Randomized Controlled Trial of Detemir vs NPH in Gestational and Type 2 Diabetes in Pregnancy: DETERMINE Study

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Background

- Diabetes mellitus (DM) is one of the most common medical complications of pregnancy
- Risks of poorly controlled DM can contribute to maternal and neonatal morbidity
- There are no randomized controlled studies that has compared rates of neonatal hypoglycemia based on insulin choice

Objective

- We sought to re-evaluate the relationship between neonatal hypoglycemia and long-acting insulin choice

Study Design

- <u>Study design:</u> Multi-center prospective, unblinded RCT comparing insulin detemir to NPH.
- Planned recruitment: 336.
- Recruitment stopped early due to discontinuation of insulin detemir, n=73
- <u>Randomization:</u> Central randomization 1:1 for detemir and NPH
- <u>Primary Outcome:</u> Rates of neonatal hypoglycemia and persistent neonatal hypoglycemia
- <u>Secondary Outcomes:</u> Maternal, antenatal, and neonatal complications
- <u>Statistics:</u> Wilcoxon Rank sum, Chi-Square or Fisher's Exact Tests were used along with Uni- and Multivariable logistic regressions were performed

Conclusion

- No difference in neonatal hypoglycemia rates based on basal insulin at this point in the study.
- The study was limited by early cessation of recruitment due to discontinuation of medication.
- Further studies will need to be performed to compare NPH with other long-acting insulins

No difference in neonatal hypoglycemia rates based on basal insulin.

Questions?
Please email Dr. Michael Richley at MRichley@uw.edu

Table 1: Patient characteristics by type of insulin (N=73)

	Total (N=73)	NPH (n=38)	Detemir (n=35)	P-value
Age at Delivery, mean (SD)	35.93 (4.51)	35.39 (4.51)	36.51 (4.51)	0.293[1]
Gravidity, n (%)				0.405[2]
1	17 (23.3%)	10 (26.3%)	7 (20.0%)	
2	21 (28.8%)	13 (34.2%)	8 (22.9%)	
3	16 (21.9%)	8 (21.1%)	8 (22.9%)	
4+	19 (26.0%)	7 (18.4%)	12 (34.3%)	
Parity, n (%)				0.121[2]
0	29 (41.4%)	16 (43.2%)	13 (39.4%)	
1	21 (30.0%)	14 (37.8%)	7 (21.2%)	
2	20 (28.6%)	7 (18.9%)	13 (39.4%)	
Race, n (%)				0.005[3]
American Indian or Alaska Native	1 (1.4%)	0 (0.0%)	1 (2.9%)	
Asian/API	18 (24.7%)	12 (31.6%)	6 (17.1%)	
Black	4 (5.5%)	0 (0.0%)	4 (11.4%)	
White	26 (35.6%)	18 (47.4%)	8 (22.9%)	
Did not identify	24 (32.9%)	8 (21.1%)	16 (45.7%)	
Ethnicity, n (%)				0.906[3]
Hispanic or Latino	32 (43.8%)	16 (42.1%)	16 (45.7%)	
Non-Hispanic or Latino	39 (53.4%)	21 (55.3%)	18 (51.4%)	
Did not identify	2 (2.7%)	1 (2.6%)	1 (2.9%)	
BMI, median (IQR)	31.5 (26.6, 38.0)	31.6 (26.9, 38.6)	31.5 (25.7, 37.0)	0.703[4]
Normal	10 (13.7%)	5 (13.2%)	5 (14.3%)	0.953[2]
Overweight	22 (30.1%)	11 (28.9%)	11 (31.4%)	
Obese	41 (56.2%)	22 (57.9%)	19 (54.3%)	
ART, n (%)				0.916[2]
No	60 (83.3%)	31 (83.8%)	29 (82.9%)	
Yes	12 (16.7%)	6 (16.2%)	6 (17.1%)	
Type of Diabetes, n (%)				0.279[2]
Gestational Diabetes	60 (82.2%)	33 (86.8%)	27 (77.1%)	
Type 2 Diabetes	13 (17.8%)	5 (13.2%)	8 (22.9%)	
Pre-Pregnancy Medications, n (%)[a]	6 (8.2%)	3 (7.9%)	3 (8.6%)	1.000[2]
Hgb A1c Intake, median (IQR)	5.9 (5.5, 7.2)	5.7 (5.5, 6.0)	6.8 (6.0, 8.7)	0.021[4]
Drug Use, n (%)	2 (2.8%)	2 (5.3%)	0 (0.0%)	0.495[3]

[1]Equal variance two sample t-test; [2]Chi-Square; [3]Fisher Exact; [4]Wilcoxon rank sum p-value;
a. Includes Metformin only (n=4), Metformin + Glyburide (n=1), and other (n=1)

Table 3: Primary and secondary FETAL outcomes by type of insulin (N=73)

