P-0379

Artificial Pancreas: First Clinical Trial in Argentina is safe and feasible

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Background: The Artificial Pancreas (AP) project has a longstanding evolution worldwide, but until this moment was never tried in Latin America where the diet and lifestyle is somehow different. Patients with type 1 diabetes mellitus (T1DM) treated with Continuous Subcutaneous Insulin Infusion (CSII) and Continuous Glucose Monitoring (CGM) still need much training and medical assistance to achieve a safe glucose profile. An AP consists of a CSII and a CGM connected by a control algorithm that aims to regulate the insulin infusion rate to maintain glycemic values in range (70-180 mg/dl) by creating a closed loop (CL) system. The main purpose of the AP system is to maintain acceptable mean glycemic ranges without increasing the number of hypoglycemic episodes, even during challenging periods of the day such as meals, exercise and overnight.

Aims: To perform the first ever AP pilot study in Latin America in which the primary outcome measure is to check adequate operation of the system and to train a team of professionals in Argentina on the use of DiAs (UVA Diabetes Assistance) containing the USS algorithm. The system is considered verified by proper operation for more than 80% of the total time and maintenance of the glycemic profile within desirable glucose range (70-180 mg/dl) or acceptable glucose range (181-250 mg/dl). Reduction of hypoglycemic events is evaluated as a secondary outcome. Furthermore, an additional aim of this study is to prepare the team for future clinical trials using a new algorithm (ARG: Automatic Regulation of Glucose) developed in Argentina by ITBA, UNQ and UNLP and adapted to be used in DiAs.

References: Maahs D, et. al. Diabetes Care. 2016 Jul;39(7):1175-9. PMID: 27330126; Kovatchev B, et. al. Diabetes Care. 2014 Jul;37(7):1789-96. 2014 Jun 14. PMID: 24929429; Ly TT, et. al. Diabetes Care. 2016 Jun 6. PMID: 27271182

Methods and Study Design: Non-randomized pilot study of five patients mean age 43±7 years old with T1DM mean 17±4 years of diagnosis and mean HbA1c 7.8±0.4%. Comparing 36 h run-in period of sensor-augmented pump (SAP) at home vs. 36 h at the hospital using AP with UVA algorithm (USS: unified safety system) programmed in the DiAs platform. Regulatory approval has been obtained as required by local laws. No AE or SAE occurred.

The Artificial Pancreas & Remote Monitoring System

System Configuration in CLC

DiAs: smartphone with GUI designed for subject use.

Subject wore Insulin Pump (Roche combo) and CGM (DexCom G4 Platinum).

Staff had access to the remote monitoring server with alerts, during the entire trial.

Study Design

Clinical trials conducted in 2 phases: (i) 36 h in home SAP use followed by (ii) 36 h in Hospital admission using AP.

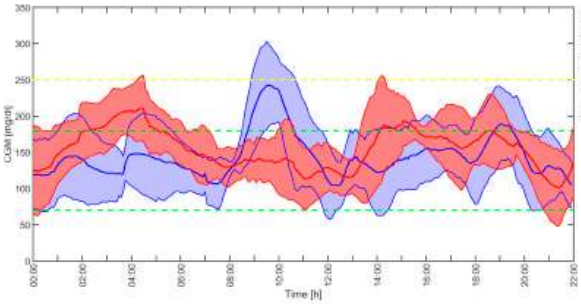
Admission 1: Sensor-augmented pump.

Provide CGM + insulin pump to participants; instruct how to use.

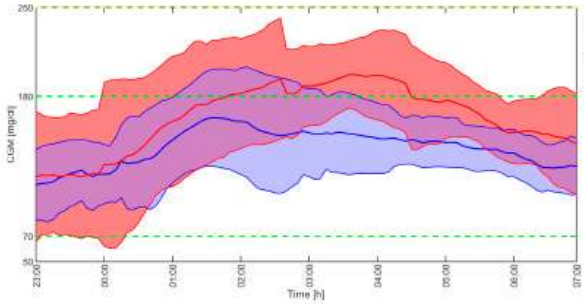
Admission 2: In hospital use of AP.

Provide AP to participants

Results



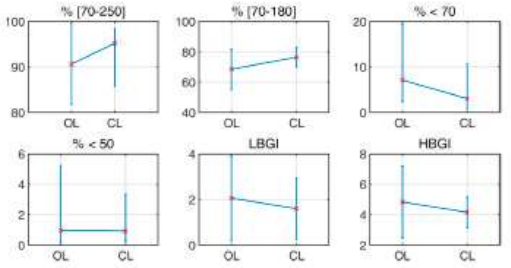
Day: Average CGM values (Dexcom G4) in OL (red) and CL (blue) during one day.



Night: Average CGM values (Dexcom G4) in OL (red) and CL (blue) during one night.

