Overnight glucose control with single- and dual-hormone artificial pancreas in type 1 diabetes with hypoglycemia unawareness versus hypoglycemia awareness: randomized controlled trial

Rémi Rabasa-Lhoret[1], Alexander Abitbol[2], Virginie Messier[1], Laurent Legault[1,3], Mohamed Smaoui[4], Martin Ladouceur[5], Ahmad Haidar[3]

[1] Institut de recherches cliniques de Montréal, Montreal, Quebec, Canada; [2] LMC Diabetes & Endocrinology, Oakville, Ontario, Canada; [3] McGill University, Montreal, Quebec, Canada; [4] Université de Montréal, Montreal, Quebec, Canada, [5] Research center of the CHUM, Université de Montréal, Montreal, Quebec, Canada

Introduction

➢ Hypoglycemia unawareness (HU): lack of autonomic symptoms in response to hypoglycemia or failure for them to occur before the development of neuroglycopenia.

➢ 20-40% of patients with type 1 diabetes have HU.

➢ Patients with HU present a 6-fold increased risk of recurrent severe hypoglycemia.

➢ Dual-hormone artificial pancreas (AP) may be more suitable in patients with HU.

This is the first study to compare the efficacy of single-hormone AP and dual-hormone AP at regulating overnight glucose levels in adult patients with and without HU.

Materials and Methods

Study Design

• A 2-week run-in period using an observational continuous glucose monitoring system (iPro Medtronic©) to document NH followed by a randomized, open-label, crossover trial comparing dual-hormone AP and single-hormone AP in 35 patients (18 patients with HU and 17 patients without HU for in-patient overnight glucose control.

• Hypoglycemia unawareness is determined by the Clarke questionnaire[1] assessing patient symptom perception.

• Each 10-hour intervention (single-hormone AP or dual-hormone AP) occurs overnight (21:00-7:00) at the clinical research facility.

Subjects

•Adult patients with T1D on insulin pump therapy for at least 3 months.

Primary Outcome

•Percentage of time with plasma glucose levels below 4.0mmol/L.

Assays

•Plasma glucose was measured every 20 minutes using YSI2300 STAT Plus Analyzer.

Statistical Analysis:

• Outcomes were calculated for the period between 11pm and 7am.

• p-values were calculated using paired t-test.

• Data is presented as median [IQR] or mean ± SD.

[1] Clarke W.L. et al. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemic frequency and associated symptoms. Diabetes Care 1195, 18(4): 517-22.

Results

Table 1. Outcomes for hypoglycemia unaware patients

	Single-hormone AP	P value	Dual-hormone AP
Time spent at glucose levels (%):			
• 4.0-8.0 mmol/L	78 [38-98]	0.46	61 [40-95]
• 4.0-10.0 mmol/L	97 [82-100]	0.20	82 [67-100]
• < 4.0 mmol/L	0 [0-10]	0.28	0 [0-0]
• < 3.5 mmol/L	0 [0-1]	0.25	0 [0-0]
• < 3.3 mmol/L	0 [0-0]	0.24	0 [0-0]
• > 10.0 mmol/L	0 [0-4]	0.06	5 [0-30]
Mean glucose (mmol/L)	6.8 ± 1.4	0.08	7.7 ± 2.1
# of hypoglycemic events	3	-	2

Table 2. Outcomes for hypoglycemia aware patients

	Single-hormone AP	P value	Dual-hormone AP
Time spent at glucose levels (%):			
• 4.0-8.0 mmol/L	59 [40-79]	0.005	84 [73-94]
• 4.0-10.0 mmol/L	77 [66-100]	0.046	100 [86-100]
• < 4.0 mmol/L	0 [0-0]	0.79	0 [0-0]
• < 3.5 mmol/L	0 [0-0]	0.94	0 [0-0]
• < 3.3 mmol/L	0 [0-0]	0.41	0 [0-0]
• > 10.0 mmol/L	18 [0-33]	0.03	0 [0-13]
Mean glucose (mmol/L)	7.9 ± 1.3	0.01	6.8 ± 1.1
# of hypoglycemic events	1	-	0

