Diabetes in *focus*

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In This Issue

Special Points of Interest

The Expanding Role of Pharmacy in Diabetes Care

Contributed by: Paul Hansen, 4th year PharmD Candidate

Approximately 25.8 million Americans are living with diabetes, and an additional 79 million are classified as pre-diabetics. Healthcare costs for a diabetic patient are 2.3 times higher than the costs for a non-diabetic patient. The total cost of diabetes on the United States healthcare system in 2007 was recorded to be $174 billion. Management must be optimized in the most cost-effective manner that also optimizes patient care.[1]

The management of diabetes involves regular blood glucose monitoring, the use of complex medication regimens, and extensive lifestyle modifications. Further, incorporation of diabetes as a risk factor in other disease states such as hypertension and hyperlipidemia changes those disease-specific treatment algorithms. As the incidence of this complex disease state continues to escalate, it is only logical that pharmacists, considered one of the most easily accessible healthcare professionals, will be increasingly called upon to help manage the care for the diabetic population.

In fact, this trend of pharmacist-managed diabetes care has already begun and is finding successful outcomes.[2,3] Clinical trials showed that pharmacist led interventions in diabetes care have shown reduced hemoglobin A1C and the achievement of better overall glycemic control. The interventions used in most trials were patient-education oriented, including one-on-one counseling with a pharmacist. By educating patients on both how to use their medications and conduct proper blood glucose monitoring and on the enormous impact diabetes can have one's health, pharmacists were able to significantly improve diabetic patient outcomes.

Pharmacists are in an ideal position to offer more extensive disease, medication, and lifestyle counseling to their diabetic patients, but this type of educational intervention is only the beginning of the potential pharmacist-led services. More clinical services could involve offering blood glucose and hemoglobin A1c screening and by offering monthly foot examinations for diabetic patients. Pharmacists have long been perceived as one of the most trusted and available healthcare professional, and this unique position will allow this profession to make a significant positive impact on diabetic patient care.

Diabetes by the Numbers

25.8 million	Diabetic Americans
79 million	Pre-diabetic Americans
$174 billion	Cost to treat diabetes
2.3	Times higher treatment costs of a diabetic compared to a non-diabetic
231,404	Deaths with diabetes as a contributing factor

References:

1. http://www.diabetes.org/diabetes-basics/diabetes-statistics. May 2012.

2. Wubben, D. P. and Vivian, E. M. (2008), Effects of pharmacist outpatient interventions on adults with diabetes mellitus: A systematic review. Pharmacotherapy, 2008; 28: 421-

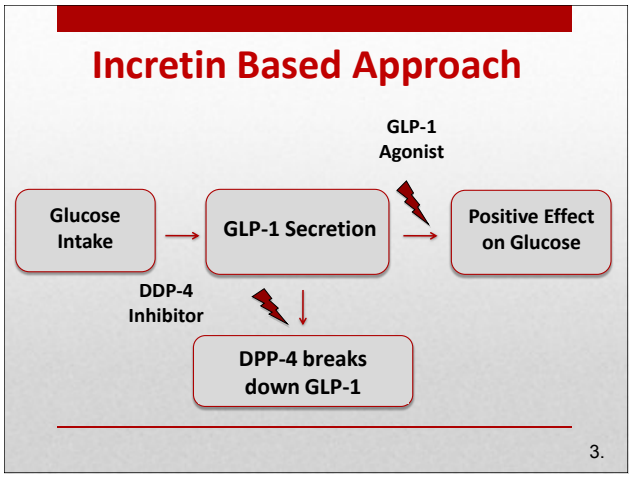
3. Choe HM, Mitrovich S, Dubay D, Hayward RA, Krein SL, Vijan S. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. Am J Manag Care. 2005;11(4):253-60.