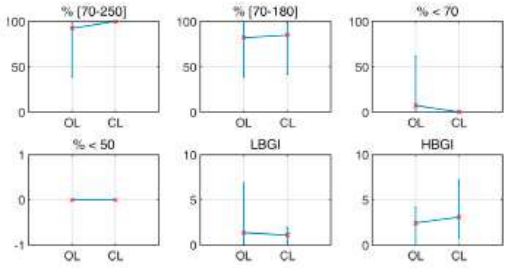
The filled areas represent ±1 STD. Dashed lines (green and orange) indicate glucose concentration limits (70-180 and 70-250 mg/dl).

Average clinical results in OL and in CL, considering a 95% CI



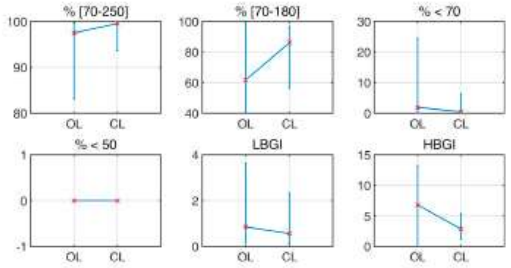
OL: From midnight of day 1 to 07:00 AM of day 2
CL: From midnight of day 1 to 07:00 AM of day 2

Average clinical results in OL and in CL, considering a 95% CI: N_1



OL: From midnight to 07:00 of day 1
CL: From midnight to 07:00 of day 1

Average clinical results in OL and in CL, considering a 95% CI: N_2



OL: From 23:00 of day 1 to 07:00 of day 2
CL: From 23:00 of day1 to 07:00 of day 2

	O				N_1				N_2			
	OL		CL		OL		CL		OL		CL	
	Mean	CI 95 %	Mean	CI 95%	Mean	CI 95 %	Mean	CI 95%	Mean	CI 95 %	Mean	CI 95%
Glucose [mg/dl]	146	[123, 169]	142	[135, 149]	131	[95, 168]	132	[104, 161]	164	[123, 204]	140	[119, 161]
% time in [70, 250] mg/dl	90.6	[81.8, 99.5]	95.2	[85.8, 98.5]	92.6	[38.5, 99.6]	100	[100, 100]	97.5	[83.0, 99.7]	99.6	[93.6, 100]
% time in [70, 180] mg/dl	68.5	[55.1, 81.9]	76.4	[70.0, 82.9]	82.1	[38.7, 97.1]	85.0	[41.7, 97.8]	61.7	[31.6, 84.9]	86.0	[56.3, 96.7]
% time < 70 mg/dl	7.1	[2.4, 19.3]	3.1	[0.8, 10.6]	7.4	[0.4, 61.5]	0.0	[0.0, 0.0]	1.9	[0.1, 24.5]	0.4	[0.0, 6.4]
% time < 50 mg/dl	1.0	[0.2, 5.2]	0.9	[0.2, 3.3]	0.0	[0.0, 0.0]	0.0	[0.0, 0.0]	0.0	[0.0, 0.0]	0.0	[0.0, 0.0]
LBGI[a]	2.1	[0.2, 3.9]	1.6	[0.3, 2.9]	1.4	[0.1, 6.9]	1.1	[0.3, 1.9]	0.9	[0.2, 3.6]	0.6	[0.1, 2.3]
HBGI	4.8	[2.5, 7.2]	4.2	[3.2, 5.2]	2.4	[0.5, 6.7]	3.1	[0.7, 7.2]	6.8	[1.7, 9.6]	2.8	[1.2, 5.3]

Average clinical results in OL and in CL.

The overall (O), and the N1 and N2 time intervals are analyzed separately.

[a] Fabris, C., Patek, S. D., & Breton, M. D. (2016). Are risk indices derived from CGM interchangeable with SMBG-based indices? J Diabetes Sci Technol,10, 50-59.

Conclusion

This is the first study done in Latin America using AP. The technology was well accepted among the participants. The period in AP reduced glucose variability and improve overall time in glycemic range more prominent at night time. The results showed that the first trial conducted with an AP in Argentina was safe and feasible. The AP system worked adequately >94% of total time and the glucose management using the USS algorithm control was in accordance with previous results performed with the same algorithm in the USA, EU and Israel using the DiAs software. It is **noteworthy the nearly absence of nocturnal hypoglycaemia**. We observed a tendency of the AP towards better glucose management compared to SAP in addition to the benefits implied in the use of an automated system. Empowering patients with chronic diseases is an imperative aim in order to deal with everyday aspects of medical care as well as to promote better quality of life. The study successfully tested the USS algorithm in our setting. This trial was followed by another one with similar design testing the ARG algorithm the results were presented at IFAC 2017 and pending publication. Larger and longer trials should be performed for efficacy.

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Acknowledgements: This research was supported by Fundación Nuria/Cellex. We thank Roche for donating the pumps used in the study.