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RPCC Pharmacy Forum

Special Interest Articles:

- Diabetes Medication Chart
- Insulin Chart
- Afreeza

Did you know?

Exanatide, marketed as Byetta, is the synthetic form of exendin-4, which was isolated from the salivary gland venom of the Gila monster. Dr. John Eng, the scientist that discovered this, built his research on studies done in the 1980's that noted that the venom of certain snakes and lizards caused inflammation of the pancreas.

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The Type 2 Diabetes Issue

In response to the type 2 diabetes epidemic, the rate of new U.S. Food and Drug Administration (FDA) approvals for type 2 diabetes has been swift in recent months. There are now 12 different categories of medications directed at the management of hyperglycemia in patients with diabetes. With sulfonylurea drug class, toxicity results almost exclusively from hypoglycemia. Many of the new medications do not cause hypoglycemia when used alone. This issue is devoted to a review of diabetes, the disease, explanations of how new drugs work, and charts that could be useful when helping patients with therapeutic errors and overdoses.

Type 2 Diabetes: The Basics

Diabetes is a life-long disease that affects the way the body handles glucose. There are about 27 million people in the US with Type 2 diabetes and another 86 million with prediabetes. The human body requires that the blood glucose level is maintained in a very narrow range. Homeostasis is regulated by two hormones, insulin and glucagon, which are both secreted by the pancreas. The production of insulin and glucagon by pancreatic cells ultimately determines if a patient has diabetes or another related problem.

Insulin
Insulin is secreted by the beta cells of the pancreas in response to high blood sugar, although a low level of insulin is always secreted by the pancreas. This is the "moving truck" that carries the glucose out of the blood stream and into the cells of the body that need it. The pancreas secretes insulin when blood sugar levels get too high. This allows for more of the sugar that is in the blood stream to now enter the cells, thus decreasing the blood sugar level.

Glucagon
Glucagon is secreted by the alpha cells of the pancreas when the blood glucose is low. Blood glucose is low between meals and during exercise. Glucagon travels to the liver and tells the liver to start turning glycogen into glucose. Glucagon causes blood glucose to increase. (see Figure 1, next page)

The Incretin Hormones
Incretin hormones are gastrointestinal hormones that interact with the pancreas and other organ tissues in response to nutrient intake. These hormones are secreted predominately by the K-cells and the L-cells in the gut. The two major incretin hormones are glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide (GIP). GLP-1 reduces blood glucose by stimulating insulin and reducing glucagon secretion. Additionally, GLP-1 effects the hypothalamus and promotes satiety in humans. GIP also stimulates insulin secretion but increases glucagon secretion.

When the body makes incretins, an enzyme called dipeptidyl peptidase-4 (DPP-4) removes it from your body.