	Total (N=73)	NPH (n=38)	Detemir (n=35)	P-value
Initial POC glucose, Median (IQR)	56.0 (47.0, 69.0)	57.5 (48.0, 69.5)	52.0 (47.0, 66.0)	0.464[1]
Hyopglycemia in 1st 24 hours, n (%)	28 (40.6%)	16 (44.4%)	12 (36.4%)	0.495[2]
Hypoglycemia in >24 hours, n (%)	4 (5.8%)	2 (5.6%)	2 (6.1%)	1.000[3]
Fetal Anomalies, n (%)	7 (9.7%)	4 (10.5%)	3 (8.8%)	1.000[3]
MVP, Median (IQR)	4.8 (4.0, 6.0)	4.9 (4.0, 6.0)	4.7 (3.8, 6.0)	0.379[1]
Polyhydramnios, n (%)	4 (5.6%)	2 (5.3%)	2 (5.9%)	1.000[3]
GA at Delivery, Median (IQR)	38.3 (37.3, 39.2)	38.9 (37.4, 39.3)	38.1 (37.1, 39.1)	0.345[1]
Birth Weight (g), Median (IQR)	3310 (3018, 3690)	3265 (2930, 3680)	3335 (3033, 3740)	0.433[1]
5 min APGAR, n (%)				0.361[3]
APGAR 8-10	67 (93.1%)	34 (89.5%)	33 (97.1%)	
APGAR 0-7	5 (6.9%)	4 (10.5%)	1 (2.9%)	
Need for Bili Lights, n (%				0.071[2]
No	58 (84.1%)	33 (91.7%)	25 (75.8%)	
Yes	11 (15.9%)	3 (8.3%)	8 (24.2%)	
NICU Admission, n (%)				0.493[2]
No	54 (78.3%)	27 (75.0%)	27 (81.8%)	
Yes	15 (21.7%)	9 (25.0%)	6 (18.2%)	

[1]Wilcoxon rank sum p-value; [2]Chi-Square p-value; [3]Fisher Exact p-value;

Table 2: Maternal outcomes by type of insulin (N=73)

	Total (N=73)	NPH (n=38)	Detemir (n=35)	P-value
Max Insulin 1st Tri, median	52.0 (30.0, 72.0)	26.0 (20.0, 34.0)	72.0 (58.0, 76.0)	0.020[2]
Max Insulin 2nd Tri, median	44.0 (16.0, 68.0)	30.0 (10.0, 48.0)	51.0 (35.0, 90.5)	0.079[2]
Max Insulin 3rd Tri, median	30.0 (16.0, 72.0)	31.0 (14.0, 58.0)	30.0 (16.0, 81.0)	0.631[2]
% Elevated Fasting, n (%)				0.619[1]
0-20	35 (47.9%)	17 (44.7%)	18 (51.4%)	
21-50	10 (13.7%)	7 (18.4%)	3 (8.6%)	
51-75	4 (5.5%)	1 (2.6%)	3 (8.6%)	
76+	8 (11.0%)	4 (10.5%)	4 (11.4%)	
Unknown	16 (21.9%)	9 (23.7%)	7 (20.0%)	
% Elevated Postprandial, n (%)				0.943[1]
0-20	42 (57.5%)	22 (57.9%)	20 (57.1%)	
21-50	6 (8.2%)	4 (10.5%)	2 (5.7%)	
51-75	3 (4.1%)	1 (2.6%)	2 (5.7%)	
76+	4 (5.5%)	2 (5.3%)	2 (5.7%)	
Unknown	18 (24.7%)	9 (23.7%)	9 (25.7%)	
Most Recent A1C, median (IQR)	5.7 (5.4, 6.1)	5.5 (5.3, 5.8)	6.0 (5.5, 6.7)	0.046[2]
Change in A1C, median (IQR)	0.0 (0.0, 1.0)	0.0 (0.0, 0.3)	0.8 (0.0, 2.7)	0.090[2]
Mode of Delivery, n (%)				0.221[3]
Vaginal	39 (54%)	18 (47.4%)	21 (61.8%)	
Cesarean delivery	33 (46%)	20 (52.6%)	13 (38.2%)	
NPO at Time of Delivery, n (%)				0.175[3]
No	30 (41.7%)	13 (34.2%)	17 (50.0%)	
Yes	42 (58.3%)	25 (65.8%)	17 (50.0%)	
Hypertensive Disorders, n (%)				0.547[1]
chronic HTN	3 (4.1%)	2 (5.3%)	1 (2.9%)	
gHTN	5 (6.8%)	2 (5.3%)	3 (8.6%)	
Preeclampsia w/o SF	5 (6.8%)	3 (7.9%)	2 (5.7%)	
Preeclampsia w/ SF	6 (8.2%)	3 (7.9%)	3 (8.6%)	
Superimposed preeclampsia	5 (6.8%)	2 (5.3%)	3 (8.6%)	
None	49 (67.1%)	26 (68.4%)	23 (65.7%)	
Other Medications, n (%)				0.887[3]
No	34 (46.6%)	18 (47.4%)	16 (45.7%)	
Yes	39 (53.4%)	20 (52.6%)	19 (54.3%)	
Insulin Drip, n (%)				0.599[1]
No	69 (95.8%)	37 (97.4%)	32 (94.1%)	
Yes	3 (4.2%)	1 (2.6%)	2 (5.9%)	
PPH, n (%)				0.005[3]
No	55 (76.4%)	24 (63.2%)	31 (91.2%)	
Yes	17 (23.6%)	14 (36.8%)	3 (8.8%)	
Chorioamnionitis, n (%)				0.485[1]
No	63 (87.5%)	32 (84.2%)	31 (91.2%)	
Yes	9 (12.5%)	6 (15.8%)	3 (8.8%)	

[1]Fisher Exact p-value; [2]Wilcoxon rank sum p-value; [3]Chi-Square p-value;