
بسم الله الرحمن الرحيم

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Can Empagliflozin be used in patients with type 1 diabetes: Results of a 12-weeks, double-blind, randomized, placebo-controlled clinical trial

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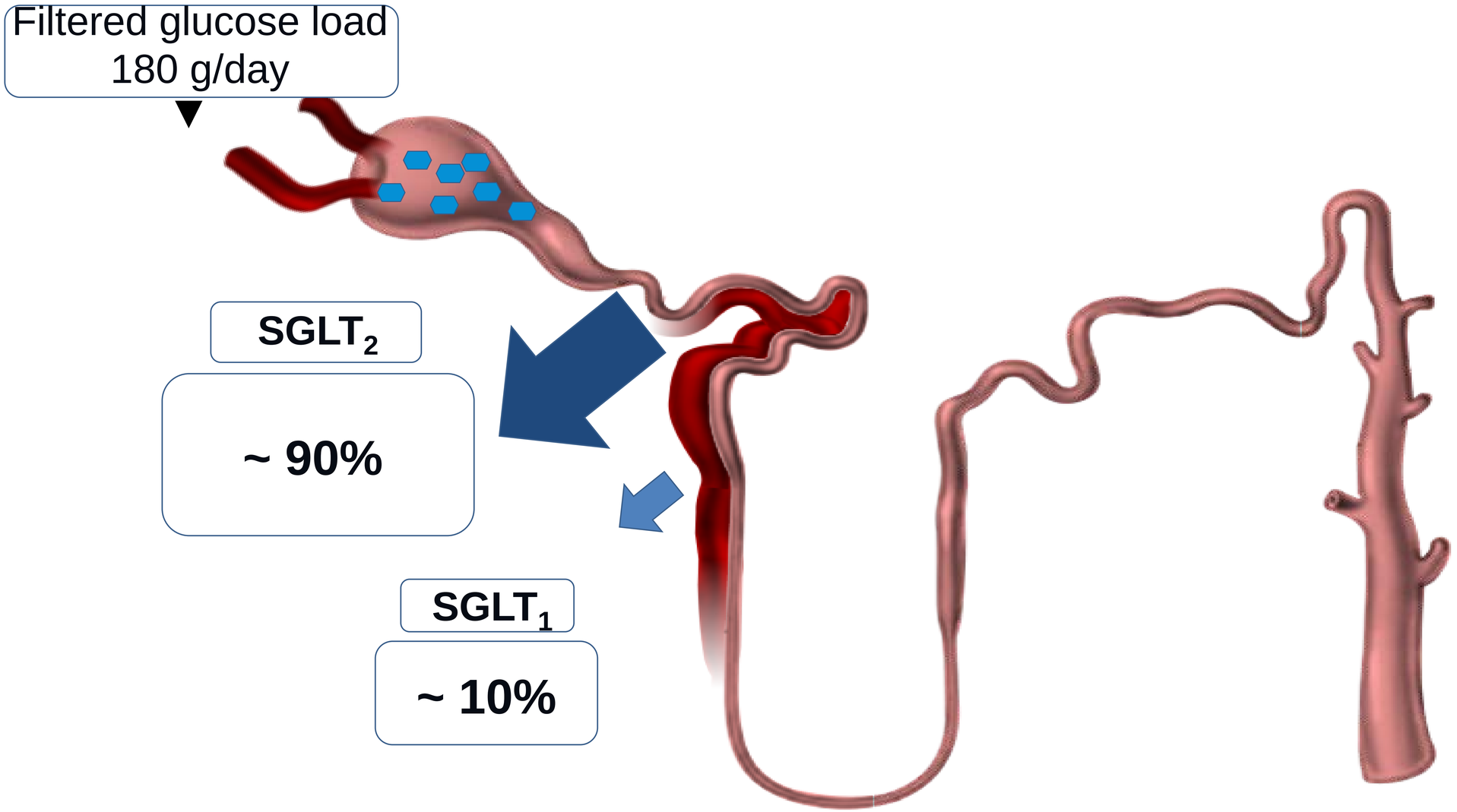
Introduction

Multiple daily injections regimen of insulin and frequent monitoring of glucose levels is an important components of type 1 diabetes management. Many patients with type 1 diabetes **do not reach treatment goals**, which is a challenge in current treatment methods of type 1 diabetes. So, improvement in patient care is needed. One new procedure is **adjunctive therapies to insulin treatment**. One of adjunctive therapy is SGLT inhibitor 2 that regulate the renal glucose reabsorption by decreasing the glucose reabsorption and increasing urinary glucose exertion which results in low plasma glucose levels in patients with diabetes.

