EVMS Emergency Medicine Journal Club
Therapy Worksheet

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Citation: Rappaport S, Endicott J, Gilbert M, Farkas J, Clouser R, McMillian W. **A Retrospective Study of Early vs Delayed Home Dose Basal Insulin in the Acute Management of Diabetic Ketoacidosis**. *J Endocr Soc*. 2019;3(5):1079-1086.

Background: The use of early basal dosing of SQ insulin has been recommended as a consideration in the management of DKA. Proponents and limited research suggest potential benefit such as less rebound hyperglycemia, faster resolution of anion gap, less ICU and hospital days. There is disparity in guideline recommendations with no mention of this practice in the American or Canadian Diabetes Associations, the Joint British Diabetes Societies and the British Society of Pediatric Endocrinology and Diabetes advocate the continuation of home dose subcutaneous basal insulin (HDBI) in patients being treated acutely for DKA.

P: In patients with acute DKA
I: Is the use of early basal dose long-acting SQ insulin
C: Compared to delayed SQ insulin
O: Associated with better outcomes (as noted above)

A. What is being studied? (Answer Below)	**Comments**
1. Study Objective	"The objective of this study was to evaluate outcomes in patients who received early vs delayed HDBI."
2. Study Design	Retrospective, cohort study, single site, 562 bed rural academic hospital in VT Compared outcomes using early vs delayed Home Dose Basal Insulin (HDBI) administration as defined as: • Early HDBI: initiation of basal insulin w/in 24 hrs of IV Insulin AND before resolution of DKA • Delayed HDBI: initiation long/intermediate acting insulin that did not meet early criteria AND w/in 6 hrs before, or any time after d/c of IV insulin.
3. Inclusion Criteria	• >= 16 yo • Dx: DKA • Admitted to ICU
4. Exclusion Criteria	• <16 yo • not admitted to ICU • required surgery w/in 48 hrs of IV insulin discontinuation • pregnant • vasopressor-dependent shock • another indication for IV insulin therapy other than DKA

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	• Patient's that did not meet criteria for early or delayed HDBI • IV Insulin d/c before resolution of DKA*
5. Interventions Compared	Early HDBI: was defined as initiation of basal insulin within 24 hours of the initiation of IV insulin and before resolution of DKA Delayed HDBI: defined as initiation of therapy that did not meet early criteria and within 6 hours before, or any time after, discontinuation of ICII
6. Outcomes Evaluated	Primary: • Incidence of transitional failure between groups o Transitional Failure defined as: ▪ Resumption of IV Insulin or recurrence of DKA b/w 2-12 hours after initial d/c of IV insulin Secondary: • Incidence of rebound hyperglycemia • Incidence of hypoglycemia • # fingerstick glucose measurements in first 24 hours • Time to close AG <= 12 mEq/L • Duration of IV insulin • Maximum rate of IV insulin • MICU length of stay • Hospital length of stay
B. Are the results of the study valid?	
1. Were patients randomized?	No. This was a retrospective analysis of ICU patients who some of whom received non-protocolized basal insulin in the management of DKA.
2. Was randomization concealed (Blinded?)	N/A
3. Were patients analyzed in the groups to which they were randomized?	N/A
4. Were patients in the treatment and control group similar with respect to known prognostic factors?	Probably. (Table 1) Demographic data on the two groups compared were similar. That stated, they did not include any comorbidities that could have had clinical significance such as baseline renal function or precipitating cause other than non-compliance which represented 40% of patients.
C. Did Experimental and Control groups retain similar prognosis after the study started?	
1. Were patients aware of group allocation	N/A
2. Were clinicians aware of group allocation	N/A
3. Were outcome assessors aware of group allocation.	The authors make no mention of blinding outcome assessors (data analysists) which in a retrospective study is the one group that can be
4. Was follow-up complete	Yes. There was no patient loss to follow-up as this was in-patient data on 106 admissions from 57 patients.
D. What were the results?	

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1. How large was the treatment effect? (difference b/w tx and control group?)	Table 2. There was **no statistical significance** in the primary or secondary outcomes between the two groups for the following Odds Ratios: Transitional failure: 0.61 (95% CI 0.06–3.47) Resume ICII 2 (6) 6 (8) 0.72 (95% CI: 0.07–4.3) Hypoglycemia 0.41 (95% CI: 0.16–1.05) Time to anion gap closure, p= 0.73 FSBG in first 24 h p= 0.06 Length of stay: ICU p= 0.83 Hospital p=0.90
2. How precise was the estimated tx effect at a 95% CI?	Statistically significant findings: **Time on ICII, h 13.8 (9.5–16.9) 17.1 (12.4–21.2) 0.04** **Rebound hyperglycemia 0.59 (95% CI 0.16–2.29)** (stat sig)
E. How can I apply the results to patient care?	
1. Were the study patients similar to my patients?	Not really: 97% of their patients were white, all had BMI's <26.0, Compliance rates probably similar. Economic status inner city vs. rural likey different. Not similar: BMI: normal in this population, less so in ours; Race: only 2 non-white patients; Highest BG was 743 and IQR was ~500-550, from those I have admitted to the ICU I would say ours are typically sicker with lower pH and larger AGs
2. Were all clinically important outcomes considered?	No. The authors state that early basal group was more predisposed to hypokalemia but they don't report and actual data. This is an important potential complication. There was a large increase in the use of basal insulin in the second two years of the study and this data was not reported separately.
3. Are the likely treatment benefits worth the potential harms and costs?	Possibly. Retrospective data on a small sample suggests some limited benefit (earlier transition off IV insulin with HDBI) and NO demonstrable harms though the study may have been underpowered to address that question. No assessment of costs, nursing and other resources reported on.

Limitations:
Retrospective data using ICD code makes potential for bias high.
No kappa scores regarding identifying patients or data analysis
"Early" basal SQ was broadly defined and could be up to 24 hours after institution of parenteral insulin Small study with 267 DKA admissions in a 3 year period – only 106 admissions met criteria
ICD-9 codes were used but they didn't say which were used – potential for missed patients
Single center rural setting
Allowed for repeat enrollees. They had 106 admissions b/w 57 patients – issues raised above regarding this no analysis of characteristics of 57 repeat patients.
Treatment protocol: They noted change in practice patterns during the study period

Clinical Bottom Line: Early use of SQ long acting insulin may improve time on IV insulin and frequency of rebound hyperglycemia.