Exenatide (Bydureon®): A Once Weekly GLP-1 Agonist

Contributed by: Robert Newsome, 4th year PharmD Candidate

Incretin-based pharmacotherapy approaches to managing type 2 diabetes mellitus are becoming a staple in the diabetic community.[1] This approach includes two classes of mediations: dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide (GLP-1) agonists. DPP-4 inhibitors increase the length of time that endogenous GLP-1 is in the bloodstream by inhibiting the enzyme that breaks down GLP-1 into its constituent amino acids. GLP-1 agonists target the GLP-1 receptor, which in turn decreases gastric motility, increases the feeling of satiety, increases insulin production, and decreases glucagon production.[1] DPP-4 inhibitors include sitagliptin (Januvia®), saxagliptin (Onglyza®), and linagliptin (Tradjeuta®). All are oral formulations. In contrast, GLP-1 agonists are subcutaneous injections and include exenatide (Byetta®, Bydureon®) and liraglutide (Victoza®).

Exenatide BID (Byetta®) was the first of the GLP-1 agonists. Due to its relatively short half-life of 4 hours, it must be given twice daily. Next liraglutide (Victoza®) was introduced to the market. A slightly different arrangement of amino acids extended the half-life to 13 hours and allowed for Victoza® to be given once daily. Exenatide once weekly (Bydureon®) contains the same active drug as Byetta®. The difference comes in its formulation, which uses slow dissolving polymers to allow for the steady diffusion of the active drug. This allows Bydureon® to be dosed once weekly, greatly enhancing patient satisfaction.



Clinical trials have shown that Bydureon® is superior to DPP-4 inhibitor sitagliptin with regards to glycemic control, and it has a more positive effect on weight gain compared to pioglitazone (Actos®).[1] Bydureon® also showed comparable efficacy in conjunction with metformin compared to the sulfonylurea glimepiride with less hypoglycemic episodes.[2] Like other GLP-1 agonists, the major adverse effect experienced with Bydureon® is nausea and vomiting; however, this side effect is seen less in Bydureon® as compared to Byetta® and Victoza® due to a less severe concentration peak.

With regards to incorporating Bydureon® into patient regimens, the American College of Clinical Endocrinologist (AACE Guidelines) recommend adding GLP-1 agonists to metformin in patients that are in need of weight loss, competent in giving subcutaneous injections, and have an A1C less than 9%. Bydureon® is priced similarly to DPP-4 inhibitors and other GLP-1 agonists.

References:

1. Bergenstal RM, Wysham C, Macconell L, et al. Efficacy and safety of exenatide once weekly versus sitagliptin or pioglitazone as an adjunct to metformin for treatment of type 2 diabetes (DURATION-2): a randomised trial. Lancet 2010;376:431-9.

2. Derosa G, Putignano P, Bossi AC, et al. Exenatide or glimepiride added to metformin on metabolic control and on insulin resistance in type 2 diabetic patients. Eur J Pharmacol 2011;666:251-6

3. Image Credit: Robert Newsome. 2012

GLP-1 Agonists Comparison

Contributed by: Brian Griffin, 4th year PharmD Candidate

Brand Name	Byetta®	Bydureon®	Victoza®
Active Drug	Exenatide	Exenatide	Liraglutide
Dose	5 -10 mcg BID prior to meal	2 mg once weekly	0.6-1.8 mg daily
Route	SUBQ	SUBQ	SUBQ
Half-life	~2.4 hours	~2 weeks	~13 hours
Titration Necessary	Yes[a,b]	No	Yes[a,c]
Cost (AWP)	$350.28	$388.13	$351.08

[A] Dose titration employed to avoid//limit GI symptoms.

[B] Byetta titration schedule: 5 mcg BID for one month, then increased to 10 mcg BID if additional effect desired