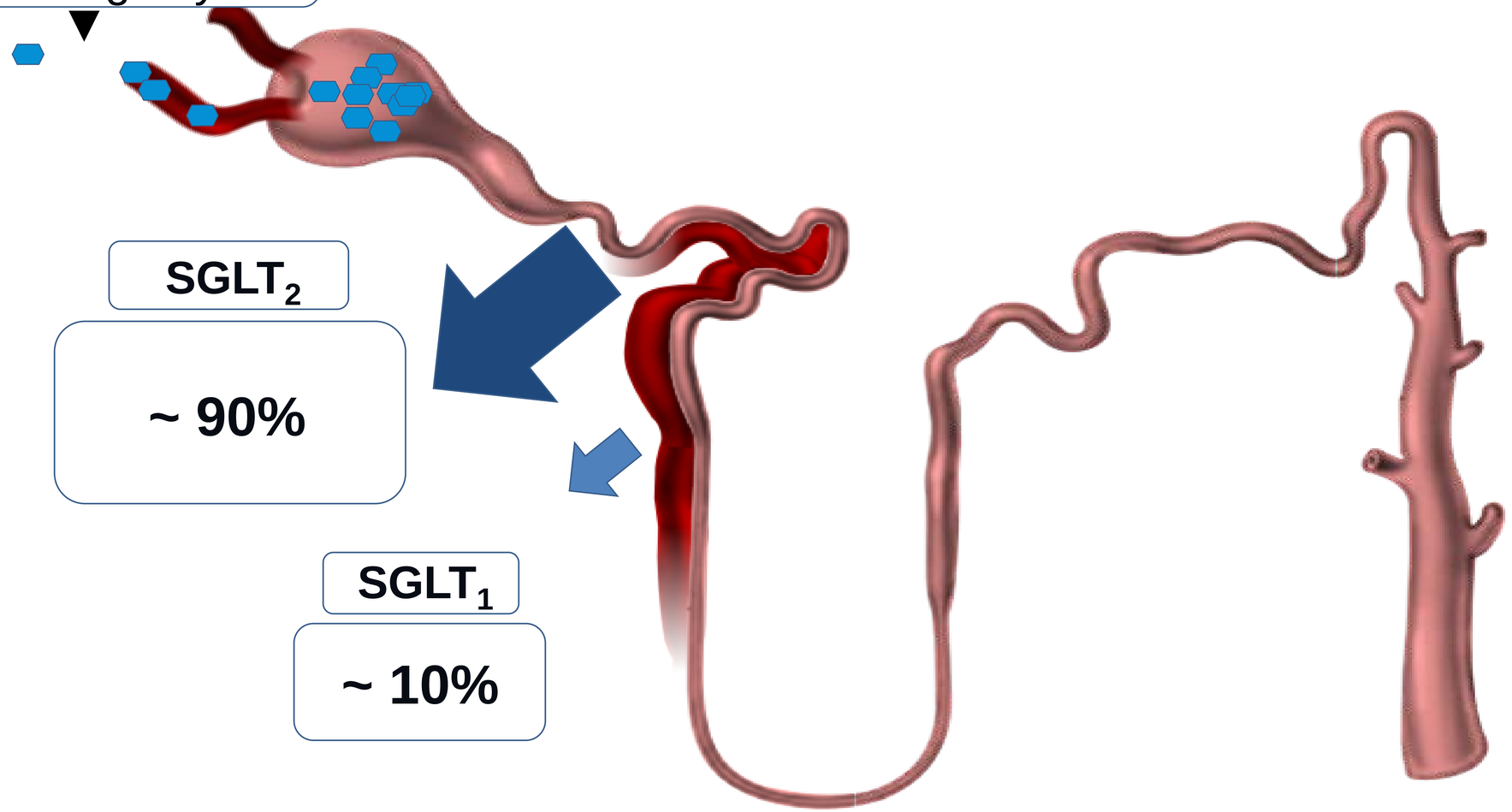
Renal glucose re-absorption in **healthy individuals**



Gerich JE. *Diabet Med*. 2010;27:136–142.

