Diabetes in Focus

UGA College of Pharmacy Student Diabetes Club

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Keeping pharmacy students informed on current and pertinent diabetes information!

In This Issue

One Less Headache: Migraines Associated with Decreased Risk of Type 2 Diabetes in Women

Written by: Camille Haile-Selassie, 3rd Year Pharm.D. Candidate

Migraine headaches have been previously associated with the development of hyperlipidemia and hypertension, as well as increased risk of cardiovascular disease. However, limited data have existed regarding the relationship between migraine and type 2 diabetes. Approximately 15 million US women have diabetes (about 1 in 9 or 11% of adult women), with roughly 90-95% of these cases being type 2 diabetes. [4] Furthermore, 18% of American women are affected by migraine, most frequently in females of reproductive age, with a declining prevalence after menopause.[1]

Migraine is an extremely incapacitating collection of neurological symptoms that usually includes a severe, throbbing, recurring pain on one or both sides of the head. Attacks last between 4 and 72 hours and are often accompanied by visual disturbances, nausea, and/or sensitivity to light and sound. [1] Aura, which occurs in 20% of migraine sufferers, is a warning sign that occurs about 5-60 minutes before a migraine. Most commonly, auras consist of visual symptoms such as flashing lights or zigzag lines.[3] Migraine with aura is especially correlated with the aforementioned cardiovascular disease risk.[1]

Reprint from Glutenfreesociety.org, Migraine Triggers

In December of 2018, JAMA Neurology published an illuminating study entitled Associations Between Migraine and Type 2 Diabetes in Women: Findings from the E3N Cohort Study.[2] This study not only identified the impact of migraine on diabetes development, but also observed if the presence of diabetes has an effect on migraine symptoms and severity.

This was a French prospective cohort study initiated in 1990. A total of 74,247 women participated, with an average age of 61 at baseline. Participants completed self-administered questionnaires sent biennially. Follow up surveying began April 1, 2004 and was continued through 2014. Three main categories were utilized: (1) no migraine history; (2) active migraine (i.e., all women who self-reported migraine on the current questionnaire cycle); and (3) prior migraine (i.e., women who reported experiencing migraine in at least 1 of the past questionnaires but not on the current questionnaire). Researchers monitored use of drugs related to migraine treatment via the drug reimbursement database from insurance plans. Type 2 diabetes was defined by pharmacological treatment with type 2 diabetes-specific medications.[2]

Between 2004 and 2014, a total of 2372 women developed type 2 diabetes, and there was a lower risk of incident type 2 diabetes in women with active migraine than in women with no migraine history. More specifically, women with active migraine had an approximate 30% decrease in the risk of developing diabetes. In addition, researchers found a clear linear decrease in the prevalence of active migraine prior to type 2 diabetes diagnosis and a stagnation of migraine prevalence after diagnosis of diabetes. Two potential mechanisms for this inverse association include[2]:

- **Hypoglycemia:** this has long been known to be a precipitating factor in migraine onset. Because plasma glucose concentration rises with time up to the point of type 2 diabetes occurrence, the prevalence of migraine symptoms may decrease.
- **Calcitonin gene-related peptide (CGRP):** this vasodilator has a role in migraine pathophysiology. Studies conducted in rats and animal models have shown varying relations but altogether underscore potential associations between CGRP, migraine pathophysiology, and glucose metabolism.[2]

Limitations of this study include:

- Migraine was self-reported
- No information on aura
- Type 2 diabetes cases not pharmacologically treated were considered non-cases, which could have reduced the magnitude of observed associations
- Study population was mainly women in post-menopause and reported as rather health-conscious[2]

These findings not only reveal an interesting association between two seemingly unrelated disease states, but they also uncover a unique long-term monitoring opportunity. Tracking the evolution and especially the decrease of migraine frequency in patients with migraine at high risk of diabetes, such as individuals with obesity, could indicate the possible emergence of increasing blood glucose levels, prediabetes, or type 2 diabetes.[2] Pharmacists detecting these patterns of disease state changes can get one step ahead in helping our patients experience one less headache.

