CALIFORNIA ASSOCIATION
OF NURSE PRACTITIONERS
MARCH 18, 2015

DIABETES MANAGEMENT WITH INSULIN
LEARNING OBJECTIVES:

• REVIEW HISTORY OF INSULIN DEVELOPMENT
• DESCRIBE DIFFERENT TYPES OF INSULINS
• STATE CURRENT RECOMMENDATIONS FOR A1C LEVELS IN PATIENTS WITH TYPE 2 DM
• IDENTIFY PATIENTS WHO ARE CANDIDATES FOR INSULIN THERAPY
• STATE THE PRIMARY ADVANTAGES AND DISADVANTAGES OF TOUJEO
HISTORY OF INSULIN

• 1869 GERMAN MEDICAL STUDENT PAUL LANGERHAM
  • DESCRIBED DECEASED PATIENTS WITH DM HAD DAMAGED PANCREASES
  • IDENTIFIED CLUSTERS OF CELLS [ THAT WERE LATER LINKED ] TO PRODUCTION OF INSULIN– BETA CELLS

• 1889, OSKAR MINKOWSKI AND JOSEPH NON MERING
  • ESTABLISHED THE LINK BETWEEN THE PANCREAS AND DM

• 1910 EDWARD ALBERT SHARPEY-SCHAFFER
  • DISCOVERED THAT PATIENTS WITHOUT DM PRODUCED A SUBSTANCE NOT FOUND IN THOSE WITH DM.
  • LABELED THE SUBSTANCE INSULIN [ IN LATIN MEANS ISLAND ] A REFERENCE TO THE ISLETS OF LANGERHANS WHERE INSULIN IS PRODUCED
1921 FREDERICK BANTING, CHARLES BEST, JOHN MCLEOD AND BERTRAM COLLIP
- Extracted beta cells from a pancreas without harming them
- Created a mixture from the isolated cells of pancreas
- Injected to sick diabetic dogs: sx were relieved
- Explored for ways to purify insulin so they could test on humans
- Were able to purify insulin while diminishing the effects of possible insulin overdose

1922 LEONARD THOMPSON
- Sick 14-year old became the first human with DM to receive an insulin injection.
- L. Thompson, near death, improved only to die of pneumonia at age 27

1923 NOBEL PRIZE FOR BANTING AND MACLEOD
Patient — J.L.
TRANSITION FROM EXTRACTED INSULIN TO BASAL INSULIN

• **1922:**
  - Eli Lilly started producing it en masse extracting it from cows and pigs.
  - Regular insulin has an onset of action of around 30 minutes and lasted for approx 4-6 hrs.

• **1936:**
  - Historically Type 1 DM was more prevalent than Type 2 DM
  - Harold Percival Himsworth wrote an article in the Lancet, he made distinction between Type 1 and Type 2 DM
  - Scientists discovered that Protamine Zinc (PZI) had a longer onset and duration of action compared to regular insulin.
  - Adding Protamine-Zinc complex to regular insulin extended the onset of action to about 4-8 hrs but made the duration of action last longer than 36 hrs with peak activity seen between 14 and 24 hrs
  - Problem: Not enough activity during the day, multiple episodes of hypoglycemia during the night
The first stills used to make insulin (early-mid 1920's).
1923
Banting and Best awarded Nobel Prize for discovery and use of insulin in the treatment of type 1 DM
NEUTRAL PROTAMINE HAGEDORN (NPH)

• **1946:**
  - NPH WAS DEVELOPED AT NORDISK LABS IN DENMARK.
  - NPH HAD LESS PROTAMINE THAN PZI AND HAD A QUICKER ONSET OF ACTION.
  - THE ONSET OF ACTION RANGED FROM ABOUT 1-3 HRS WITH A DURATION OF ACTION SLIGHTLY SHORTER COMPARED TO PZI AT 24 TO 28 HRS.
  - THE QUICKER ONSET ELIMINATED THE RISKS OF DAYTIME HYPERGLYCEMIA AND NIGHTTIME HYPOGLYCEMIA.

• **1950:**
  - NPH WAS MARKETED
  - PZI WAS DISCONTINUED IN USA
• 1955:
  • FREDERICK SANGER HAD FINISHED SEQUENCING THE LONG AMINO ACID CHAINS FOUND IN BOVINE INSULIN WHICH WOULD PROVE INVALUABLE IN DETERMINING THE STRUCTURE OF INSULIN.