Renal glucose re-absorption in patients with **Diabetes**

Filtered glucose load
> 180 g/day



$SGLT_2$

~ 90%

$SGLT_1$

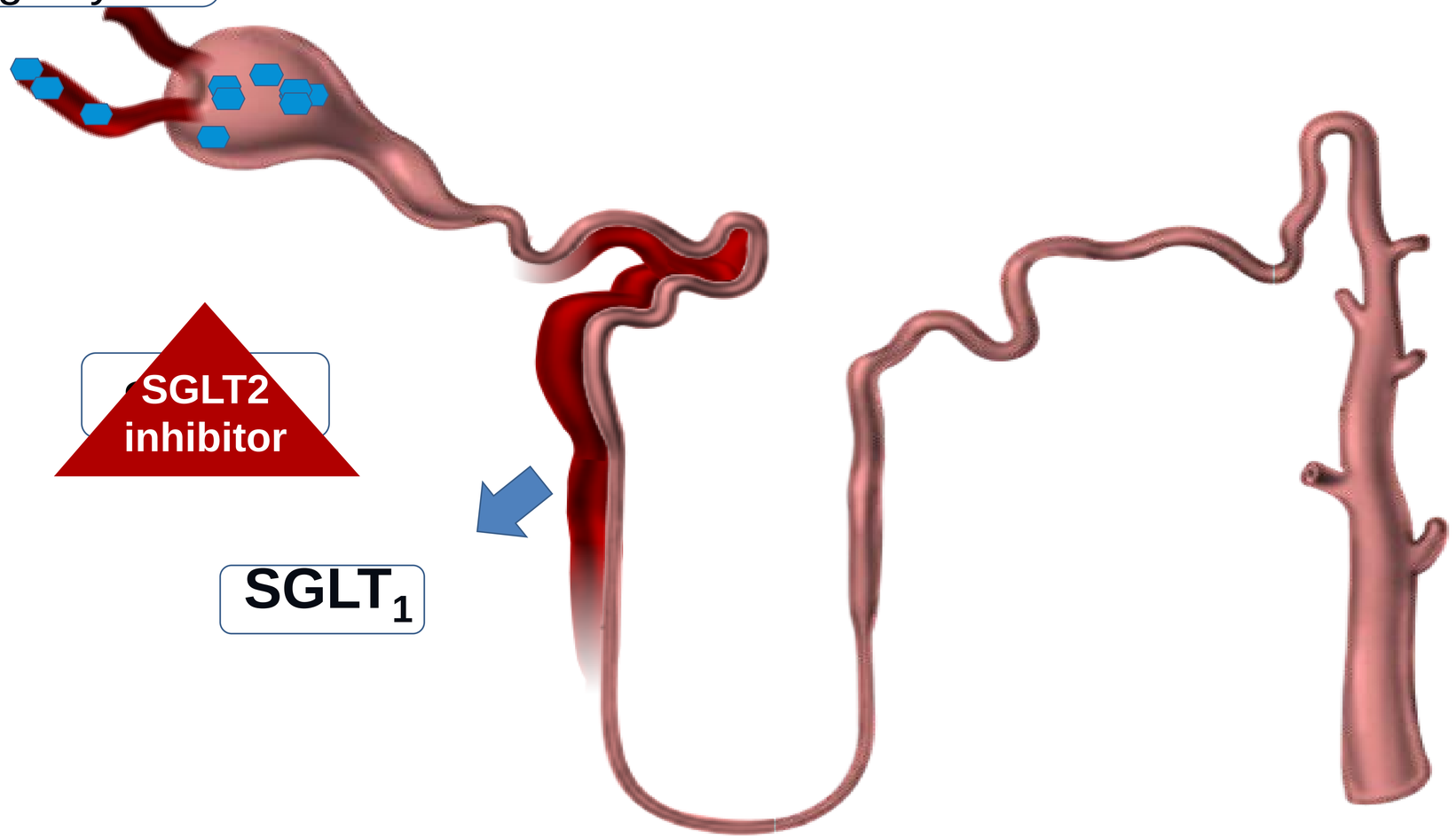
~ 10%

When blood glucose increases above the renal threshold *(~ 180 mg/dL),* the capacity of the transporters is exceeded, resulting in urinary glucose excretion

Gerich JE. *Diabet Med*. 2010;27:136–142.