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Smart Insulin Patch: The Future of Diabetes Management

Written by: Andrea Ampuero, 3rd year Pharm.D. Candidate

An estimated 6 million Americans currently use insulin daily to manage their diabetes and blood sugar levels.[1] For patients living with type 1 diabetes, insulin injections may be required three to four times a day. These injections can be painful, uncomfortable and inconvenient. Conversely, people with type 2 diabetes will often initiate insulin therapy with two injections a day which may increase up to four injections daily if necessary, to maintain glycemic control. Insulin administration requires diabetics to monitor their blood sugar often to achieve normoglycemic levels. When a patient is initially starting an insulin regimen, the prescriber may have to adjust the regimen often to achieve proper blood glucose control. Despite proper management of insulin administration, patients may still struggle to control their blood sugars appropriately. Under development is a new insulin patch that may help ease the painful needle burden for diabetic patients.

Researchers at the University of North Carolina and North Carolina State have developed a smart insulin patch that will circumvent the frequent need to inject insulin and check blood sugars. [2] This patch mimics the body's pancreatic beta cells or the insulin generators. Beta cells have tiny sacs called vesicles which make and store insulin. When blood glucose levels start to rise, beta cells quickly respond by secreting stored insulin while simultaneously increasing production of the hormone. The Joint Department of Biomedical Engineering at UNC and NC State created artificial vesicles that perform the same function as beta cells.[3]

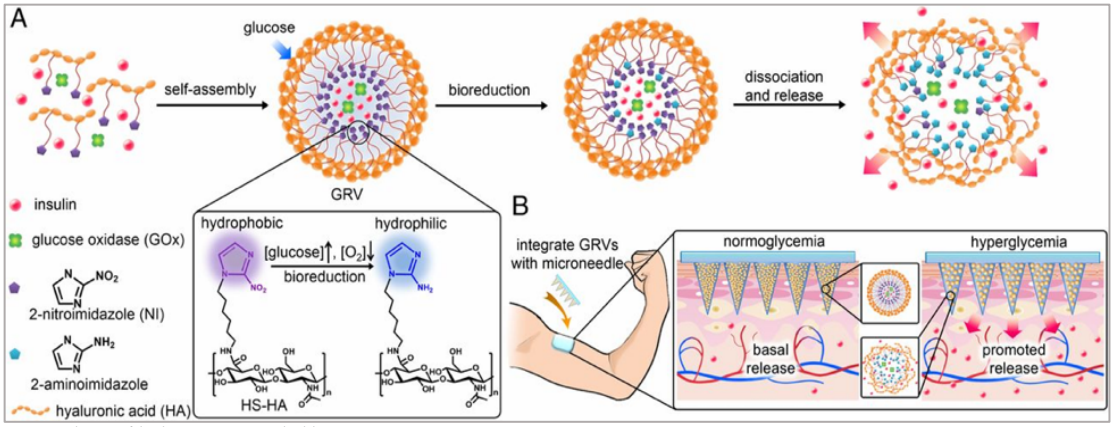

Figure 1: Schematic of the glucose-responsive insulin delivery system

The patch contains artificial vesicles which are composed of hyaluronic acid and 2-nitroimidazole. Scientists combined the two materials to create a brand new molecule that self assembles into a vesicle. The vesicle is created due to the hydrophilic, hyaluronic acid, and hydrophobic, 2-nitroimidazole properties of both materials. Each vesicle contains insulin and glucose sensing enzymes. In lab experiments, when blood sugar rose, glucose sensing enzymes converted the glucose into gluconic acid, while consuming oxygen. The hypoxic environment causes 2-nitroimidazole to become hydrophilic thus releasing insulin from the artificial vesicle. The vesicles were then inserted into tiny microneedles made of hyaluronic acid. A single patch contains more than one hundred of these microneedles. Once the painless patch is placed on the skin the microneedles pierce through the skin to access the blood as depicted in Figure 1.[3]

In mice experiments, mice were given either an injection of insulin or wore the insulin patch. Mice who wore the insulin patch had better control of blood glucose compared to those that received the injection of insulin.[3] The patch group blood sugar controlled within 30 minutes and maintained normoglycemic levels for a couple hours. Interestingly, scientists are able to adjust the amount of insulin within every vesicle to maintain a specific blood glucose target.

Currently, the insulin patches have only been tested in mice, but human trials should be underway in the foreseeable future. The development and use of this patch in diabetes therapy could be revolutionary in terms of the burden placed on patients. Researchers are planning to develop a patch that lasts approximately three days for human use. With this revolutionary technology, it is expected that patients will be able to manage their blood sugars more easily than before with fewer risks that are usually associated with regular insulin.