• 1978:
  • BECKMAN RESEARCH INST & GENENTECH PRODUCED THE FIRST RECOMBINANT SYNTHETIC HUMAN INSULIN USING PLASMIDS IN BENIGN E COLI BACTERIA

• 1981:
  • NOVO NORDISK CHEMICALLY AND ENZYMATICALLY CONVERTED PORCINE INSULIN TO HUMAN INSULIN.

• 1982:
  • ELI LILLY AND CO WERE ABLE TO BRING THE MARKET, THE FIRST DNA RECOMBINANT PRODUCT EVER- HUMULIN

• 1988:
  • NOVOLIN WAS MARKETED.

• 1999:
  • MYRIAD OF INSULIN ANALOGS HAVE BEEN DEVELOPED.
STATISTICS

• APPROX. 29 MILLION AMERICANS HAVE DM

• GOAL OF DM MANAGEMENT IS TO PREVENT COMPLICATIONS:
  • HTN
  • KIDNEY
  • PVD
  • CAD
  • STROKE
  • CERTAIN CANCERS
23.6 MILLION

Number of Americans with diabetes:

Emergency-room costs attributed to diabetes every year: $3.9 billion

Good control of blood glucose decreases eye, kidney and nerve disease by 25%

Lower-limb amputations of diabetics per year: 71,000

Amount of blood Americans lose every year for blood-glucose testing: 1,600 gallons

Number of glucose-testing strips Americans use every year: ABOUT 6 BILLION
NORMAL PHYSIOLOGY

- **High blood sugar**
  - Promotes insulin release
  - Glucagon
  - Pancreas

- **Glycogen**
  - Liver
  - Stimulation of glycogen breakdown
  - Insulin
  - Stimulation of glycogen formation
  - Lowers blood sugar
  - Low blood sugar
  - Tissue cells

- **Glucose**
  - Raises blood sugar
  - Stimulates glucagon uptake from blood
  - Promotes glucagon release
ETIOLOGIC CLASSIFICATION OF DIABETES MELLITUS

**TYPE 1**
- \(\beta\)-CELL DESTRUCTION WITH LACK OF INSULIN PRODUCTION
- LITTLE TO NO INSULIN SECRETION
- OBESITY NOT CHARACTERISTIC
- TYPICALLY DEPENDENT ON EXOGENOUS INSULIN FOR SURVIVAL

**TYPE 2**
- INSULIN RESISTANCE AND INSULIN DEFICIENCY
- RISK INCREASES WITH AGE, LACK OF PHYSICAL ACTIVITY, AND OBESITY
- INDIVIDUALS TYPICALLY OBESE
- HTN AND DYSLIPIDEMIA COMMON
- MAY IMPROVE WITH WEIGHT LOSS OR PHARMACOLOGIC THERAPY

TYPE 2 DIABETES:

TWO DEFECTS

Genes → Impaired Insulin Secretion

Genes → Insulin Resistance

±Environment → IGT

±Environment → IGT

Type 2 Diabetes

LIFESTYLE MODIFICATIONS 3-6 MONTHS

- **REGULAR PHYSICAL ACTIVITY**
  - 150 MINUTES / WEEK
  - MODERATE ACTIVITY: DANCING, SWIMMING, WALKING

- **WEIGHT REDUCTION**
  - 5%-10% OF CURRENT WT
  - BMI < 25 KG/M

- **HEART HEALTHY DIET**
  - 500 -1000 KCAL REDUCTION
  - HIGH FIBER FOODS
  - LIMIT SWEETS
  - LIMIT SATURATED FATS
A1C GOALS

- AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGIST (AACE):
  - $\leq 6.5\%$
  - PRE PRANDIAL $< 120 \text{ MG/DL}$
  - 2 HOURS POST PRANDIAL $< 140 \text{ MG/DL}$
  - $< 7\%$ WITH COMORBIDITIES
    - SHORTER LIFE EXPECTANCIES
    - SIGNIFICANT HYPOGLYCEMIA OR UNAWARENESS
    - POOR MOTIVATION
ADA GLYCEMIC RECOMMENDATIONS FOR NONPREGNANT ADULTS WITH DIABETES

A1C

<7.0%*

Preprandial capillary plasma glucose

70–130 mg/dL* (3.9–7.2 mmol/L)

Peak postprandial capillary plasma glucose†

<180 mg/dL* (<10.0 mmol/L)

*Goals should be individualized based on these values.
†Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.
TREATMENT INITIATION