Urinary glucose excretion via $SGLT_2$ inhibition

Filtered glucose load
> 180 g/day



$SGLT_2$ inhibitors reduce glucose re-absorption in the proximal tubule, leading to urinary glucose excretion* and osmotic diuresis

***Loss of ~ 80 g of glucose/day**

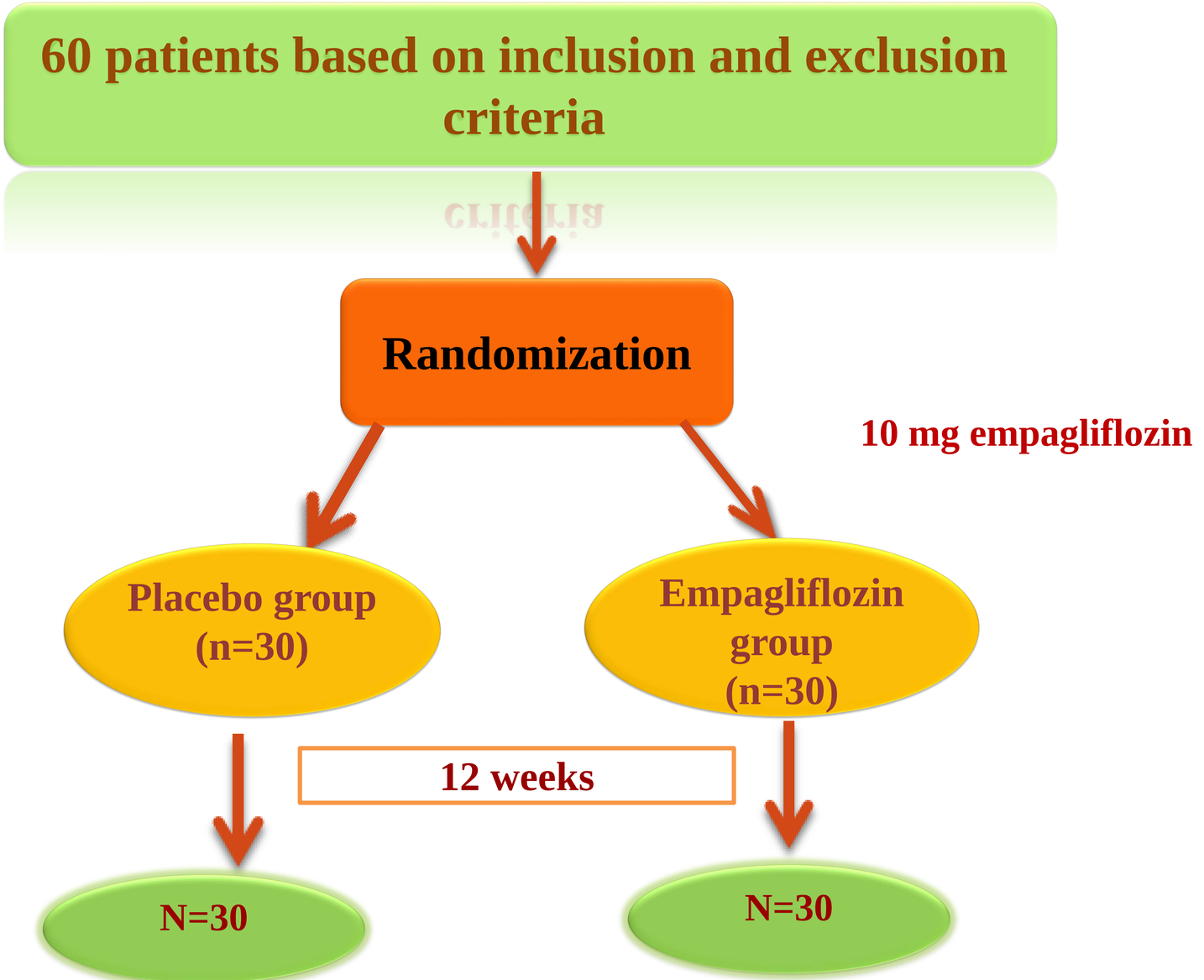
Gerich JE. *Diabet Med*. 2010;27:136–142.