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Type 2 Diabetes and Cognitive Decline

Written by: Ashley Austin, 3rd Year Pharm.D. Candidate

Citing years of research, diabetes mellitus has been linked to reductions in cognitive function and changes in brain structure. Specifically, the data collected show a stronger association between dementia and type 2 diabetes than type 1.[1] Typically, type 2 diabetes is diagnosed at an older age and is commonly associated with obesity, insulin resistance, hypertension, and dyslipidemia, all of which can have a negative impact on the brain.[2] However, the underlying mechanism and risk factors that may lead to the development of severe cognitive dysfunction in a number of diabetes patients is not well understood. Type 2 diabetes mellitus is associated with a 50% increase in the risk for dementia along with impaired attention, processing & motor speed, executive functioning, and verbal memory.[2] While there is a significant concern for dementia among the elderly population, the growing rate of type 2 diabetes in all age groups could lead to an increase in prevalence of diabetes-related cognitive dysfunction in the future.[2]

For example, neuroimaging has exposed structural changes in the brains of patients with type 2 diabetes. Brain magnetic resonance spectroscopy (MRS) analyzing the diabetic brain has shown changes consistent with dementia. In general, excitatory neurotransmitters (i.e., glutamate and glycine) are increased, inhibitory neurotransmitters are decreased, and N-acetylaspartate levels are decreased, indicating loss of neuronal integrity.[3] In patients without dementia, MRI findings display modest brain atrophy, increased burden of small vessel disease, and disturbed structural connectivity. When compared to non-diabetic controls, patients with type 2 diabetes have lower total gray, white, and hippocampal volumes.[3] These reductions in brain volume occur slowly over a period of years at a rate that only slightly exceeds normal age-related loss of brain volume. Progression of cerebral atrophy in these patients has also been linked to accelerated cognitive decline.[3]

Furthermore, diabetes mellitus has been associated with different stages of cognitive dysfunction, ranging from mild cognitive impairment to dementia. Future research is needed to develop specific diagnostic criteria and determine which patients will most benefit from such testing. In the meantime, healthcare providers may continue to counsel patients on the importance of glycemic control and weight management. Since there are no existing therapies targeting cognitive impairment in diabetes patients, practitioners should abide by the same treatment guidelines used to treat cognitive impairment or dementia in patients without diabetes.

Strategies such as reviewing patient profiles regularly to prevent medication errors and individualizing therapy based on patient-specific factors (age, comorbidities, and weight) are effective ways to improve patient outcomes. Consider screening for cognitive dysfunction in patients with cognitive complaints or in elderly patients with type 2 diabetes, especially if there is evidence of deterioration in everyday functional ability.

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Trailblazing in CGM monitoring: Spike Diabetes Application

Written by: Kayla Saxton, 2nd Year Pharm.D. Candidate

Since the discovery of insulin in the spring of 1921, our breadth of knowledge on the diabetic disease state and the development of treatments has remarkably increased, however this has not stemmed a cure.[2] With an increase in the diabetic population being predicted by the Institute of Alternative Futures to reach a staggering 54% between 2015-2030, it puts into perspective how important understanding this disease state is for medical professionals and patients. [3]

Figure 1:Reprint from Apktada.com[5]

In 2018, with an increase in knowledge and technological advancements, the Spike mobile assistant app was released. The Spike app is designed to aid patients with diabetes to achieve better glycemic control in regard to self-monitoring blood glucose values. Spike monitors a patient's daily behavior and is therefore able to provide reminders and tips regarding insulin requirement, food, activity, etc. In addition, Spike has the capability to store the patient's data for further analysis that can be shared with doctors and caregivers.[4]

According to research conducted by Spike developers, almost 75% of diabetics are not well educated on how to select healthy food options when eating.[4] This results in suboptimal eating patterns that can negatively impact the blood glucose levels of the patient. The Spike application contains a feature that detects which restaurant the patient is entering and consequently sends healthy food recommendations based on the menu at the

restaurant. This unique feature allows for patients with suboptimal skills in proper glycemic management strategies, such as carbohydrate counting, to be more conscientious of the carbohydrates they are consuming.