- **MONOTHERAPY:** A1C 6.5%-6.9%
  - NEWLY DXED
  - METFORMIN: MOST COMMONLY PRESCRIBED WORLDWIDE
  - TITRATION Q 2-3 MONTHS
- **DUAL THERAPY:** A1C: 7%-9%
# Antihyperglycemic Therapy in Type 2 Diabetes

### Healthy eating, weight control, increased physical activity

<table>
<thead>
<tr>
<th>Metformin</th>
<th>High risk</th>
<th>Low risk</th>
<th>Neutral/loss</th>
<th>GI/lactic acidosis</th>
<th>Low risk</th>
</tr>
</thead>
</table>

If needed to reach individualized HbA1c target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):

<table>
<thead>
<tr>
<th>Metformin +</th>
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<th>Thiazolidinedione +</th>
<th>DPP-4 Inhibitor +</th>
<th>GLP-1 receptor agonist +</th>
<th>Insulin (usually basal) +</th>
</tr>
</thead>
<tbody>
<tr>
<td>High HbA1c</td>
<td>High</td>
<td>High</td>
<td>Intermediate</td>
<td>High</td>
<td>Highest</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>Low risk</td>
<td>Low risk</td>
<td>Low risk</td>
<td>High</td>
<td>High risk</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Gain</td>
<td>Gain</td>
<td>Neutral</td>
<td>High</td>
<td>High gain</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Hypoglycemia</td>
<td>Edema, HF, Fx’s</td>
<td>Rare</td>
<td>GI</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Low HbA1c</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Variable</td>
</tr>
</tbody>
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<tbody>
<tr>
<td>TZD</td>
<td>SU</td>
<td>SU</td>
<td>SU</td>
<td>SU</td>
<td>TZD</td>
</tr>
</tbody>
</table>
# When Oral Combination Therapy is No Longer Enough

<table>
<thead>
<tr>
<th>Rate</th>
<th>5% to 10% per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs</td>
<td>FPG &gt;140 mg/dL</td>
</tr>
<tr>
<td></td>
<td>A1C &gt; 7%</td>
</tr>
<tr>
<td>Causes</td>
<td>Same as those for monotherapy</td>
</tr>
<tr>
<td></td>
<td>Decreasing β-cell function</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
</tr>
<tr>
<td></td>
<td>Insufficient physical activity</td>
</tr>
<tr>
<td></td>
<td>Intercurrent illness</td>
</tr>
</tbody>
</table>
OBJECTIVES OF INSULIN THERAPY

• SURVIVAL
• PREVENTION OF HYPERGLYCEMIA & KETOACIDOSIS
• LIVING FULL & ACTIVE LIFE
• PREVENTION OF LONG TERM COMPLICATIONS IF POSSIBLE
• FUNCTION AS SUBSTITUTE FOR ENDOGENOUS HORMONE
• EFFECTS ARE SAME AS NORMAL ENDOGENOUS INSULIN
• HUMAN INSULIN
  • DERIVED USING RECOMBINANT DNA TECHNOLOGIES
  • RECOMBINANT INSULIN PRODUCED BY BACTERIA AND YEAST
• RESTORES THE DIABETIC PATIENT’S ABILITY TO:
  • METABOLIZE CARBOHYDRATES, FATS, AND PROTEINS
  • STORE GLUCOSE IN THE LIVER
  • CONVERT GLYCOGEN TO FAT STORES
TYPE 2 DIABETES.....
A PROGRESSIVE DISEASE

OVER TIME, MOST PATIENTS WILL NEED INSULIN TO REACH TARGET

Physiologic Insulin Secretion: 24-Hour Profile

- **Insulin (µU/mL)**
  - Basal Insulin
  - Breakfast
  - Lunch
  - Dinner

- **Glucose (mg/dL)**
  - Basal Glucose

**Time of Day**

7 A.M. - 9 P.M.
INSULIN THERAPY

• MIMICS NORMAL PHYSIOLOGIC INSULIN RELEASE
• STRIVES FOR IDEAL RELEASE OF INSULIN
• GOAL IS: REACHING A TARGETED CONTROLLED GLUCOSE OF <100 MG /DL
• USED TO TREAT:
  • TYPE 1 DM
  • TYPE 2 DM WITH PROGRESSIVE BETA-CELL LOSS
  • GDM
EXOGENOUS INSULIN THERAPY

- Low constant basal level of insulin is needed at all times to maintain:
  - Normal cellular metabolism
  - Balance hepatic glucose production