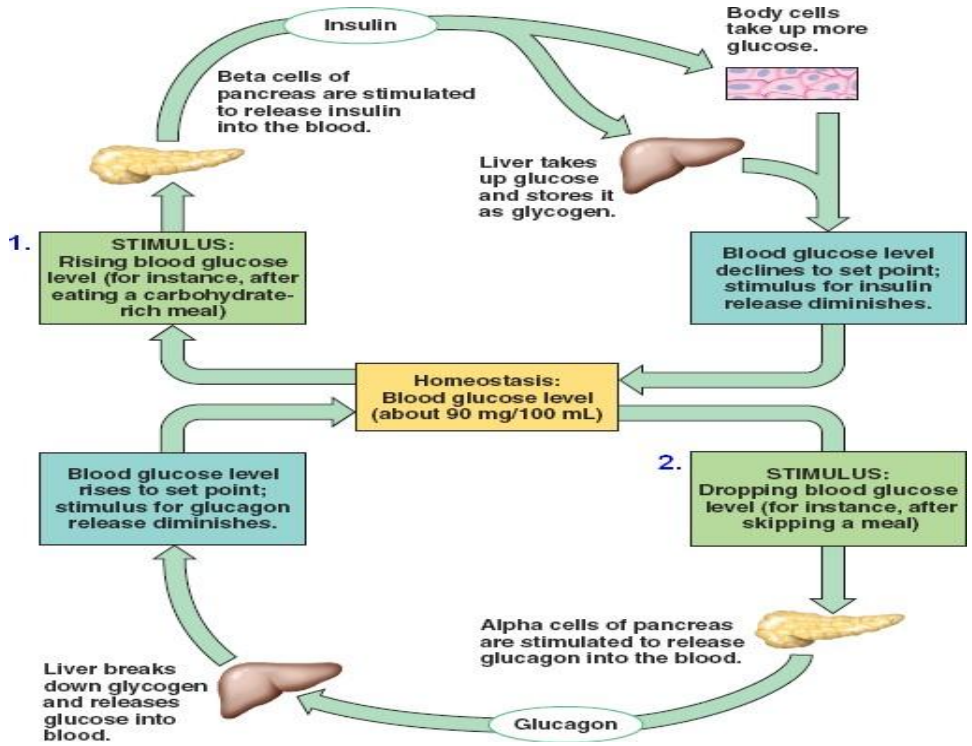

Figure 1

"There are 27 million people in the US with Type 2 diabetes and another 86 million with prediabetes."

Amylin
Amylin is a peptide hormone that is cosecreted with insulin from the pancreatic beta-cell. It inhibits glucagon secretion, delays gastric emptying and acts as a satiety agent.

Sodium-Glucose Co-Transporter-2
The sodium-glucose co-transporter-2 (SGLT2) is a low-affinity transport system that is specifically expressed in the kidney and plays an important role in renal glucose reabsorption in the proximal tubule. This transporter is responsible for ~ 90% of glucose reabsorption in the kidney. When this transporter is antagonized, excess glucose in the renal tubules is not reabsorbed, and glucose is excreted in the urine. This results in a net loss of glucose and a reduction in hyperglycemia.

Alpha-glucosidase
Alpha glucosidase is an enzyme located in the brush border of the small intestine that breaks down starch and disaccharides to glucose.

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Type 2 Diabetes Medications

Drug Class	***Drugs***	***Mechanism of Action***	***Route and Initial Dose***	***Overdose Effects***
Alpha- glucosidase inhibitor	Acarbose (Precose) Miglitol (Glyset)	Slows intestinal carbohydrate digestion/absorption	PO 25 mg Tablet TID 25 mg Tablet TID	-No hypoglycemia when used alone -GI effects -Hepatotoxicity (rare)
Amylin Analog	Pramlintide (Symlin)	Slows gastric emptying, regulates food intake due to centrally-mediated modulation of appetite, prevention of the postprandial glucagon secretion which leads to suppression of endogenous glucose output from the liver	Injectable 60 mcg SQ prior to major meals	-No hypoglycemia when used alone -GI effects -Vasodilation -Tachycardia -Usually reserved for Type 1 diabetics
Biguanide	Metformin (Glucophage)	Decreases the amount of glucose produced in liver, enhances insulin sensitivity in muscle and fat	PO 500 mg BID	-No hypoglycemia when used alone -Lactic acidosis
Dipeptidyl peptidase-4 inhibitor or DPP-4 or "gliptin"	Alogliptin (Nesina) Linagliptin (Tradjenta) Saxagliptin (Onglyza) Sitagliptin (Januvia) All of these are also made in combination with metformin	Protects the endogenous incretin hormones and enhances their actions. This results in increased insulin secretion, decreased glucagon secretion, slowed gastric emptying and increased satiety	PO Alogliptin-25 mg once daily Linagliptin-5 mg once daily Saxagliptin-2.5-5 mg once daily Sitagliptin- 100 mg once daily	-No hypoglycemia when used alone -Insignificant QTc prolongation has been reported at *8 times the therapeutic dose with sitagliptin; it has not been reported with saxagliptin. -GI effects -Pancreatitis (rare) -Increased heart failure risk with saxagliptin and alogliptin
Glucagon-like peptide 1 (GLP-1) agonist or incretin mimetic	Albiglutide (Tanzeum) Dulaglutide (Trulicity) Exenatide (Byetta) Exenatide ER (Bydureon) Liraglutide (Victoza)- FYI- Liraglutide (Saxenda) is marketed as weight loss drug for obese patients Usually used as an add on to Metformin and other Type 2 medications	Stimulation of GLP-1 receptors results in increased insulin secretion in response to elevated glucose, decreased glucagon secretion, slowed gastric emptying, and increased satiety	Injectable Albiglutide- 30 mg SQ once weekly Dulaglutide- 0.75 SQ once weekly Exenatide- 5 mcg SQ BID Exenatide ER- 2 mg SQ once weekly Liraglutide- 0.6 mg SQ once daily for 1 week, then increase to 1.2 mg SQ once daily	-No hypoglycemia when used alone -Headache -GI effects -Pancreatitis