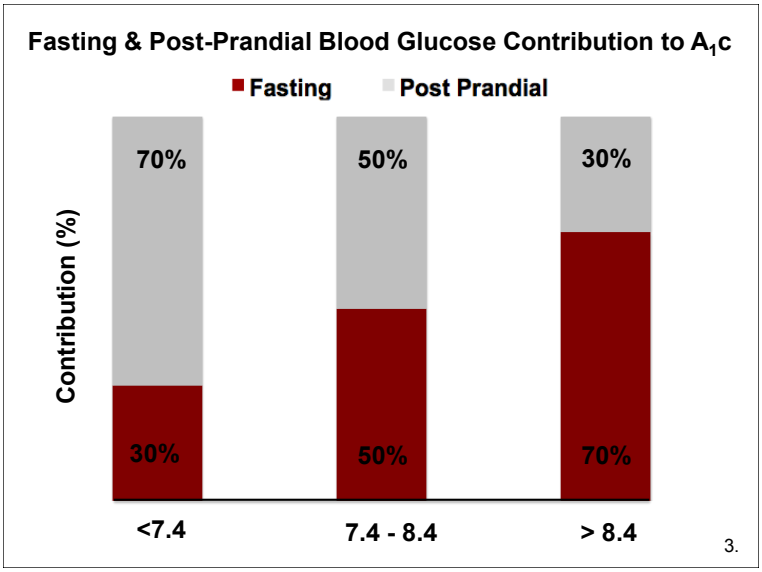
[C] Victoza titration schedule: 0.6 mg daily for 1 week, then increase to 1.2 mg daily. May increase dose to 1.8 mg daily if optimal glycemic response not seen with lower doses. If greater than 3 doses missed in a row, re-titration required.

Clinical Pearls: Fasting & Post-Prandial Glucose Levels and A1C

Contributed by: Andrea Sikora, 4th year PharmD Candidate

A_1c or glycated hemoglobin is considered the gold standard of assessing glycemic status in diabetic patients. Lowering A_1c significantly reduces the risk and progression of diabetic complications including retinopathy, amputations, and cardiovascular events.[1]

The power of A_1c is its ability to give a global picture of a patient's diabetic control as opposed to having to muddle through many individual glucose readings. Indeed, A_1c is used to guide the intensification of medication therapy according to diabetic guidelines, but this simple test also offers further insights.



Monnier and colleagues found that therapy, as well as blood glucose testing, should be tailored based on A_1c because post-prandial glucose and fasting glucose had varying contributions depending on the A_1c level.[1] Fasting glucose is a greater contributor when A_1c is greater than 8.4% whereas post-prandial glucose peaks are a greater contributor when A_1c is less than 8.4%.

The figure to the left depicts the general contributions of fasting vs. post-prandial blood glucose to A_1c based on the A_1c range. For a patient with an A_1c of 7.1%, the primary offending factor is the blood glucose spikes directly after meals. This patient would probably benefit more from therapy that targets post-prandial glucose levels such as rapid-acting mealtime bolus insulin. In contrast, a patient with an A_1c of 8.7% would probably benefit more from a long-acting basal insulin therapy that would target the primary offender of fasting blood glucose.

References:

1. Monnier L, Lapinski H, Colette C, Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations with increasing levels of HbA(1c). Diabetes Care 2003;26: 881–885.

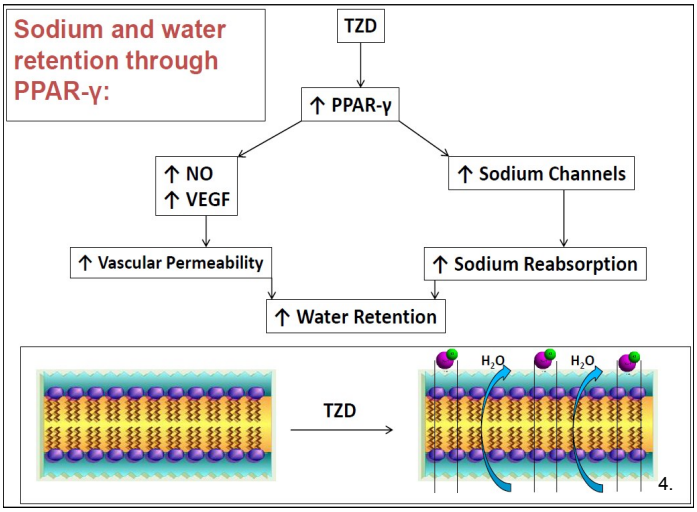
2. The DCCT Research Group, The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N. Engl. J. Med. 1993;329:977–986.

3. Image at left adapted from Schrot, RJ. Targeting Plasma Glucose: Preprandial versus Postprandial. Clinical Diabetes. 2004. Vol 22 No 4. 169-172.