- **Type 1:**
  - Hormone replacement therapy
  - Usually bolus basal regimen

- **Type 2:**
  - More complex in Type 2 than Type 1
  - No preferred or standard insulin regimen
  - Antidiabetic medications are used in combination with insulin
  - Increase workload for patient
  - Risk of hypoglycemia
INSULIN THERAPY INDICATIONS

• GLUCOSE CANNOT BE CONTROLLED ADEQUATELY

• A1C > 8%

• LONG STANDING HX

• INSULIN MORE ROBUST OPTION THAN ADDING 3\textsuperscript{RD} ORAL AGENT

• AACE SUGGESTS A1C > 9%, SIGNIFICANT SXS

• ADA & EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES (EASD) RECOMMEND A1C ≥ 10%
INSULIN THERAPY INITIATION

• AACE AND ADA

• STARTING DOSE: 0.1 - 0.2 UNITS/KG IF A1C <8%

• 0.2-0.3 UNITS/KG IF A1C LEVELS 8-10%
TYPES OF INSULIN

• 15 TYPES OF INSULIN
• TREATMENT OF TYPE 1
• TREATMENT OF TYPE 2
  • 25.8 % LONG ACTING
  • 17.8 % SHORT ACTING
  • 16.5 % RAPID ACTING
  • 5.3% MIXED
CLASSIFICATION

- RAPID ACTING
- SHORT ACTING
- INTERMEDIATE ACTING
- LONG ACTING
<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting</td>
<td>NovoLog</td>
<td>Insulin aspart</td>
<td>15 minutes</td>
<td>30 to 90 minutes</td>
<td>3 to 5 hours</td>
</tr>
<tr>
<td></td>
<td>Apidra</td>
<td>Insulin glulisine</td>
<td>15 minutes</td>
<td>30 to 90 minutes</td>
<td>3 to 5 hours</td>
</tr>
<tr>
<td></td>
<td>Humalog</td>
<td>Insulin lispro</td>
<td>15 minutes</td>
<td>30 to 90 minutes</td>
<td>3 to 5 hours</td>
</tr>
<tr>
<td>Short-acting</td>
<td>Humulin R</td>
<td>Regular (R)</td>
<td>30 to 60 minutes</td>
<td>2 to 4 hours</td>
<td>5 to 8 hours</td>
</tr>
<tr>
<td></td>
<td>Novolin R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting</td>
<td>Humulin N</td>
<td>NPH (N)</td>
<td>1 to 3 hours</td>
<td>8 hours</td>
<td>12 to 16 hours</td>
</tr>
<tr>
<td></td>
<td>Novolin N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting</td>
<td>Leveimir</td>
<td>Insulin detemir</td>
<td>1 hour</td>
<td>Peakless</td>
<td>20 to 26 hours</td>
</tr>
<tr>
<td></td>
<td>Lantus</td>
<td>Insulin glargine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-mixed NPH (intermediate-acting) and regular (short-acting)</td>
<td>Humulin 70/30</td>
<td>70% NPH and 30% regular</td>
<td>30 to 60 minutes</td>
<td>Varies</td>
<td>10 to 16 hours</td>
</tr>
<tr>
<td></td>
<td>Novolin 70/30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Humulin 50/50</td>
<td>50% NPH and 50% regular</td>
<td>30 to 60 minutes</td>
<td>Varies</td>
<td>10 to 16 hours</td>
</tr>
<tr>
<td>Pre-mixed insulin lispro protamine suspension (intermediate-acting) and insulin lispro (rapid-acting)</td>
<td>Humalog Mix 75/25</td>
<td>75% insulin lispro and 25% insulin lispro</td>
<td>10 to 15 minutes</td>
<td>Varies</td>
<td>10 to 16 hours</td>
</tr>
<tr>
<td></td>
<td>Humalog Mix 50/50</td>
<td>50% insulin lispro protamine and 50% insulin lispro</td>
<td>10 to 15 minutes</td>
<td>Varies</td>
<td>10 to 16 hours</td>
</tr>
<tr>
<td>Pre-mixed insulin aspart protamine suspension (intermediate-acting) and insulin aspart (rapid-acting)</td>
<td>NovoLog Mix 70/30</td>
<td>70% insulin aspart protamine and 30% insulin aspart</td>
<td>5 to 15 minutes</td>
<td>Varies</td>
<td>10 to 16 hours</td>
</tr>
</tbody>
</table>
## Insulin Products Comparison Chart

