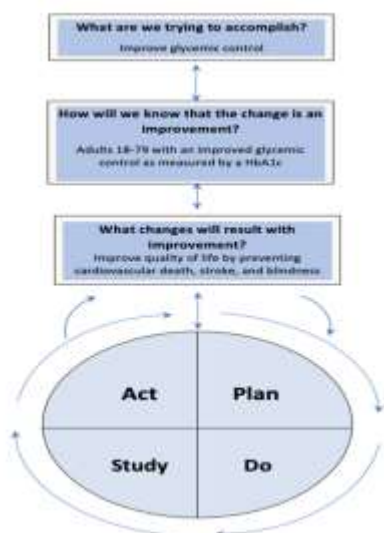
Do: I documented baseline HbA1c levels before initiating treatment. Patients were scheduled for a two-week post-treatment follow-up to assess drug tolerance and HbA1c levels.

Study: I compared HbA1c levels before and after two weeks of treatment.

Act: Based on the analysis of the results of HbA1c testing, I determined the efficacy of these drug regimens at improving blood glucose levels in patients 18-79 using an evidence-based intervention.

Figure 3

PDSA QI for T2DM



IRB application and work site 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: A work letter from work site manager approval letter to implement a QI project, submit QI project proposal and application to UTEP IRB.

On November 9, 2021, UTEP IRB letter of approval was obtained for this QI project entitled “Empagliflozin and/ or metformin: A combination approach for uncontrolled Type II diabetes. 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 November 01, 2021, I was granted permission by the worksite manager at Ben Archer to conduct the QI project.

Study of interventions

The QI project was performed during a six-week time frame that started on January 21, 2022. During the first four weeks, the patients were evaluated, and interventions were initiated. The final two weeks were for follow-up. Patients who met inclusion criteria for the QI project were between 18–78 years of age with new-onset or a known diagnosis of T2DM with an HbA1c level >7%. I recorded the HbA1c levels at the initial visit and determined whether or not the patient was taking metformin. I encouraged the patients to measure their fasting blood glucose levels every morning and to bring their glucose logs to their two-week follow-up visit. The patient was then capable of making an informed decision to accept or decline the intervention. The patients who took part in the QI project returned to the clinic two weeks after the initiation of the intervention. I recorded a post-intervention HbA1c level during the follow-up visit to evaluate the efficacy of the treatment. I also recorded weight and blood pressure at each 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

The results of my completed DNP project will have a direct impact on my patients as they will have improved glycemic control on an evidence-based treatment with empagliflozin. Overall, improved fasting glucose levels may also be used to monitor the improved management of T2DM. Additional visits will provide us with the opportunity to address this and other concerns.

Analysis

Quantitative data reflecting pre- and post-intervention HbA1c levels were collected to determine the impact of each drug regimen. Evaluation of data is presented on one line graph for pre and post HbA1c (figure 4). Nineteen patients (eighteen females and one male) met the criteria for the QI project. Nine patients were < 60 years of age and 10 were >60 years of age. Although not quantified, a pie graph (figure 5) represents the percentage of weight loss.

HbA1c measurements are a standard of care for testing and monitoring diabetes, particularly in patients diagnosed with T2DM. The HbA1c level is an indirect measure of a patient's average blood glucose level over the previous two to three months (Hillson & Alberti, 2012) and is strongly correlated with fasting plasma glucose levels. HbA1c is a reliable measure of chronic glycemia and correlates with the risk of long-term diabetes complications (John et al., 2012). Additional qualitative data gathered at follow-up visits provided me with insight into improved adherence and quality of life.

Ethical Considerations

Patient Inclusion. Inclusion criteria for the QI project required adults 18-78 years of age with uncontrolled T2DM. Patients who qualified for the QI project were consulted regarding the decision to initiate the new treatment. I reviewed the intervention and its intended results with each patient and also discussed the most common side effects of the medication that are currently listed in Epocrates (<https://www.epocrates.com/>) and the literature. The patient was then capable of making an informed decision to accept or decline the intervention.

Clinical data. I collected, managed, and analyzed all patient data. The patient data remained in the electronic medical record throughout the QI project. Non-identifying data were collected together with initial (pre-intervention baseline) and follow-up (post-intervention) HbA1c levels.