Drug-Induced Heart Failure with Thiazolidinediones

Contributed by: Robert Newsome, 4th year PharmD Candidateand Andrea Sikora, 4th year PharmD Candidate

Diabetes increases the risk of cardiac complications; however, thiazolidinediones (TZD) are associated with drug-induced heart failure (HF) at a higher rate than what would be expected of a typical diabetic patient.[1] The incidence of HF in patients on TZD's is 8.2% as compared to 5.3% in patients on other diabetic therapies.[2] TZDs include rosiglitazone (Avandia®) and pioglitazone (Actos®). The mechanism of toxicity is through their mechanism of action: activation of PPAR-γ. PPAR-γ is responsible for multiple pathways in the human body including insulin regulation and insulin sensitivity; however, PPAR-γ also increases vascular permeability through nitric oxide (NO) and VEGF and increases the number of sodium channels in the kidneys. As a result, more water is absorbed due to an increase in sodium and water absorption. This leads to water retention and an increased work load on the heart.[3] Rosiglitazone and pioglitazone has an extensive risk evaluation and mitigation system (REMS) program that must be adhered to for a patient to receive the drug. Both drugs carry the same black box warning, contraindicating their use in NYHA Class III and IV heart failure patients. Further, cautious TZD use in diabetic patients that are at increased risk for heart failure (previous MI, reduced left ventricular ejection fraction, hypertension) is warranted.



References:

1. *Maxwell CB, Jenkins AT. Drug-induced heart failure. Am J Health Syst Pharm. 2011 Oct 1;68(19):1791-804.*
2. *Patel RR. Thiazolidinediones and congestive heart failure: a judicious balance of risks and benefits. Cardiology in review 2009;17:132-5*
3. *Yang T, Soodvilai S. Renal and vascular mechanisms of thiazolidinedione-induced fluid retention. PPAR research 2008;2008:943614.*
4. *Image credit: Andrea Sikora & Robert Newsome. 2012.*

The Formation of the Student Diabetes Club

Diabetes is a chronic disease state with a large and growing population. Proper care involves extensive lifestyle modifications over a period of time, complex pharmacotherapy plans, and cognizance of how diabetes can be a prominent risk factor for other diseases and conditions. Because pharmacists are considered experts in drug knowledge and have the opportunity to regularly interact with patients, pharmacist directed diabetic patient care is an emerging reality that will only grow as concepts like Medication Therapy Management gain popularity.

Pictured (left to right): Robert Newsome (Editor), Andrea Sikora (Editor), Paul Hansen (Vice President), Brian Griffin (President)

As we discussed this new role for our profession, we realized that creating an organization focused solely on pharmacist-oriented diabetic patient care could be an excellent way for us to prepare the next generation of pharmacists as well as to become more involved with this population. Thus, the Student Diabetes Club (SDC) was born.

Our mission is to improve patient care through developing pharmacy student knowledge of diabetes as well as their experience with diabetic patients through educational events and outreach activities.

Through journal clubs and the *Diabetes in Focus* newsletter, we hope to educate students about evidence-based guidelines, pharmacist-led interventions, new research in the field of diabetes, and many other topics. Through outreach activities such as health fairs and diabetes classes, we hope to spark pharmacy students interest in the diabetic population.

We hope to see you at some of our events as we explore this dynamic field.

Sincerely, SDC

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Please forward comments, topic requests or questions to The Student Diabetes Club at sdcuga@gmail.com

August

Tues., Aug 28:
Interest Meeting

Fri., Aug 31:
Gourmet Lunch Fundraiser

September

Tues., Sept. 11:
Journal Club and Spaghetti Dinner

Sat., Sept 29:
ADA Step Out Walk in Grant Park, Atlanta

October

Tues., Oct 2:
SDC Meeting

Sat., Oct 6:
ADA North Metro Step Out Walk in Alpharetta

Thurs., Oct 25:
Diabetes in Focus Issue 2 launch

Wed., October17:
Dawgtoberfest

Note: All dates are subject to change. Please look for updates via e-mail.