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Brand Name/ Formulary Status/ Manufacturer</th>
<th>Concentration</th>
<th>May Be Mixed With</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Administration in Relation to Meals</th>
<th>Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basal and Prandial Premixed Combinations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70% Insulin aspart protamine 30% Insulin aspart</td>
<td>NovoLog® 70/30 (NF)* Novo Nordisk</td>
<td>100 units/mL</td>
<td>do not mix with other insulins</td>
<td>10 to 20 minutes</td>
<td>1 to 4 hours</td>
<td>15 to 18 hours</td>
<td>within 15 minutes of meal initiation</td>
<td>cloudy</td>
</tr>
<tr>
<td>70% NPH 30% Regular</td>
<td>Novolin® 70/30 (NF)* Novo Nordisk</td>
<td>100 units/mL</td>
<td>do not mix with other insulins</td>
<td>30 to 60 minutes</td>
<td>2 to 12 hours</td>
<td>10 to 16 hours</td>
<td>30 minutes before meals</td>
<td>cloudy</td>
</tr>
<tr>
<td>50% NPH 50% Regular</td>
<td>Humulin® 50/50 (NF)* Lilly</td>
<td>100 units/mL</td>
<td>do not mix with other insulins</td>
<td>30 to 60 minutes</td>
<td>2 to 5.5 hours</td>
<td>10 to 16 hours</td>
<td>30 minutes before meals</td>
<td>cloudy</td>
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<td>70% NPH 30% Regular</td>
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<tr>
<td>75% Insulin lispro protamine 25% Insulin lispro</td>
<td>Humalog® 75/25 (NF)* Lilly</td>
<td>100 units/mL</td>
<td>do not mix with other insulins</td>
<td>15 to 30 minutes</td>
<td>1 to 6.5 hours</td>
<td>up to 24 hours</td>
<td>within 15 minutes of meal initiation</td>
<td>cloudy</td>
</tr>
</tbody>
</table>
INSULINS

• SHORT-ACTING
  • REGULAR INSULIN (HUMULIN R)
  • ONSET 30 TO 60 MINUTES
  • THE ONLY INSULIN PRODUCT THAT CAN BE GIVEN BY IV BOLUS, IV INFUSION, OR EVEN IM
INSULINS

• INTERMEDIATE-ACTING
  • INSULIN ISOPHANE SUSPENSION (ALSO CALLED NPH)
  • NPH NEUTRAL PROTAMINE HAGEDORN
    • CLOUDY APPEARANCE NPH NEUTRAL PROTAMINE HAGEDORN
    • SLOWER IN ONSET AND MORE PROLONGED IN DURATION THAN ENDogenous INSULIN
Replace B3 asparagine with lysine and B29 lysine with glutamic acid.
INSULIN ANALOGS

- PRODUCED FROM RECOMBINANT DNA TECHNOLOGY MODIFIED FROM HUMAN INSULIN
- HAVE SAME COMPOSITION, PROPERTIES AND ACTIONS AS HUMAN INSULIN
- RAPID ACTING ANALOGS
- COVER MEALS TO LOWER POSTPRANDIAL
- ONSET: < 15 MINUTES
- PEAK: 1-2 HRS
- DURATION: 3-5 HRS
TWICE-DAILY SPLIT-MIXED REGIMENS

LONG ACTING INSULINS

• SINCE 2000 IN USA
• A1C REDUCTION 1.5% - 1.8%
• BASAL LONG ACTING INSULIN ANALOG
• FLAT EFFECT FOR UP TO 24 HRS
• GLARGINE (LANTUS) U 100 (18-24 HRS) ONSET: 70 MIN 1X/D, MORE STEADY ABSORPTION, NO PEAK
• DETEMIR (LEVEMIR) U 100 (24 HRS) : 1-2 X/DAY, ERRATIC ABSORPTION RATE DEPENDS ON DOSE, LARGE DOSES NOT ABSORBED WELL
• GLARGINE (TOUJEO) U 300
GLARGINE

- **LANTUS VIAL U 100**
- **LANTUS SOLOSTAR PEN U 100**
  - PREFILLED DISPOSABLE STORAGE LIFE 28 DAYS AT ROOM TEMP
  - WIDELY UTILIZED
  - SAFE AND EFFECTIVE
Multiple Daily Injections (MDI)