Results

Nineteen patients met the inclusion criteria of this QI project. Eighteen were female between the ages of 23–78 years; sixteen of these patients were Hispanic, and two were Caucasian. The one male patient who elected to undergo treatment with empagliflozin was a Hispanic between 40 to 50 years of age. All 19 patients who elected to undergo treatment with empagliflozin completed the recommended follow-up visit scheduled for two weeks following the initiation of treatment. The outcomes of this QI project are shown in Figure 4. The average pre-intervention HbA1c level was 8.08%. The average post-intervention HbA1c level was 7.87%, representing an overall improvement of 0.21% (Figure 4).

Figure 4

Pre- and Post-Intervention HbA1c levels

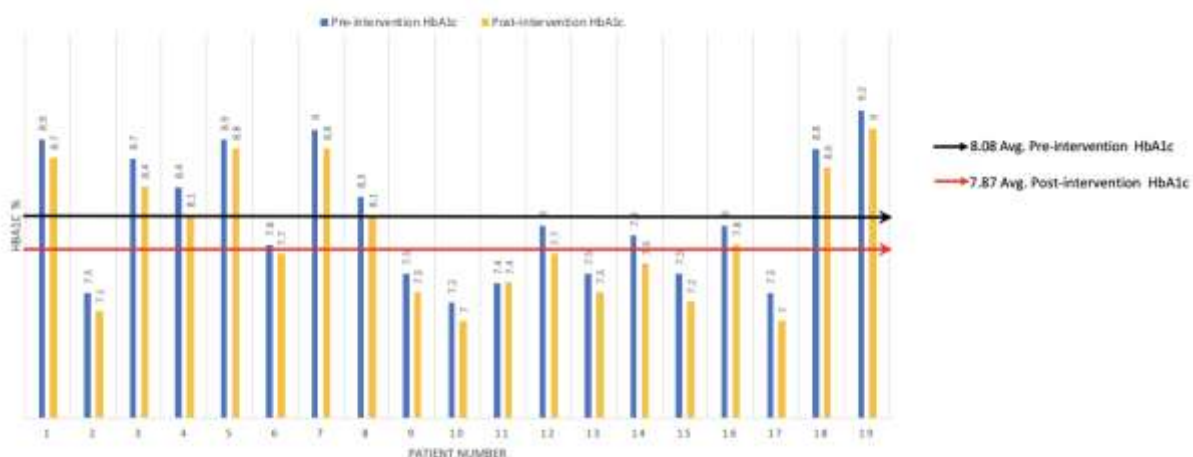
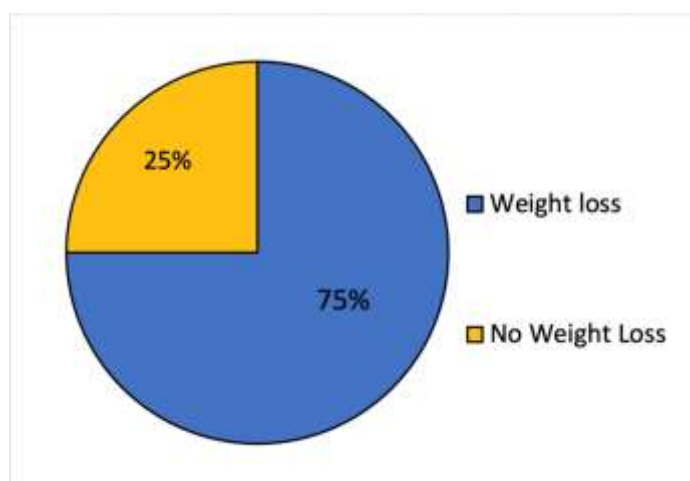


Figure 5



Note. Data from N = 19 patients.

Seventeen patients met inclusion criteria for combination empagliflozin and metformin while only 2 patients were started on empagliflozin as a monotherapy. In the patients who were on monotherapy, one didn't have any improvement in HbA1c while the other exhibited a 0.3% reduction in HbA1c at two weeks post-intervention.

In addition to reductions in HbA1c, I observed several other secondary outcomes, including weight loss (Figure 5), increased mental clarity, stronger motivation to manage their T2DM, and improved satisfaction with their treatment regimens.

Interestingly, the two patients who met criteria for monotherapy with empagliflozin exhibited more weight loss than the other seventeen patients. These two patients each lost six pounds during the two-week interval, possibly secondary to the diuretic effect of this drug. Some patients experienced no weight loss. However, most patients who did lose weight dropped one to three pounds over the two-week QI project period. Many patients reported that they performed regular glucose monitoring which helped them to remain accountable for their food choices throughout the day. Education was also a critical component of empowering patients as part of this QI project.