Results

Figure 1. Glucose profile of hypounaware patients with single-hormone AP

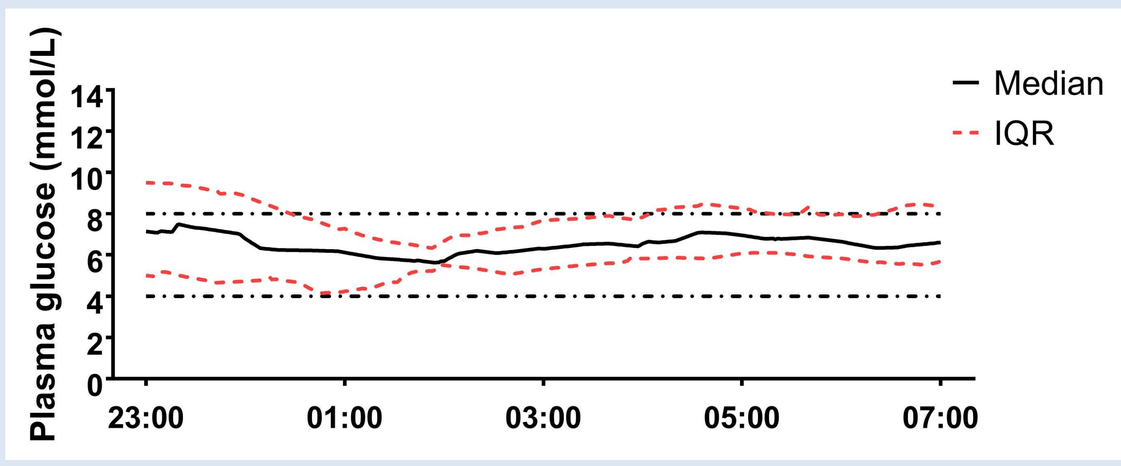


Figure 2. Glucose profile of hypounaware patients with dual-hormone AP

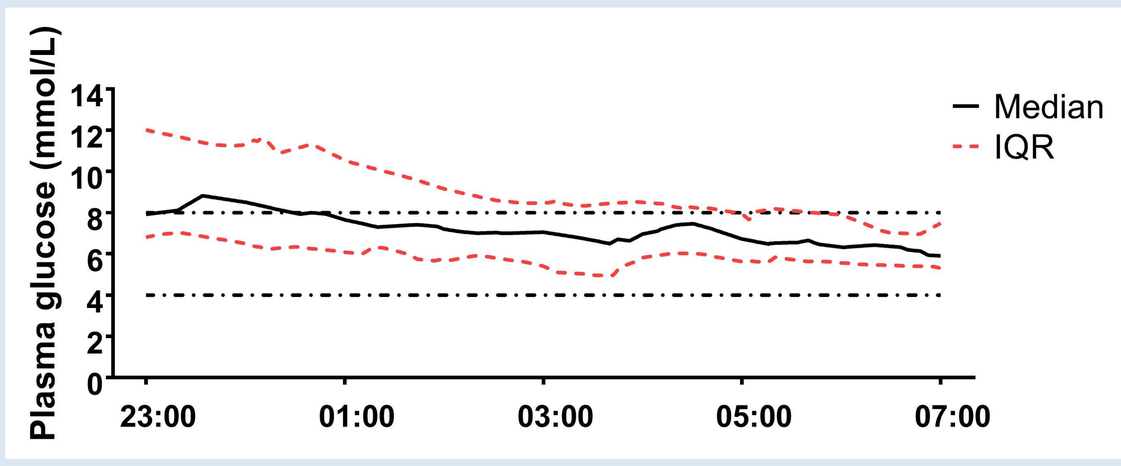


Figure 3. Glucose profile of hypoaware patients with single-hormone AP

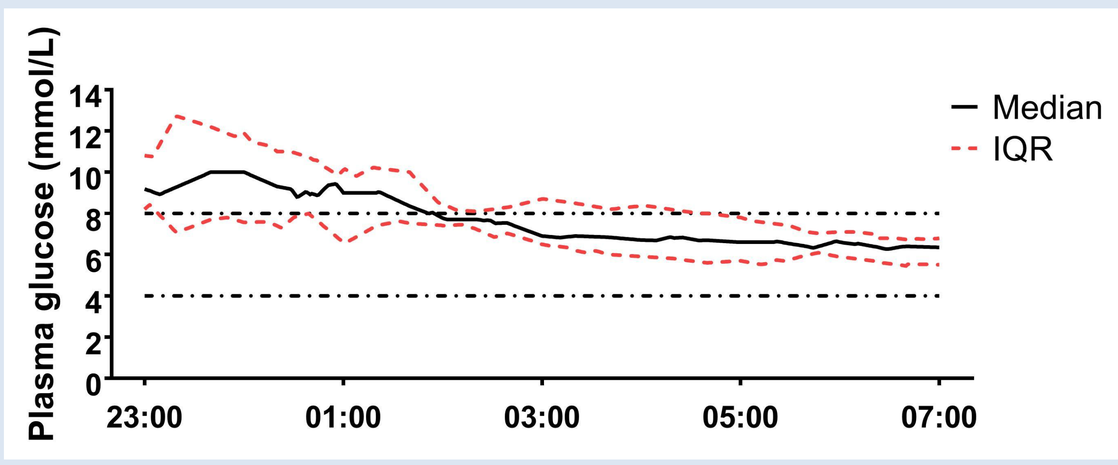
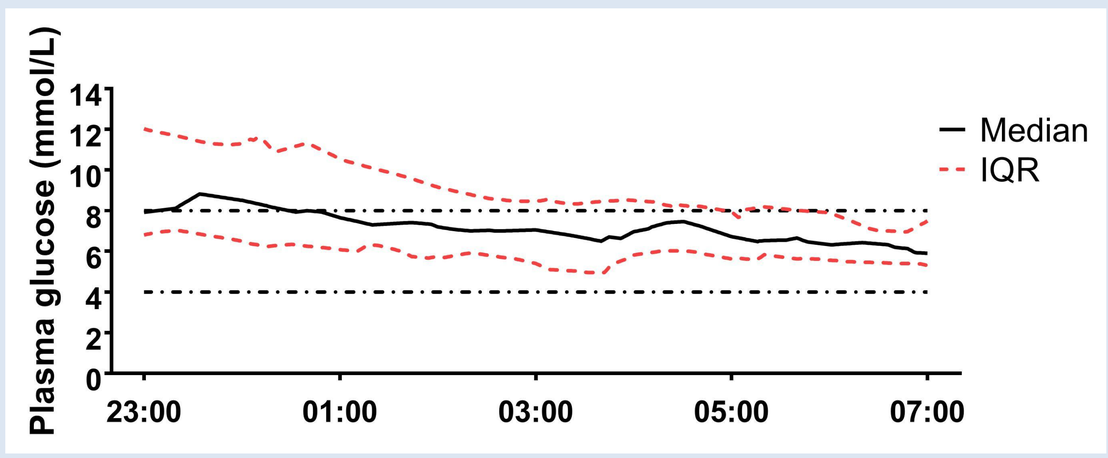


Figure 4. Glucose profile of hypoaware patients with dual-hormone AP



Conclusions

- Both single- and dual-hormone AP were effective at preventing nocturnal hypoglycemia
- Single-hormone AP might be sufficient for hypoglycemia-free overnight control in patients with HU
- Day-and-night studies are needed to evaluate the potential benefits of adding glucagon to the AP for patients with HU

Acknowledgements

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