



4.6 Effects of Combined Therapy of Empagliflozin and Linagliptin Versus Metformin and Insulin Glargine on Blood Pressure and Vascular Function in Patients with Type 2 Diabetes

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ABSTRACT

Background: Combination of insulin with oral antidiabetic drugs is a valid option, but oral combination therapy emerged as an alternative treatment in type 2 diabetes (T2DM). However, the effects on blood pressure (BP) and vascular function of such combination therapies is less clear.

Methods: In this study 101 patients with T2DM were randomized to receive either empagliflozin 10 mg and linagliptin 5 mg (E+L group) orally or metformin and insulin glargine (M+I group, with dose adjustments according to glucose levels), for 3 months. Patients underwent BP and vascular examination at baseline and after 12 weeks of treatment, including measurement of office and ambulatory BP and vascular function under clinical and ambulatory conditions by validated systems.

Results: In comparison to baseline, office, 24-hour ambulatory BP and central blood and pulse pressure (PP) values decreased significantly after 12 weeks of treatment with E+L, whereas there was no significant change in vascular parameters in the M+I group (Table 1). Comparing the 2 groups, there were significant decreases in 24-h ambulatory peripheral systolic (mean difference between the 2 groups: -5.2 ± 1.5 mmHg, $p = 0.004$), diastolic BP (-1.9 ± 1.0 mmHg, $p = 0.036$) and PP (-3.3 ± 1.0 mmHg, $p = 0.007$) in favour of E+L. Central systolic BP (-5.56 ± 1.9 mmHg, $p = 0.009$), forward pressure pulse height (-2.0 ± 0.9 mmHg, $p = 0.028$) and 24-h ambulatory central systolic (-3.6 ± 1.4 mmHg, $p = 0.045$), diastolic BP (-1.95 ± 1.1 mmHg, $p = 0.041$) and 24-h pulse wave velocity (-0.14 ± 0.05 m/s, $p = 0.043$) were reduced to a greater extent in the E+L group than in the M+I group.

Conclusion: The combination of E+L significantly improves BP and vascular function in contrast to the combination of M+I.

Table 1

	E+L			M+I		
	Baseline	12 weeks	p-value	Baseline	12 weeks	p-value
Peripheral (brachial) BP values						
24-h ambulatory SBP [mmHg]	131 ± 10.9	127 ± 8.8	<0.001	131 ± 9.7	131 ± 8.6	0.438
24-h ambulatory DBP [mmHg]	81.5 ± 7.1	79.7 ± 7.0	0.013	81 ± 7.1	81 ± 7.5	0.976
Clinical (laboratory) central vascular parameters						
Central SBP [mmHg]	123 ± 9.6	117 ± 10.4	<0.001	121 ± 9.9	121 ± 8.3	0.944
Central PP [mmHg]	44.4 ± 8.0	41.4 ± 6.6	0.004	43.5 ± 8.6	42.8 ± 7.5	0.471
Forward pressure pulse height [mmHg]	33 ± 5.7	30.2 ± 4.6	<0.001	32.5 ± 5.6	31.8 ± 4.5	0.216
Central office PWV [ms]	82 ± 1.6	8.0 ± 1.5	0.039	8.4 ± 1.3	8.3 ± 1.2	0.400
24-h ambulatory central vascular parameters						
Central 24-h SBP [mmHg]	120.5 ± 9.3	117.3 ± 7.9	0.007	121 ± 9.1	121 ± 8.0	0.608
Central 24-h DBP [mmHg]	83.2 ± 7.3	81.1 ± 6.9	0.016	82.4 ± 7.1	82.4 ± 7.7	0.928
Central 24-h PWV [ms]	8.9 ± 1.3	8.8 ± 1.3	0.010	9.0 ± 1.4	9.0 ± 1.3	0.349

Changes in BP and vascular function after 12 weeks of treatment with E-L and M-I in comparison to baseline. Data are given as mean ± standard deviation. E, empagliflozin; L, linagliptin; M, metformin I, insulin glargine; SBP – systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; PWV, pulse wave velocity.

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