The Efficacy and Safety of Predictive Low Glucose Suspend Feature in Decreasing Hypoglycemia in Children with Type 1 Diabetes Mellitus: a systematic review and meta analysis

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Introduction

- Hypoglycemia is a common adverse consequence of insulin replacement therapy and it is a major barrier towards optimal T1DM management in term of worry and fear of that can affect the quality of life of both children with T1DM and their caregivers and in term of accepting higher blood glucose levels in order to avoid hypoglycemia (1,2).
- That creates the need for major advancements in insulin pump technology that improves the glycemic control while it reduces the risk of hypoglycemia.
- PLGS system works through a predictive algorithm that utilizes the glucose value obtained through a subcutaneously inserted glucose sensor to suspended insulin delivery from the insulin pump if the predicted glucose is expected to reach hypoglycemia range in the next 30 minutes (3).

Therefore, the aim of this study is systematically synthesize the evidence on the efficacy and safety of utilizing PLGS system for children and adolescents with T1DM.

Methods

- The protocol was registered in PROSPERO, registration No. CRD42018115829

Eligibility Criteria:

Type of studies: Randomized and quasi randomized controlled trials.

Type of Participants: Children and adolescents age 2-18 years known to have T1DM diagnosed more than 6 months.

Type of intervention:

SAP+PLGS

Type of control:

Insulin pump with no continuous glucose sensor or with subcutaneous sensor with PLGS feature turned off.

Outcomes:

Primary outcomes:

- Percentage of time with hypoglycemia defined as sensor glucose (SG) <3.9 mmol/l (<70mg/dl).
- Percentage of time with nocturnal hypoglycemia defined as hypoglycemia SG <3.9 mmol/l (< 70 mg/dl).

Secondary outcomes:

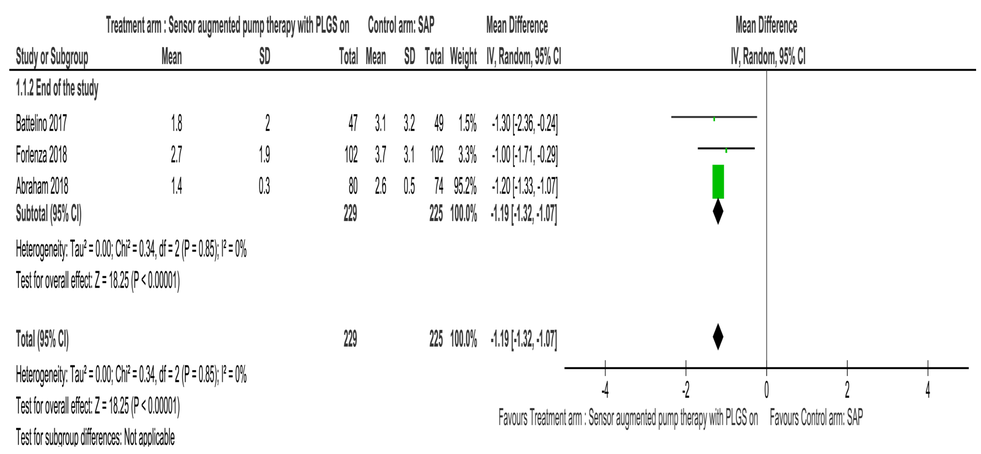
- Percentage of time spent with severe hypoglycemia defined as SG <2.8 mmol/l (<50 mg/dl), or altered level of consciousness or seizure.
- Percentage of time spent with hyperglycemia based on SG > 10 mmol/l (>180 mg/dl) and >13.8 mmol/l (250 mg/dl).

- Two review authors independently selected trials for inclusion, assessed trial quality, and extracted the data.
- We examined heterogeneity amongst studies with the Chi2 and I2 statistics and used GRADE methodology to assess the quality of evidence
- Data analysis were done through Review Manager software (RevMan version 5.3).

