

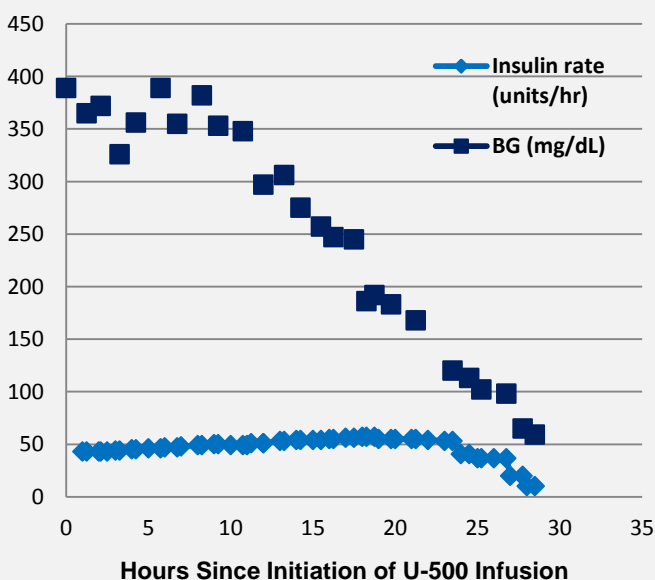
Introduction

- Insulin resistance is a marker of disease severity in critically-ill patients and is associated with increased morbidity and mortality.^{1,2}
- Guidelines recommend targeting BG between 140-180 mg/dL or <180 mg/dL in critically-ill patients in order to achieve adequate glycemic control while minimizing hypoglycemia.^{1,2}
 - IV insulin infusions allow for rapid titration to achieve and maintain goal range.
- Limited literature exists describing strategies to overcome insulin resistance when maximum rates of insulin infusion are reached.
 - Concentrated insulin may be considered in these rare scenarios
- We report two cases of severe insulin resistance treated with IV infusions of U-500 regular insulin

Case 1

- 66-year-old male (119.7 kg) with DM2, CAD, and atrial fibrillation presents with acute pancreatitis.
- On day 3, he was intubated for acute respiratory distress syndrome.
- Insulin aspart (U-100) intravenous infusion protocol was initiated on day 4 in response to BG levels above 200 mg/dL.
- On days 6-8, the patient developed acute kidney injury and BG ranged 280-389 mg/dL despite maximum insulin infusion at 40 units/hr. He was transitioned to U-500 infusion at 43 units/hr with titration per physician order.
- BG trended from 389 to 120 mg/dL on day 9. U-500 was discontinued and the patient was transitioned back to insulin aspart infusion.
- The patient expired from PEA cardiac arrest on day 10.

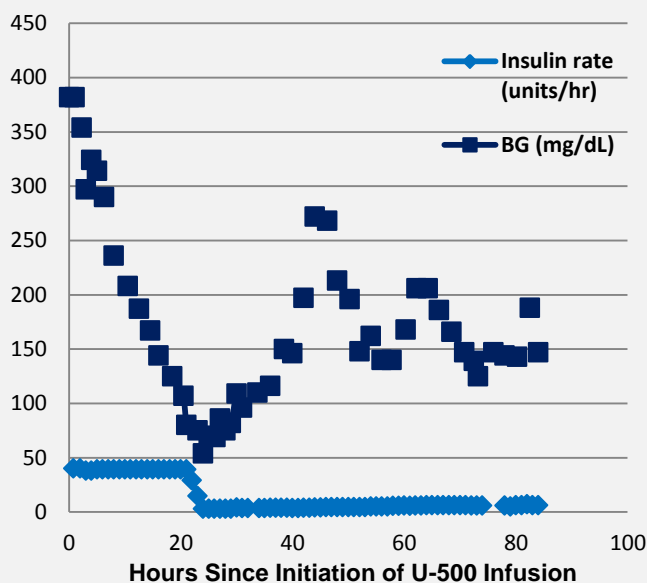
BG and U-500 Insulin Infusion Over Time



Case 2

- 51-year-old male (109.8 kg) with DM2 and hypertension presented with ST-elevation myocardial infarction.
- Insulin aspart (U-100) infusion protocol was initiated on day 1 for BG above 500 mg/dL. Despite insulin aspart 40 units/hr, BG trended only from 504 to 387 mg/dL.
- Day 2, he was transitioned to U-500 infusion at 40 units/hr with titration per physician order, and after 14 hours BG reduced to 144 mg/dL.
- Patient remained on U-500 infusion until care was withdrawn on day 5.

BG and U-500 Insulin Infusion Over Time



Discussion/Conclusions

- U-500 insulin is a short-acting, concentrated insulin product with a pharmacokinetic and pharmacodynamic profile similar to intermediate-acting insulin when administered subcutaneously.³
 - Differences in metabolism of concentrated insulin may account for attainment BG control.
- Equipotent doses of U-500 vs. U-100 IV infusion achieved target BG in our cases.
 - Slower metabolism and elimination of U-500 may account for improved glycemic control even when administered via IV route.
- One published case report describes use of IV U-500 insulin infusion to successfully treat DKA in a patient with Rabson-Mendenhall syndrome, an autosomal recessive disorder causing mutations in the insulin receptor gene leading to decreased insulin binding at the receptor site.⁴
- Measures to ensure safety and prevent errors with concentrated insulin storage, dosing, dispensing, and administration must be in place.
- IV U-500 insulin infusion may be considered for refractory insulin resistance.
 - Future studies are needed to fully elucidate the mechanism for use in severe critical-illness insulin resistance.

References

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4. Moore MM, et al. Treatment of DKA with IV U-500 insulin in a patient with Rabson-Mendenhall syndrome. J Pharm Pract. 2016. [Epub ahead of print]