Main objective

- FDA has approved drugs of SGLT2 inhibitors class for patients with type 2 diabetes. However, there is insufficient clinical evidence to recommend them for type 1 diabetes.

the effect of empagliflozin was not investigated in Iranian participants whose BMI, body composition and diet are different from other populations, the present clinical trial conducted to evaluate the potential therapeutic benefits of empagliflozin in patients with type 1 diabetes.

A randomized, double-blind, placebo-controlled clinical trial study



Results

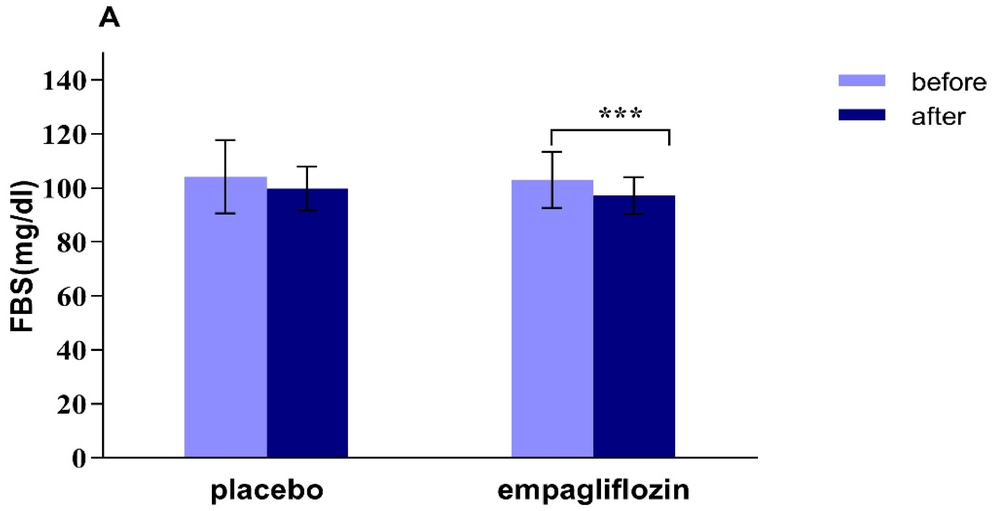
Table 1: Baseline characteristic of the study participants.

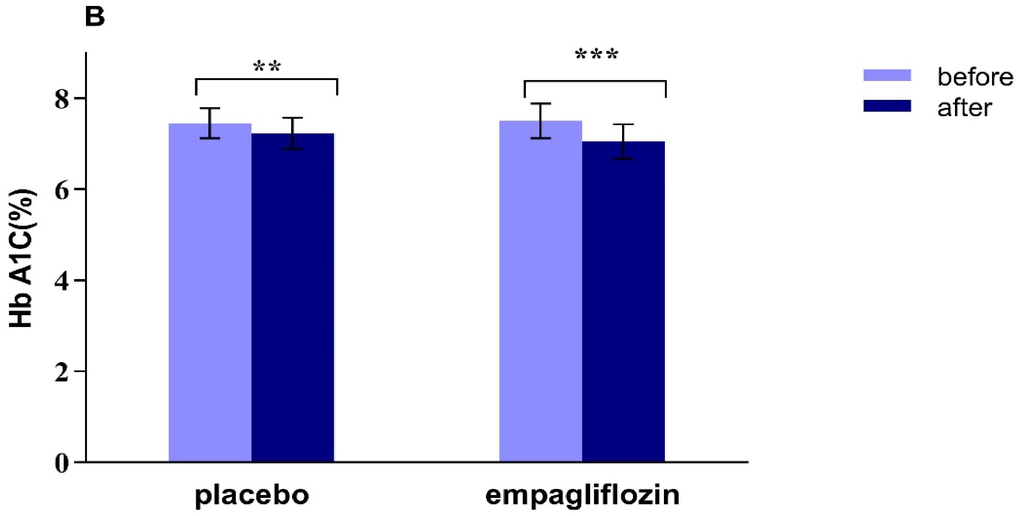
Variable	Placebo (n=30) Mean ± SD	Empagliflozin (n=30) Mean ± SD	p-value
Age (yr.)	23.13 ± 4.50	25.40 ± 9.94	0.26[a]
Weight (Kg)	63.20 ± 7.97	69.13 ± 6.31	0.002[a]
Height (cm)	164.10 ± 7.06	160.55 ± 5.51	0.137[a]
BMI (Kg/m^2)	23.43 ± 2.25	24.85 ± 1.31	0.004[a]
WC (cm)	75.20 ± 5.03	76.97 ± 6.27	0.234[b]
HC(cm)	82.10 ± 7.94	84.07 ± 6.73	0.051[a]
HbA1C(%)	7.45 ± 0.33	7.5 ± 0.38	0.610[a]
FBS(mg/dl)	104.24 ± 13.558	103.03 ± 10.367	0.24[a]
Duration(yr.)	4.37 ± 1.92	5.67 ± 3.15	0.061[a]
Sex	N(%)	N(%)	
Female Male	22(66.7) 8(33.3)	18(60) 12(40)	0.592[C]