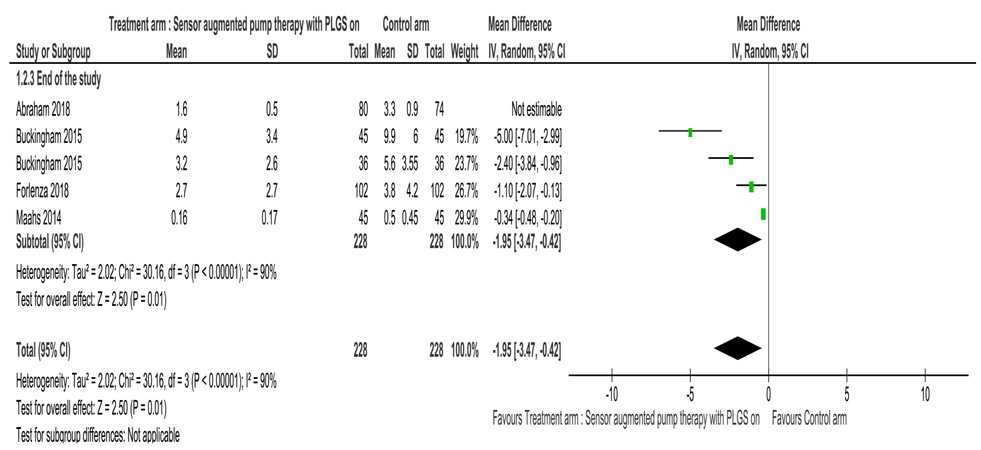
Results

- We included five randomized controlled trials with total sample size of 493 participants and study duration ranging between 2 weeks to 6 months.
- All the included studies have at least one domain with high risk of bias except one study with low risk of bias.
- We planned to conduct a subgroup and sensitivity analysis based on pre-specified sources of expected heterogeneity. However, there were not enough studies to conduct this analysis.

Percentage of time with hypoglycemia defined as sensor glucose (SG) < mmol/l (< mg/dl)



Percentage of time with nocturnal hypoglycemia defined as sensor glucose (SG) < 3.9 mmol/l (<70mg/dl)



Summary of findings for the main comparison

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	PLGS	SAP	Relative (95% CI)	Absolute (95% CI)		
% of time with hypoglycemia sensor glucose <3.9 mmol/l (<70 mg/dl) (follow up: range 2 weeks to 24 weeks)												
3	Randomised trials	serious	not serious	not serious	not serious	publication bias strongly suspected strong association	229	225	-	MD **17.1 minutes lower** (15.4 lower to 19 lower)	⊕⊕⊕◯ MODERATE	CRITICAL
% of time with nocturnal hypoglycemia sensor glucose <3.9 mmol/l (<70 mg/dl) (follow up: range 2 weeks to 24 weeks)												
5	Randomised trials	serious	not serious	not serious	not serious	publication bias strongly suspected very strong association dose response gradient	308	302	-	MD **28 Min lower** (6 lower to 50 lower)	⊕⊕⊕◯ High	CRITICAL
% of time with sever hypoglycemia sensor glucose <2.8 mmol/l (<50 mg/dl) (follow up: range 2 weeks to 24 weeks)												
3	Randomised trials	serious	not serious	not serious	not serious	publication bias strongly suspected	229	225	-	MD **1.6 minutes lower** (0.3 lower to 2.88 lower)	⊕⊕◯◯ LOW	CRITICAL
% of time with hyperglycemia sensor glucose >10 mmol/l (>180 mg/dl) (follow up: range 2 weeks to 24 weeks)												
3	Randomised trials	serious	serious [a]	not serious	serious [b]	publication bias strongly suspected	229	225	-	MD **11.6 min higher** (25 lower to 49 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
% of time with hyperglycemia sensor glucose >13.8 mmol/l (>250mg/dl) (follow up: range 2 weeks to 24 weeks)												
3	Randomised trials	serious	serious	not serious [c]	not serious	publication bias strongly suspected	229	225	-	MD **1.6 min higher** (5 higher to 8.2 lower)	⊕◯◯◯ VERY LOW	IMPORTANT

Conclusion

- Hypoglycemia is an important patient outcome that can affect quality of life of both patients and their caregivers and can affect indirectly HbA1c as well.
- There is moderate quality evidence that PLGS is superior to SAP in decreasing hypoglycemia<3.9 mmol/l.
- There is high quality evidence that PLGS is superior to SAP in decreasing nocturnal hypoglycemia <3.9 mmol/l.
- There is low quality of evidence that PLGS is superior to SAP in decreasing hypoglycemia<2.8 mmol/l.
- There is no increase in the % of hyperglycemia with PLGS use.

Reference

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