Type 2 Diabetes Medications Continued

Drug Class	*Drugs*	*Mechanism of Action*	*Route and Initial Dose*	*Overdose Effects*
Insulin	Various		Injectable	-Hypoglycemia
Meglitinide or "glinides"	Nateglinide (Starlix) Repaglinide (Prandin)	Stimulates pancreatic insulin secretion, similar to sulfonylureas, but glucose dependent and diminishes with low glucose concentrations	PO Nateglinide- 60-120 mg TID with meals Rapaglinide- 0.5 mg TID with meals	-Hypoglycemia if taken without food or if severe renal impairment -Glinides can cause hypoglycemia, but they do so at a rate lower than that observed with the sulfonylureas.
Sodium-glucose co-transporter 2 (SGLT2) inhibitor or "flozins"	Canagliflozin (Invokana) -with metformin (Invokamet) Dapagliflozin (Farxiga) Empagliflozin (Jardiance) -with linagliptin (Glyxambi) -with metformin (Synjardy)	Blocks glucose reabsorption in kidney, increases glucosuria	PO Canagliflozin- 100 mg once daily Dapagliflozin- 5 mg once daily Empagliflozin- 10 mg once daily	-No hypoglycemia -Hypotension -Possible association with ketoacidosis
Sulfonylurea- 1st generation	Chlorpropamide (Diabinese) Tolazamide (Tolinase) Tolbutamide (Orinase)	Stimulates pancreatic insulin secretion	PO Chlorpropamide- 100-250 mg once daily Tolazamide- 250 mg once daily Tolbutamide- 1 gram once daily	-Hypoglycemia, more common than with 2nd generation -GI upset
Sulfonylurea- 2nd generation	Glyburide (Diabeta, Glynase, Micronase) Glipizide (Glucotrol) Glimepiride (Amaryl)	Stimulates pancreatic insulin secretion	PO Glyburide- 2.5 mg once daily Glipizide- 5 mg once daily Glimepiride- 1 mg once daily	-Hypoglycemia -GI upset
Thiazolidinedione (TZDs)	Pioglitazone (Actos) Rosiglitazone (Avandia)	Increases insulin sensitivity in muscle and fat	PO Pioglitazone- 15 mg once daily Rosiglitazone- 4 mg once daily	-No hypoglycemia when used alone -GI effects -Water retention, congestive heart failure, and hepatotoxicity in chronic therapy
Bile Acid Sequestrant	Colesevelam (Welchol)	May reduce hepatic glucose, may increase incretin levels and decrease GI glucose absorption	PO Comes in oral powder and tablet 3.75 grams per day	-No hypoglycemia when used alone -GI effects -Not systemically absorbed, so low toxicity
Dopamine agonist	Bromocriptine (Cycloset)	May centrally regulate metabolism, increase insulin sensitivity	PO 0.8 mg once daily	-No hypoglycemia when used alone -Dizziness -GI effects -Diaphoresis -Severe hypotension -Confusion and hallucinations -Repetitive yawning

Insulin Therapy

Brand	Onset	Peak	Duration
Rapid Acting • Humalog • NovoLog • Apidra	 - 15-30 min - 10-20 min - 25 min	 - 30 min- 2.5 h - 40-50 min - 45-48 min	 - 3-6.5 hours - 3-5 hours - 4-5.3 hours
Short Acting • Humulin R • Novolin R	 - 30 min - 30 min	 - 3 hours - 1.5-3.5 hours	 - 8 hours - 8 hours
Intermediate-acting • Humulin N • Novolin N	 - 1-2 hours - 90 min	 - 6.5 hours - 4-12 hours	 - 16-24 hours or longer - Up to 24 hours
Long Acting • Lantus • Levemir • Toujeo	 - 1.1 hour - 1.1-2 hours - Develops over 6 hours	 - No significant peak on any	 - 10.8 to >24 h - 7.6 to >24 h - >24 h
Ultra Long-acting • Tresiba	Will be approved in early 2016 - 30-90 min	 - No peak	 - 42 hours

Top Selling Branded Diabetes Drugs

Lantus Solostar
Januvia
Lantus
Humalog
Novolog Flexpen
Novolog
Janumet
Invokana
Levemir Flexpen
Levemir Flextouch
Levemir
Victoza 3-pack

New Inhaled Insulin for Diabetes

Afreeza (insulin human) is an inhaled insulin and could be used as an alternative to rapid-acting injections. Afreeza is easier to use than the first inhaled insulin that was approved (Exubera), and is small, about the size of a whistle. Afreeza is recommended for special situations, such as for certain patients who need mealtime insulin but balk at giving the injections. Afreeza is used at the beginning of a meal.