Importantly, this application can be used for blood glucose monitoring in patients with Type I or Type II diabetes. The only requirement is that the patient must also wear a continuous blood glucose monitor (CGM) which is a device that allows for diabetics to check blood glucose readings at any point in time, predict future glucose events up to an hour in advance, and informs patients of glucose patterns.[1] By using a CGM in conjunction with Spike, the system will automatically receive glucose readings at a set time interval (i.e. every 5 minutes) and this data will be stored in the Spike application. The glucose readings can also be shared with health care providers.[4] Since frequent doctor visits are not always feasible, it provides a way for medical professionals to track a patient's glucose levels remotely which promotes better diabetes management.

Furthermore, Spike includes a feature that promotes medication adherence that is termed by the company as guardian connection.[4] This feature allows for the patient to add family members or others to a notification system. By using the guardian connection, caregivers will receive a notification when the patient takes his/her medication. It also includes a monthly report that can be sent to any member of the patient's healthcare team.[4] Additionally, the product also allows the patient to set alarms as reminders to take his/her medication(s).

With the user-friendly design and presentation of the material, the Spike Diabetes app is currently available on both Apple and Android devices for free and can be synced with devices such as the Apple watch.

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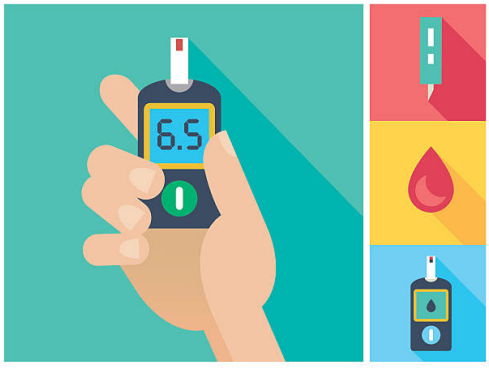
Are You Testing Your Blood Sugar Too Often?

Written by: Ansley Gayle, 3rd Year Pharm.D. Candidate

In January 2019, the American Diabetes Association (ADA) published their most recent recommendations on diabetes care. A major change in the new guidelines is the content of Section 6 "Glycemic Targets," which now focuses primarily on the importance of A1c testing and goals. The recommendations for self-monitoring of blood glucose (SMBG) were removed from Section 6 and are now included a new section of the guidelines entitled "Diabetes Technology." This section also includes a discussion of insulin delivery devices, blood glucose meters, and continuous glucose monitors.[1]



Who should be checking blood glucose routinely?

Despite these recent changes in the Diabetes Standards of Care, the ADA continues to recommend routine blood glucose assessment as a crucial component of diabetes management for patients using intensive insulin regimens, such as multiple-doses of insulin or insulin pump therapy. Research supports the benefit of a multi-modal approach that includes structured SMBG monitoring to reduce acute complications associated with diabetes in insulin-treated patients with diabetes mellitus.[2] Similarly, the ADA also acknowledges that continuous glucose monitoring (CGM) may be used to assess glucose levels in patients treated with intensive insulin regimens. Results of frequent blood glucose values inform both clinicians and patients on the efficacy of therapy and are valuable for making insulin dose adjustments.

What if my patient is not on an intensive insulin regimen?

The efficacy of routine SMBG is less apparent in patients who are not currently using an intensive insulin regimen. This issue has long been a topic of uncertainty, and the optimal frequency of blood glucose assessment has not been well defined for patients on less rigorous insulin regimens, such as basal insulin.[1] However, SMBG values still have a role in therapy for all patients on insulin. In contrast to the frequent self-monitoring recommending for those on intensive insulin regimens, patients on less complicated insulin regimens should be counseled to occasionally record fasting SMBG values, as this data is often used for dose adjustments in outpatient settings.[3]

When should patients on intensive insulin therapy perform SMBG?

- Prior to meals and snacks
- At bedtime
- Post-prandially (occasionally)
- Prior to exercise
- If they suspect low blood sugar
- After treating low blood sugar (continue to check every 15 minutes until normoglycemic)
- Prior to critical tasks, such as driving

Should I recommend routine SMBG to patients only taking oral agents?

The latest recommendations from the ADA acknowledge several randomized clinical trials suggesting limited utility of SMBG in patients with diabetes who are not currently on insulin therapy.[1,4,5] To confuse matters, a handful of studies have also detected a slight benefit from SMBG in patients on oral antidiabetic therapy. A Cochrane review published in 2012 indicated that SMBG induced a slight reduction A1c during the first six months; unfortunately, the statistical significance of this reduction was no longer seen after one year.[6] Once blood glucose control is achieved and the results of self-monitoring stabilize, most individuals do not benefit from repeated testing if not using a hypoglycemic agent.[7]

The cost-effectiveness of SMBG in this non-insulin treated population has also been brought into question, given a large amount of SMBG results that remain unused or do not impact therapy.[8] When considering the role of blood glucose assessment in patients with diabetes, the potential benefits of frequent self-monitoring should be weighed against the additional costs incurred by the patient.