Discussion

Summary

The results of the QI project support the findings already published in the literature. Consistent with evidence-based diabetes guidelines and recommendations, my findings suggest that administration of empagliflozin either alone or in combination with metformin improves glycemic control in adult patients with T2DM. Although not assessed quantitatively, the results of my project suggest that this regimen also promotes weight reduction and reductions in systolic blood pressure and thus provides a measure of cardioprotective and renal protective benefit to patients with T2DM.

Interpretation

After completion of the QI project, patients who began treatment with empagliflozin were more motivated to monitor their blood glucose levels. Most of the QI project patients

brought their blood sugar logs to their follow-up visits and made additional dynamic behavioral changes. Patients also reported a weight loss and a decrease in leg edema weight loss secondary to the diuretic effect of this drug. Other reported responses included reductions in blurred vision and considerable improvement in mental clarity. Overall, patients were satisfied with the new medication regimen.

Limitations

The QI project was implemented at a federally qualified health center over the course of six-weeks. The simplicity of the QI project allows for its application in other settings. However, the sustainability of these findings will depend on whether these results can be replicated by different providers in other clinical settings as well as overall access to and coverage provided for this medication.

The FQHC has an on-site pharmacy that carries many new drugs, including empagliflozin being one of them. The cost of a 90-day supply of empagliflozin either (10 mg or 25 mg tablets) has a cost of \$6.88. Furthermore, the QI project was not longitudinal and thus I was unable to assess the long-term sustainability and impact of treatment. However, information from the literature indicates that empagliflozin continues to work well over time with no loss of efficacy. Another limitation to this QI project was that I relied on HbA1c measurements taken <12 weeks apart. While this was not ideal, the results clearly suggested an overall improvement in HbA1c. Similarly, patient monitoring logs also revealed improvements in fasting blood glucose levels over a period of 14 days.

Conclusion

The QI project aimed to improve glycemic control in patients with uncontrolled T2DM using empagliflozin alone or together with metformin as a combination treatment. This QI

project showed that the use of an SGLT2 inhibitor to treat T2DM is a safe, tolerable, and effective evidence-based option that will reduce HbA1c and fasting blood glucose levels.

References

- American Diabetes Association. (2018) Economic costs of diabetes in the U.S. in 2017. *Diabetes Care*, 41(5), 917–928. <https://doi.org/10.2337/dci18-0007>
- American Diabetes Association. Diabetes Care. Standards of Medical Care in Diabetes. (2020). *The Journal of Applied Research and Education*, 43(Suppl. 1), S1–S212.
- Babar, H. M., & Aktar, A. L. (2021). Comparison of Efficacy and safety profile of empagliflozin as combination therapy in obese type 2 diabetes patient. *Journal of Ayub Med Coll Abbottabad*, 33(3), 188–191.
- Burnes, B. (2004). Kurt Lewin and the planned approach to change: A re-appraisal. *Journal of Management Studies*, 41(6), 977–1002. <https://doi.org/10.1111/j.1467-6486.2004.00463.x>
- Burnes, B., & Bargal, D. (2017). Kurt Lewin: 70 years on. *Journal of Change Management*, 17(2), 91–100. <https://doi.org/10.1080/14697017.2017.1299371>
- Chen, Z., & Li, G. (2019). Sodium-glucose co-transporter 2 inhibitors compared with sulfonylureas in patients with type 2 diabetes inadequately controlled on Metformin: A meta-analysis of randomized controlled trials. *Clinical Drug Investigation*, 39(6), 521–531. <https://doi.org/10.1007/s40261-019-00781-w>
- Donnan, J. R., Grandy, C. A., Chibrikov, E., Marra, C. A., Aubrey-Bassler, K., Johnston, K., Swab, M., Hache, J., Curnew, D., Nguyen, H., & Gamble, J.-M. (2019). Comparative safety of the sodium-glucose co-transporter 2 (sglt2) inhibitors: A systematic review and meta-analysis. *BMJ Open*, 9(1), e022577. <https://doi.org/10.1136/bmjopen-2018-022577>
- Fuchigami, A., Shigiyama, F., Kitazawa, T., Okada, Y., Ichijo, T., Higa, M., Hiyoshi, T., Inoue, I., Iso, K., Yoshii, H., Hirose, T., & Kumashiro, N. (2020). Efficacy of dapagliflozin