Clear Solution pH 4

Dissolution

Hexamers $10^3 M$ → Dimers $10^5 M$ → Monomer $10^8 M$

Precipitation

Capillary Membrane

Insulin in Blood
TOUJEO

- FDA APPROVAL ON FEBRUARY 2015, ON MARKET 2015
- U 300, 3 X THE STANDARD FOR MOST INSULIN THERAPIES
- LONG ACTING, 1X/D
- DISPOSABLE PREFILLED PEN, 450 U OF GLARGINE INSULIN
- MORE EVEN STEADY DELIVERY 24-30 HRS
- 0.4 UNITS/KG – 0.5 UNITS /KG
- MAX DOSE OF 80 UNITS / INJECTION
- **LANTUS TO TOUJE O** CONVERSION: IS UNIT TO UNIT
- MAXIMUM STABILITY/EFFECT IS 5 DAYS, TITRATE Q 3-4 DAYS
- **NPH TO TOUJE O CONVERSION**: 2 X NPH INJECTION, 80 % OF TOTAL NPH, OR 50% AND THEN TITRATE
- EVERY 3 DAYS INCREASE BY 2 UNITS TILL FBS REACHES TO 100 (3-2-1 ALGORYTHM)
TOUJEO

- AVAILABLE AS PREFILLED 1.5 ML PENS, EACH MILLILITER CONTAINING 300 UNITS OF ACTIVE INSULIN.
- SIDE EFFECTS: HYPOGLYCEMIA, INJECTION SITE REACTION, PRURITIES, LIPODYSTROPHY, RASH, EDEMA AND WEIGHT GAIN
- 31% LESS NIGHT TIME HYPOGLYCEMIA COMPARED TO LANTUS
- 14% LESS ANYTIME HYPOGLYCEMIA COMPARED TO LANTUS
TOUJEO

- 3X MORE CONCENTRATED THAN LANTUS, USES 1/3 LESS LIQUID
- BENEFICIAL TO PATIENTS WHO ARE INSULIN RESISTANT AND REQUIRE LARGE INSULIN DOSES.
- 80 UNITS OF LANTUS AND MORE, NEED TO SPLIT THEIR DOSE INTO TWICE DAILY DOSING.
- MIGHT NEED HIGHER DOSE THAN LANTUS TO RECEIVE THE SAME GLYCEMIC CONTROL
NEW BASAL INSULIN: TRESIBA & RYZODEG

- TRESIBA (DEGLUDEC) AND RYZODEG 70/30 (INSULIN DEGLUDEC/INSULIN ASPART)
- IN ADULTS
- TRESIBA: LONG ACTING DURATION 42 HRS
- U-100 AND U-200 FORMATION
- SIDE EFFECT: HYPOGLYCEMIA
- RYZODEC 70/30 IS A MIXTURE OF INSULIN DEGLUDEC A LONG ACTING INSULIN ANALOG AND INSULIN ASPART A RAPID ACTING HUMAN INSULIN ANALOG.
- RESULTS FROM ALL TRIALS SHOWED RYZODEG 70/30 PROVIDED REDUCTIONS IN A1C COMPARED TO OTHER PREVIOUSLY APPROVED LONG ACTING OF PREMIXED INSULIN
TERESIBA

• BENEFICIAL FOR PATIENTS WITH
  • BUSY LIFESTYLE
  • CANNOT TAKE THE INJECTION AT THE SAME TIME
  • ARE NON COMPLIANT

• AVAILABLE IN U-100 AND U-200

• WHEN CONVERTING FROM U-100 TO U-200 THERE IS NO NEED FOR DOSAGE CONVERSION

• MISSED DOSE NEED TO BE ADMINISTERED AS SOON AS POSSIBLE, 8 HRS APART FROM THE FOLLOWING DOSE

• START 10 UNITS WITH INSULIN NAÏVE PATIENTS

• USE SAME DOSAGE WITH PATIENTS ALREADY ON INSULIN

• NO HEPATIC OR RENAL ADJUSTMENT IS NECESSARY BLOOD GLUCOSE SHOULD BE MONITORED CLOSELY WITH PATIENTS IN HEPATIC OR RENAL IMPAIRMENT AND INSULIN ADJUSTMENTS MADE ACCORDINGLY
# COMPARISON

## LANTUS
- U100/ML
- A1C REDUCTION SIMILAR (BOLLI ET AL, 2015)
- NOCTURNAL HYPOGLYCEMIA
- PHARMACOKINETIC, PHARMACODYNAMIC:
- MODE OF ACTION:
- DURATION: 18-24 HRS