Although the majority of the evidence suggests that routine SMBG should be avoided among patients with diabetes treated with non-insulin therapy, it is important to note that some individuals in these clinical trials did experience reduction of A1c when structured SMBG was included as part of a treatment regimen (despite not being statistically significant when the data from all participants was pooled).[5] Therefore, the ultimate decision to initiate SMBG in patients with diabetes should come from shared decision making between the patient and the provider. In addition, there are a few exceptions in these patients in which more frequent monitoring of blood glucose may be necessary. Consider implementing SMBG in individuals experiencing weight fluctuations, significant A1c changes, acute illness, and changes in therapy, along with those who require monitoring to maintain targets.[7]

Situations to consider implementing routine SMBG in patients on oral antidiabetic agents:

- During acute illness
- When adding or removing medications
- When weight fluctuates
- If significant changes in A1c are observed
- In individuals who need monitoring to maintain targets

Optimizing self-monitoring strategies

Among patients who utilize SMBG or CGM, clinicians have a vital role in ensuring optimal monitoring. Frequent reevaluation of the patient's blood glucose monitoring technique is necessary to ensure accuracy. At each visit, the need and frequency for ongoing self-monitoring should be determined.[1] It is important for providers to counsel patients on the utility of their blood glucose values and educate on self-management strategies in diabetes. Self-monitoring is beneficial as long as our patients are learning and adjusting therapy based on the result of the monitoring.[7] Clinicians should also be aware of factors that can impact the accuracy of blood glucose test results, such as variation among blood glucose meters, use of counterfeit strips, storing meters in extreme temperatures, and certain physiologic and pharmacologic substances.[1]

Summary

In summary, when recommending frequent assessment of blood glucose, providers should assess multiple factors and collaborate with patients to determine the best plan to manage diabetes and prevent future complications. Among patients who utilize SMBG or CGM, frequent reevaluation of monitoring technique, as well as the need and frequency for ongoing self-monitoring is necessary.

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Congratulations on Matching!

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Test Your Knowledge

1. SS is a 53-year-old female who was diagnosed with Type 2 Diabetes almost 10 years ago. Her current diabetes regimen includes metformin, glipizide, insulin glargine, and insulin aspart. Last week her A1c was 9.4%. How should SS be counseled to monitor her blood glucose at home?
    a. Her current therapy is not considered to be an "insulin intensive" regimen. She should not perform routine SMBG unless a new injectable agent has been added.
    b. Based on the A1c value, her current therapy is not controlling her blood glucose. Therefore, SMBG should be performed once a day after her largest meal, as this will provide the most information on the efficacy of her current insulin therapy.
    c. Her current therapy is considered to be "insulin intensive" regimen. Therefore, she should perform SMBG once a day after her largest meal and during acute illness.
    d. Her current therapy is considered to be "insulin intensive" regimen. Therefore, routine SMBG is indicated. She should be counseled to at least perform SMBG before meals or snacks, before exercise or operating a vehicle, if she feels that her blood sugar may be low or if is treating her low blood sugar, and before bedtime.

2. Which is a proposed mechanism for the inverse association between migraine and type 2 diabetes?
    a. Hyperglycemia is a precipitating factor in migraine onset
    b. Hypoglycemia is a precipitating factor in migraine onset
    c. The vasoconstrictor CGRP may also be associated with glucose metabolism
    d. Migraine and type 2 diabetes are not inversely related

3. Which of the following patient populations is most at risk for cognitive decline associated with diabetes?
    a. Adolescents
    b. Young adults
    c. Adults
    d. Elderly
4. How many diabetics are not well educated on selecting healthy food options?
    a. 90%
    b. 80%
    c. Almost 75%
    d. 50%

5. A single smart patch contains more than _____vesicles filled with insulin.
    a. 1
    b. 10
    c. 100

Enter Drawing*:

1. Scan QR code
2. Submit Responses

**drawing ends April 26, 2019 – online quiz will remain active*