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**U-500 Insulin**

- Understand differences between U-500 concentrated insulin and standard insulin formulations
- Recognize benefits and risks associated with U-500 insulin use
- Understand typical U-500 dosing regimen
Patient Case: Mr. S.

- 58 yo male
- Wt 298 lbs (140 kg), BMI 42
- 12 year history of DM2
- PMH
  - CAD, HTN, hyperlipidemia, peripheral neuropathy, DM2, sleep apnea

Current Insulin
- NPH insulin 80 units BID
- Aspart insulin 42 units with breakfast and lunch, 65 units with evening meal

HgbA1c
- 8.4% ⇒ 8.8% ⇒ 9.1% ⇒ 10.7%

Daily BG readings
- Morning Noon Evening Bed
  - Average: 259 275 339 280

Patient Case: Mr. S.
Introduction

- Increasing obesity epidemic and increasing occurrence of insulin resistance with uncontrolled diabetes
- Escalating insulin dose requirements, usually associated with poor diabetes control
- Excessive number of daily injections
- Absorption of high insulin volumes becomes unpredictable

Insulin Resistance Dose Response

4. Cochran E, Musso C, Garden P
• U-500 regular insulin (u500R)
• Available since the 1950’s
  • Humulin R – 1997
• Five-fold concentrated insulin

What is it

U-500 Insulin
• 500 units / mL
• 10,000 units per 20mL vial

Standard Insulin
• 100 units / mL
• 1000 units per 10mL vial

What is it
• Higher Concentration of U-500 alters its pharmacokinetic profile
  • Onset of action within 30 minutes
  • Peak action 8 hours
  • Duration of action 12 hours (reports of up to 24 hours)

• Onset of action similar to Regular (U-100) Insulin
• Duration of action similar to Neutral Protamine Hagedorn (NPH) Insulin
• Has action resembling both basal & bolus insulin

What is it

Insulin Duration of Action
Insulin Duration of Action

- Those with high dose requirements – severe insulin resistance
  - Greater than 200 - 300 units per day
    - (2 units/kg/day)
    - Multiple daily injections required to achieve dose
  - Assess the ability of patient to appropriately monitor and manage dosing
  - Rule out
    - Cushings, acromegaly, glucagonoma, pheochromocytoma
    - Other high resistance syndromes

Who gets it
Patient Case: Mr. S.

• 58 yo male
• Wt 298 lbs (140 kg), BMI 42
• 12 year history of DM2
• PMH
  • CAD, HTN, hyperlipidemia, peripheral neuropathy, DM2, sleep apnea

• Current Insulin
  • NPH insulin 80 units BID
  • Aspart insulin 42 units with breakfast and lunch, 65 units with evening meal
• HgbA1c
  • 8.4% ➔ 8.8% ➔ 9.1% ➔ 10.7%
• Daily BG readings
  • Morning  Noon  Evening  Bed
    Average:  259  275  339  280
Patient Case: Mr. S.

- Current Insulin
  - NPH insulin 80 units BID
  - Aspart insulin 42 units with breakfast and lunch, 65 units with evening meal
  - *Total daily dose 309 units*

- HgbA1c
  - 8.4% ➔ 8.8% ➔ 9.1% ➔ 10.7%

- Daily BG readings
  - Morning Noon Evening Bed
  - Average: 259 275 339 280
  
*Uncontrolled daily bg levels, rising A1c, despite escalating insulin dose*

No Formal dosing guidelines

<table>
<thead>
<tr>
<th>Total Daily Dose</th>
<th>(percent of total daily dose divided with meals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>150-300 units</td>
<td>Twice Daily Injections (60 / 40)</td>
</tr>
<tr>
<td></td>
<td>May Consider Three Daily Injections (40 / 30 / 30), (45 / 35 / 20), (40 / 40 / 20)</td>
</tr>
<tr>
<td>300-600 units</td>
<td>Three Daily Injections</td>
</tr>
<tr>
<td></td>
<td>May Consider Four Daily Injections (30 / 30 / 30 / 10)</td>
</tr>
<tr>
<td>Greater than 600 units</td>
<td>Four Daily Injections (30 / 30 / 30 / 10), (25 / 25 / 25 / 25)</td>
</tr>
</tbody>
</table>

How to use it

Adapted from 7. Reutrakul S, Wroblewski K, Brown R.
What is it

• *HIGH POTENTIAL FOR ERROR*
  • Use tuberculin syringe for administration
  • Prescribe by both volume and actual units
  • FDA issued safety label changes to express the prescribed
dose in actual units of U-500 along with corresponding
markings on the syringe the patient is using
  • Provide a dose conversion chart

How to use it

• Dosage adjustment similar to standard insulin
  • Titrate by percentage of total dose
  • 10% of total daily dose

• Alternate dosing methods
  • Insulin pump
  • Basal / bolus regimens
Example U-500 dose conversion chart

<table>
<thead>
<tr>
<th>U-500 actual unit dose</th>
<th>U-100 syringe unit marking</th>
<th>Volume of tuberculin syringe (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 units</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td>50 units</td>
<td>10</td>
<td>0.1</td>
</tr>
<tr>
<td>75 units</td>
<td>15</td>
<td>0.15</td>
</tr>
<tr>
<td>100 units</td>
<td>20</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Adapted from 7. Reutrakul S, Wroblewski K, Brown R.

- Current Insulin
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- HgbA1c
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- Daily BG readings
  - Morning Noon Evening Bed
  - Average: 259 275 339 280

Patient Case: Mr. S.
Dose Initiation

Total Daily Insulin Dose = 309 units

- 20% reduction
  - 247 units == BID dosing
    - 145 units (0.29 ml) U-500 insulin with breakfast
    - 100 units (0.2 ml) u-500 insulin with dinner

- 20% reduction
  - 247 units == TID dosing
    - 100 units (0.2 ml) U-500 insulin with breakfast
    - 100 units (0.2 ml) u-500 insulin with lunch
    - 45 units (0.09 ml) u-500 insulin with dinner

Mr. S. Case

- Reduced from 5 injection a day to 2 (or 3) daily injections
- Reduced total daily volume of injections from 3.09 ml to 0.49 ml
- Additional room for dose titration to reach target BG goals
Patient Education Points

- Discuss properties of U-500 concentrated insulin
- Clear liquid, concentrated form comes in a larger bottle and has a small red triangle to mark it as U-500 concentrated insulin
- Store U-500 concentrated insulin away from other insulin products
- Use of tuberculin syringes, including drawing up appropriate and precise amount of insulin
- Hold U-500 concentrated insulin for skipped meals
- Hypoglycemia treatment
- Importance of carrying information letter indicating that patient uses U-500 concentrated insulin and explaining conversion with tuberculin syringes
- Contact information to call during business hours or emergencies

Boise VA Medical Center Criteria for Use U-500 Concentrated Insulin

Take away points

- Five times more concentrated than regular U-100 insulin (500 units/mL)
- Supplied as 20 mL vials (10,000 units per vial)
- For subcutaneous use only
- Pharmacokinetics with onset similar to Regular Insulin and duration similar to NPH Insulin
- Dose typically given twice daily (dosing customized to patient case)
- Due to prolonged duration of action, hypoglycemic reactions may develop 18-24 hours after injection
1. Boise VA Medical Center Criteria for Use U-500 Concentrated Insulin. August 2014