## TOUJEO
- U300/ML
- A1C REDUCTION SIMILAR @ 6 MO
- LESS EPISODES IN TYPE 1 & 2 AT WK 9 TO 6 MO
- MORE EVEN STEADY STATE, CONSTANT, PERSISTENT
- LONGER DURATION OF ACTION
- EXTENDED BEYOND 24 HRS (BECKER ET AL, 2015)
Toujeo

**ADVANTAGES**
- ↓ NOCTURNAL HYPOGLYCEMIA
- AVAILABLE IN DISPOSABLE SOLOSTAR PEN, DOSAGE ACCURACY, ↓ PT ERROR
- DELIVERED LESS VOLUME
- 24-30 HRS, GOOD OPTIONS FOR THOSE REQUIRING BID DOSING
- ↓ WT GAIN THAN LANTUS
- LIVE 1TO 1 SYNCRONIZED PT SUPPORT (TEXT, PHONE, EMAIL OR WEBINARS) BY CDE FOR 120 DAYS
- PT ASSISTANCE PROGRAM

**DISADVANTAGES**
- RISK FOR HYPOGLYCEMIA
- WT. GAIN
- AVAILABLE ONLY IN PEN
- TZD NEED ↓ WHEN DOSED CONCOMITANTLY
- NOT INDICATED FOR AGES ↓ 18
- ALLERGIC INJECTION SITE REACTION, LIPODYSTROPHY, PRURITIS, RASH, EDEMA (ALTHOUGH LESS THAN GLARGINE)
CAUSES OF HYPERGLYCEMIA

• ADDITIONAL CALORIC INTAKE
• NOT ADEQUATE INSULIN
• LACK OF EXERCISE
• STRESS
• STEROIDS
CAUSES OF HYPOGLYCEMIA

• BLOOD GLUCOSE < 50-60 MG/DL (2.7-3.3 MMOL/L)
• TOO MUCH INSULIN
• TOO MUCH ORAL HYPOGLYCEMIC AGENTS
• TOO LITTLE FOOD
• EXCESSIVE PHYSICAL ACTIVITY
Time of Activity of Human Insulins

Rapid-Acting
Humalog®
also available in vial

Short-Acting
Humulin®R

Intermediate-Acting
Humulin®N
also available in vial
Humulin®L

Long-Acting
Humulin®U

Premixed
Humalog® Mix 75/25
also available in vial

Premixed
Humulin® 70/30
also available in vial

Premixed
Humulin® 50/50

Insulin Glargine
(Lantus)
<table>
<thead>
<tr>
<th>Type of Insulin &amp; Brand Names</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Role in Blood Sugar Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humalog or lispro</td>
<td>15-30 min.</td>
<td>30-90 min.</td>
<td>3-5 hours</td>
<td>Rapid-acting insulin covers insulin needs for meals eaten at the same time as the injection. This type of insulin is often used with longer-acting insulin.</td>
</tr>
<tr>
<td>Novolog or aspart</td>
<td>10-20 min.</td>
<td>40-50 min.</td>
<td>3-5 hours</td>
<td></td>
</tr>
<tr>
<td>Apidra or glulisine</td>
<td>20-30 min.</td>
<td>30-90 min.</td>
<td>1-2½ hours</td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular (R) humulin or novolin</td>
<td>30 min. -1 hour</td>
<td>2-5 hours</td>
<td>5-8 hours</td>
<td>Short-acting insulin covers insulin needs for meals eaten within 30-60 minutes</td>
</tr>
</tbody>
</table>
## Approach to Management of Hyperglycemia

<table>
<thead>
<tr>
<th>Factor</th>
<th>More Stringent</th>
<th>Less Stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia, other adverse events</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Disease duration</td>
<td>Newly diagnosed</td>
<td>Long-standing</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>Long</td>
<td>Short</td>
</tr>
<tr>
<td>Important comorbidities</td>
<td>Absent</td>
<td>Severe</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>Absent</td>
<td>Severe</td>
</tr>
<tr>
<td>Resources, support system</td>
<td>Readily available</td>
<td>Limited</td>
</tr>
</tbody>
</table>

GLYCEMIC RECOMMENDATIONS FOR NONPREGNANT ADULTS WITH DIABETES

• GOALS: INDIVIDUALIZED BASED ON
  • DURATION OF DIABETES
  • AGE/LIFE EXPECTANCY
  • COMORBID CONDITIONS
  • KNOWN CVD OR ADVANCED MICROVASCULAR COMPLICATIONS
  • HYPOGLYCEMIA UNAWARENESS

• INDIVIDUAL PATIENT CONSIDERATIONS
HOW TO INITIATE INSULIN?

