OKLAHOMA STATE UNIVERSITY CENTER FOR HEALTH SCIENCES

Time to resolution of ketoacidosis comparing weight based and non-weight based insulin dosing for diabetic ketoacidosis

Zachary Dunn, PharmD[1] (PGY1); Josh Burton, DO[2] (PGY3); Ben Jacobs, PharmD[1]; (Faculty Advisors) John Bury, PharmD[1], BCPS, MBA; Kelly Murray, PharmD, BCACP[1,2] Oklahoma State University Medical Center | Department of Pharmacy[1], Department of Emergency Medicine[2]

BACKGROUND

- Diabetic ketoacidosis (DKA) is characterized by uncontrolled hyperglycemia, metabolic acidosis, and ketonemia[1]
- Insulin's role in DKA is to halt lipolysis and ketogenesis eventually resolving acidosis[2]
- The American Diabetes Association (ADA) insulin drip rates in managing DKA: (1) 0.14 units/kg/hour infusion or (2) 0.1 unit/kg bolus followed by 0.1 units/kg/hour infusion[1]
- Insulin rates lower than the ADA doses may be used to avoid hypoglycemia or hypokalemia, but no research has been done to assess the effectiveness of this strategy
- Despite euglycemia, appropriate weight-based dosing is necessary to avoid delaying resolution of DKA and resolving ketonemia[2]
- Doses lower than 0.1 unit/kg/hour may be enough to suppress lipolysis and ketogenesis[3]

OUTCOMES

- Compare time to resolution of ketoacidosis based on weight-based versus non-weight-based insulin drip rates started in the ED
- Describe adverse outcomes associated with insulin drip rates

ENDPOINTS

- **Primary**: time to resolution of ketoacidosis defined as – blood glucose < 200 and at least 2 of the following: (1) serum bicarbonate $\geq$ 15 mEq/L, (2) venous pH > 7.3, and/or (3) anion gap $\leq$ 12 mEq/L
- **Secondary**: time of ICU and hospital stay, time to start of subcutaneous insulin, hypoglycemic events, hypokalemic events, and death

DISCLOSURES & REFERENCES

REFERENCES

1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic Crises in Adult Patients with Diabetes. Diabetes Care 2009;32(7):1335-1343
2. French EK, Donihi AC, Korytkowski MT. Diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome: review of acute decompensated diabetes in adult patients. BMJ 2019;365:I1114.
3. Cardoso L, Vicente N, Rodrigues D, et al. Controversies in the management of hyperglycaemic emergencies in adults with diabetes. Metabolism Clinical and Experimental 2017;68:43-54.
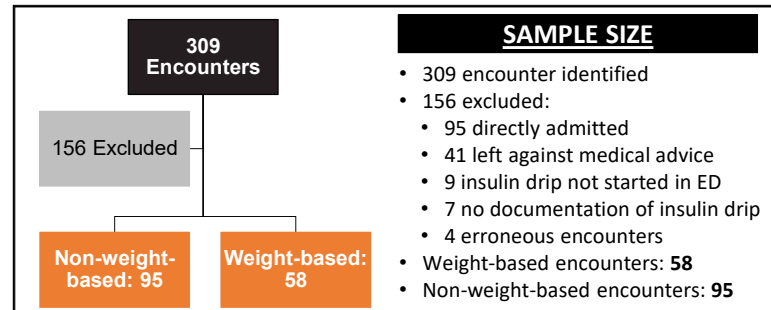
METHODS

- Retrospective cohort chart review from January 1, 2018 to December 31, 2019

INCLUSION CRITERIA	EXCLUSION CRITERIA
• Diagnosis code of DKA • Admitted through the ED	• Left against medical advice • Directly admitted/not admitted • Did not received insulin drip in ED

- Baseline characteristics and labs on arrival were collected
- Other data collected included drip rates, length of stay in ICU and hospital, number of hypoglycemic and hypokalemic events, and death to assess endpoints
- Independent variables including time to resolution assessed with ANOVA tests; dichotomous variables, including hypoglycemic events and death, assessed with Chi squared tests of independence

POPULATION RESULTS

309 Encounters

156 Excluded

Non-weight-based: 95   **Weight-based: 58**

SAMPLE SIZE

- 309 encounter identified
- 156 excluded:
  - 95 directly admitted
  - 41 left against medical advice
  - 9 insulin drip not started in ED
  - 7 no documentation of insulin drip
  - 4 erroneous encounters
- Weight-based encounters: **58**
- Non-weight-based encounters: **95**

BASELINE DEMOGRAPHICS

- No difference between groups

CATEGORY	NON-WEIGHT-BASED (N = 95)	WEIGHT-BASED (N = 58)
Age – mean	37	36
Female – no. (%)	36 (38)	17 (29)
Caucasian – no. (%)	56 (59)	41 (71)
Type 1 Diabetes – no. (%)	70 (74)	41 (71)
Precipitating factor – no. (%):		
Non-compliance	63 (66)	41 (71)
Infection	9 (10)	6 (10)
Weight – mean kg	76.2	70.8
Initial laboratory findings:		
Venous/arterial pH – mean	7.16	7.16
Anion gap – mean mEq/L	26.3	27.5
Blood glucose* – mean mg/dL	557	633
Severity of DKA – no.:		
Severe (%)	51 (54)	34 (59)

* Blood glucose p = 0.058

OUTCOME RESULTS

| OUTCOME	NON-WEIGHT-BASED (N = 95)	WEIGHT-BASED (N = 58)	P - VALUE
Primary outcome:			
Time to resolution – mean hrs.	17.72	17.62	0.971
Secondary outcomes:			
Length of ICU stay – mean hrs.	43.4	32.9	0.353
Length of hospital stay – mean hrs.	65.4	70	0.725
Time to first SQ insulin – mean hrs.	20.9	26.7	
Hypoglycemic events – no.			0.212
0 events (%)	77 (81)	42 (72)	
1 or more events (%)	18 (19)	16 (28)	
Hypokalemic events – no. (%)	54 (56)	31 (53)	0.682
Death – no. (%)	3 (3)	1 (2)	0.638
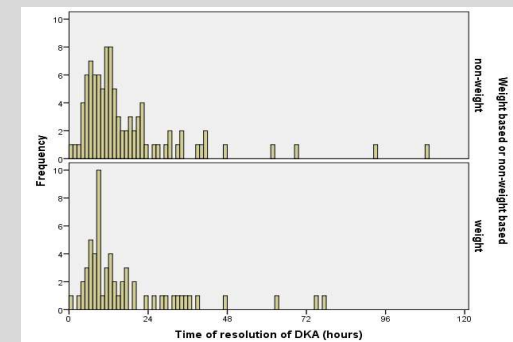
Figure 1: Primary outcome: time to resolution of DKA based on insulin drip rates

DISCUSSION

We saw no statistically significant difference in time to resolution of DKA between groups

- Between groups had similar baseline demographics – all not statistically significant. Of note however, blood glucose on arrival was marginally significant with a P = 0.058 where patients in the weight based group were more likely to have a higher glucose on arrival
- All secondary outcomes were also not statistically significant. Length of ICU stay was numerically shorter in time between groups 43.4 hours vs 32.9 hours favoring weight-based regimen.
- This study was unable to achieve an adequate power as the mean time to resolution between groups was similar, but it is important to appreciate the similarities in the groups including similar percentages of hypoglycemic events and hypokalemic events.