- versus sitagliptin on cardiometabolic risk factors in Japanese patients with type 2 diabetes: A prospective, randomized study (diversity-CVR). *Cardiovascular Diabetology*, 19(1). <https://doi.org/10.1186/s12933-019-0977-z>
- Garber, A. J., Handelsman, Y., Grunberger, G., Einhorn, D., Abrahamson, M. J., Barzilay, J. I., Blonde, L., Bush, M. A., DeFronzo, R. A., Garber, J. R., Garvey, W., Hirsch, I. B., Jellinger, P. S., McGill, J. B., Mechanick, J. I., Perreault, L., Rosenblit, P. D., Samson, S., & Umpierrez, G. E. (2020). Consensus statement by the American association of clinical endocrinologists and American college of endocrinology on the comprehensive type 2 diabetes management algorithm – 2020 executive summary. *Endocrine Practice*, 26(1), 107–139. <https://doi.org/10.4158/cs-2019-0472>
- Hadjadj, S., Rosenstock, J., Meinicke, T., Woerle, H. J., & Broedl, U. C. (2016). Initial combination of empagliflozin and metformin in patients with type 2 diabetes. *Diabetes Care*, 39(10), 1718–1728. <https://doi.org/10.2337/dc16-0522>
- Hussain, M., Elahi, A., Iqbal, J., Ghafoor, M., Rehman, H., & Akhtar, S. (2021). Comparison of efficacy and safety profile of sodium-glucose cotransporter-2 inhibitors as add-on therapy in patients with type 2 diabetes. *Cureus*, 13(4): e14268. <https://doi.org/10.7759/cureus.14268>
- John, W., Hillson, R., & Alberti, S. (2012). Use of hemoglobin A1c (HbA1c) in the diagnosis of diabetes mellitus. The implementation of World Health Organisation (WHO) guidance 2011. *Practical Diabetes*, 29(1), 12–12a. <https://doi.org/10.1002/pdi.1648>
- Lewin, K. (1958). Group Decision and Social Change. In E. E. Maccoby, T. M. Newcomb, & E. L. Hartley (Eds.), *Readings in social psychology* (pp. 197–211) Holt, Rinehart, & Winston.

- Molugulu, N., Yee, L., Ye, Y., Khee, T., Nie, L., Yee, N., Yee, T., Liang, T., & Kesharwani, P. (2017). A systematic review of metformin monotherapy and dual therapy with sodium-glucose co-transporter 2 inhibitor (sglt-2) in treatment of type 2 diabetes mellitus. *Diabetes Research and Clinical Practice*, *132*, 157–168.
<https://doi.org/10.1016/j.diabres.2017.07.025>
- Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T., C., Mulrow, C. D., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*;372:n71.
<https://doi.org/10.1136/bmj.n71>
- Rowley, W. R., Bezold, C., Arikan, Y., Byrne, E., & Krohe, S. (2017). Diabetes 2030: Insights from yesterday, today, and future trends. *Population Health Management*, *20*(1), 6–12.
<https://doi.org/10.1089/pop.2015.0181>
- Scheen, A. J. (2020). SGLT2 inhibitors as add-on therapy to metformin for people with type 2 diabetes: A review of placebo-controlled trials in Asian versus non-Asian patients. *Diabetes, Metabolic Syndromes and Obesity: Targets and Therapy*, *13*, 2765–2779.
<https://doi.org/10.2147/dms0.s193528>
- Tsapas, A., Karagiannis, T., Kakotrichi, P., Avgerinos, I., Mantsiou, C., Tousinas, G., Manolopoulos, A., Liakos, A., Malandris, K., Matthews, D. R., & Bekiari, E. (2021). Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: A systematic review and network meta-analysis. *Diabetes, Obesity and Metabolism*, *23*(9), 2116–2124. <https://doi.org/10.1111/dom.14451>

- Usman, M., Siddiqi, T., Memon, M., Khan, M., Rawasia, W., Talha Ayub, M., Sreenivasan, J., & Golzar, Y. (2018). Sodium-glucose co-transporter 2 inhibitors and cardiovascular outcomes: A systematic review and meta-analysis. *European Journal of Preventive Cardiology*, 25(5), 495–502. <https://doi.org/10.1177/2047487318755531>
- Zou, C.-Y., Liu, X.-K., Sang, Y.-Q., Wang, B., & Liang, J. (2019). Effects of sglT2 inhibitors on cardiovascular outcomes and mortality in type 2 diabetes. *Medicine*, 98(49), e18245. <https://doi.org/10.1097/md.00000000000018245>