- WT IN KG. MULTIPLY BY 0.4-0.5 = TDD
- 50% TDD = BASAL
- TITER DOSAGE TILL FBS IS TARGET 110-120 MG/DL
- 50% TDD = BOLUS
- BOLUS DIVIDE BY 3.
- ADMINISTER AC MEALS
**INSULIN SENSITIVITY FACTOR**

- Refers to # of points 1 unit of rapid acting insulin lowers BLD GLU
- Goal of ISF, is to bring blood glu level to target if elevated.
- If ISF is set correctly, BLD GLU should ↓ into target range 3-4 hours after the correction bolus is given.
- ISF is determined by using the “1800 rule.”
  - Determine average total daily insulin dose (TDD)
  - Divide 1800 by TDD
HUMALOG INSULIN AT RATIO 1 UNIT/15 GM OF CHO WITH EACH MEAL AND SNACK. 36 UNITS OF LANTUS INSULIN AT BEDTIME.

BELOW IS THE CALCULATION OF HIS ESTIMATED TDD.

BREAKFAST: 8 UNITS HUMALOG LUNCH: 5 UNITS HUMALOG
SNACK: 3 UNITS HUMALOG DINNER: 8 UNITS HUMALOG
BEDTIME: 36 UNITS LANTUS TDD: 60 UNIT

ISF 1800/60=30. 1 UNIT OF INSULIN WILL LOWER BLD. GLU BY 30
BEFORE DINNER TODAY BLD GLU 250. TARGET IS 120

130 ABOVE TARGET. 130/30=4.3. 4 UNITS NEEDED TO CORRECT
SLIDING-SCALE INSULIN DOSING

- SQ SHORT-ACTING OR REGULAR INSULIN DOSES ADJUSTED ACCORDING TO BLOOD GLUCOSE TEST RESULTS
- USED IN HOSPITALIZED DIABETIC PATIENTS OR THOSE ON TOTAL PARENTERAL NUTRITION (TPN) OR ENTERAL TUBE FEEDINGS
- SQ INSULIN IS ORDERED IN AMT THAT ↑ AS THE BLD GLU ↑
- DISADVANTAGE: DELAYS INSULIN ADMINISTRATION UNTIL HYPERGLYCEMIA OCCURS; RESULTS IN LARGE SWINGS IN GLUCOSE CONTROL
GLUCAGON INJECTION

• USED TO TREAT VERY LOW BLOOD SUGAR WHICH MAY OCCUR IN PEOPLE WHO TAKE INSULIN.

• ADMINISTERED IV, SQ OR IM IF THE PERSON IS:
  • UNCONSCIOUS,
  • HAVING SEIZURE
  • DISORIENTED AND UNABLE TO EAT SUGAR OR SUGAR-SWEETENED PRODUCTS

• ONE VIAL CONTAINS 1 MG (1 UNIT) GLUCAGON AND 1 ML STERILE WATER FOR RECONSTITUTION
GLUCAGON INJECTION
TACTICS AND TECHNIQUES

• TREAT TO TARGETS DEFINED BY EPIDEMIOLOGIC AND INTERVENTIONAL EVIDENCE
  • $\text{AIC} \leq 7\%$
  • BLOOD PRESSURE $< 130/80$ MM HG
  • LDL-CHOLESTEROL $\leq 100$ MG/DL
TACTICS AND TECHNIQUES

• BASIC TREATMENT TACTICS INCLUDE
  • DSME / MNT / PHYSICAL ACTIVITY
  • FOR GLYCEMIC CONTROL
    • ORAL AND ORAL-INSULIN COMBINATIONS
  • FOR BLOOD PRESSURE CONTROL
    • ACE-INHIBITOR, β-BLOCKER, CA-CHANNEL BLOCKERS, ARB II AND DIURETIC COMBINATIONS
  • FOR LDL-CHOLESTEROL CONTROL
    • STATINS, FIBRATES
  • FOR VASCULAR PROTECTION
    • ASA 81 TO 325 MG DAILY

REFERENCES

• DUGAN (2016), MANAGING DIABETES IN WOMEN OF CHILDBEARING AGE, CLINICIAN REVIEW, FEB, 51-54.
• SAYLOR (2016). TRANSITIONING YOUNG ADULTS WITH TYPE 1 DIABETES TO CAMPUS LIFE. THE JOURNAL OF NURSE PRACTITIONER, VOL 12, NO 1, 41-46.