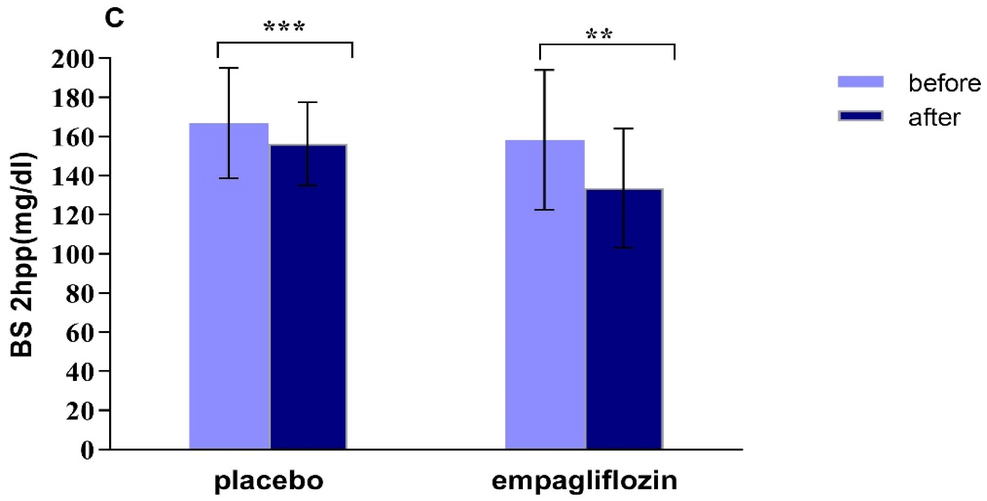
Table2: Anthropometric indices of the study participants throughout the study.

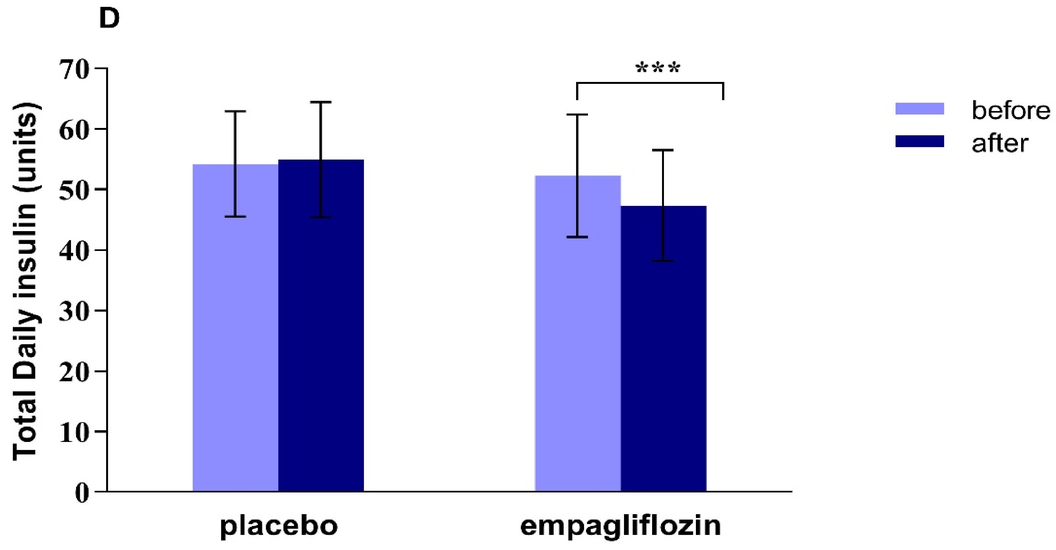
	Placebo (n= 30) Mean ± SD	Empagliflozin (n= 30) Mean ± SD	MD (95 % CI), P-value	Pvalue[C]
BMI				
Baseline	23.43± 2.25	24.85 ± 1.31	1.42(0.46,2.37),0.004[b]	
Post-treatment	23.33 ± 2.16	23.79± 1.22	-0.560(-0.649,1.46), 0.002[b]	<0.001[c]
MD (95 % CI)	0.36 (0.415, -0.078)	-1. 62(-1.974, -0.808)		
P	0.058[a]	<0.001[a]		
WHR				
Baseline	0.92 ± 0.09	0.89 ± 0.07	-0.025(-0.068,0.017),0.23[g]	
Post-treatment	0.92 ± 0.09	0.88 ± 0.06	-0.039(-0.081,0.003),0.069[g]	0.070[c]
MD (95 % CI)	0.0001 (-0.004 , 0.005)	-0.013 (-0.020, -0.007)		
P	0.938[f]	0.06[a]		
WHtR				
Baseline	0.45 ± 0.033	0.46± 0.031	0.002(-0.013,0.198), 0.724[b]	
Post-treatment	0.45 ± 0.034	0.45 ± 0.030	-0.010(-0.022,0.0108),0.4[b]	0.505[c]
MD (95 % CI)	0.010(0.002, 0.038)	0.01 (0.008, 0.013)		
P	0.055[a]	0.058[a]		

Results(cont.)

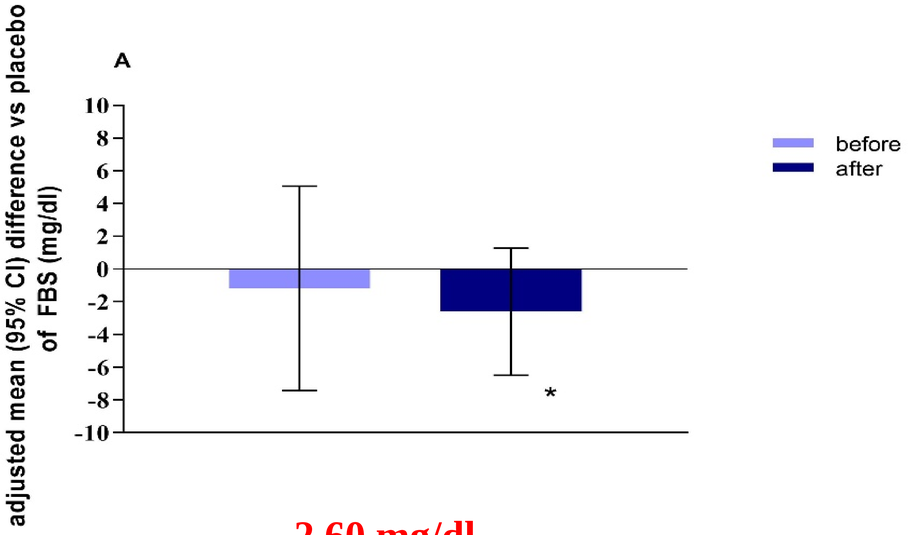




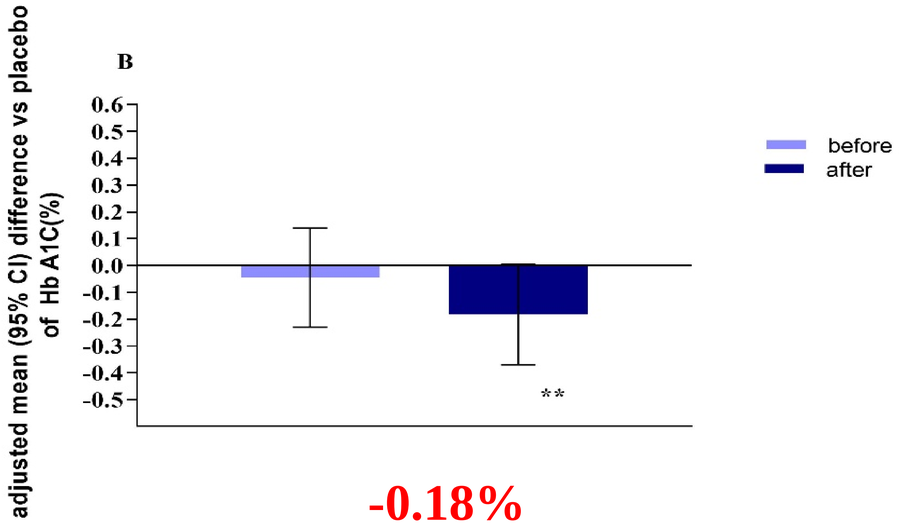




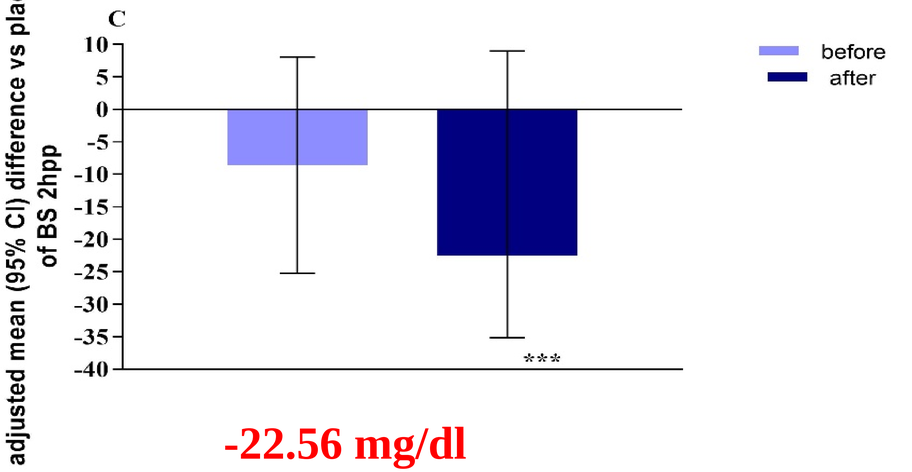
Results(cont.)



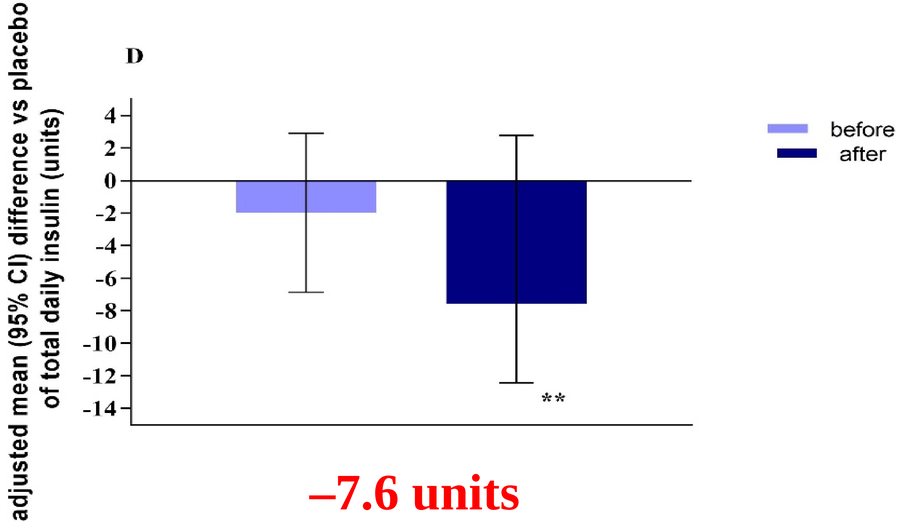
–2.60 mg/dl



-0.18%



-22.56 mg/dl



–7.6 units

Conclusion

- In this trial, Empagliflozin 10 mg/d for 12 weeks improved glycemic control and reduced total daily insulin doses and BMI in patients with type 1 diabetes.
- In this study, a 0.5% reduction in A1C was observed with Empagliflozin 10 mg, which is a clinically significant finding.
- In the current study, no cases of diabetic ketoacidosis were reported which is considered an important finding,
- The possible reason for no DKA events in the present study is daily ketone monitoring and instructions implemented about insulin dose during the study.

Conclusion (cont.)

- According to the empagliflozin's insulin-independent mechanism of action, hypoglycemia events were not observed in the present study .

- Empagliflozin was well tolerated in patients with type 1 diabetes. No events consistent with genital infection were reported.

SGLT2 inhibitors are approved for type 1 diabetes in Europe and Japan, with **off label** use in type 1 in the US.

Diabetes Spectr. 2021, 34, 42–51.


Thank you!