P25

Effect of linagliptin on AVI and API, indices of vascular stiffness evaluated by an automatic blood pressure monitor

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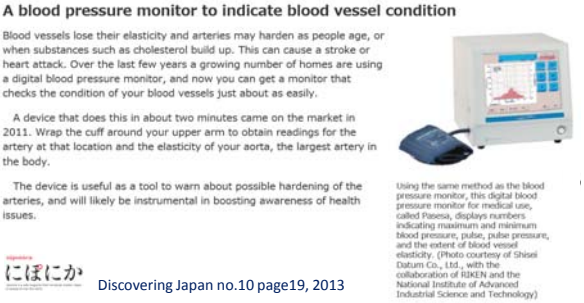
BACKGROUND AND AIMS

Dipeptidyl peptidase 4 inhibitors (DPP4i) have been widely used for the treatment of type 2 diabetic patients. Effect of DPP4i on cardiovascular system is still controversial. Among drugs in this class, linagliptin has been shown to have beneficial effects to reduce incident of cardiovascular events in early preliminary analysis. Pasesa® blood pressure monitor (Shisei Datum, Tokyo, Japan) has received approval for medical use in Japan, this automatic blood pressure monitoring apparatus measures blood pressure, heart rate, and pulse pressure, while simultaneously displaying the condition of central arteries near the heart (AVI) and the stiffness of peripheral blood vessels (API).
In this study, we evaluated AVI and API when type 2 diabetic patients received linagliptin in clinical settings.

METHODS

Medical records of patients visiting to the diabetic clinic at the Saitama Medical Center, Saitama Medical University were analyzed. Linagliptin 5mg q.d. was prescribed by the decision of physicians in charge. The application of this drug and clinical practice is conducted by physicians who practice based on clinical guidelines issued from the Japan Diabetes Society. The prescription of linagliptin was started from April 2013, and we observed the data obtained until June 2014 or any changes of anti-diabetic agents of anti-hypertensive agents or lipid-lowering agents. Pasesa® (AVE-1000, Shisei Datum, Machida, Tokyo, Japan) was used to evaluate AVI and API on each visit. The analysis was approved by the ethical committee of the Saitama Medical Center, Saitama Medical University.



A blood pressure monitor to indicate blood vessel condition

Blood vessels lose their elasticity and arteries may harden as people age, or when substances such as cholesterol build up. This can cause a stroke or heart attack. Over the last few years a growing number of homes are using a digital blood pressure monitor, and now you can get a monitor that checks the condition of your blood vessels just about as easily.

A device that does this in about two minutes came on the market in 2011. Wrap the cuff around your upper arm to obtain readings for the artery at that location and the elasticity of your aorta, the largest artery in the body.

The device is useful as a tool to warn about possible hardening of the arteries, and will likely be instrumental in boosting awareness of health issues.

Using the same method as the blood pressure monitor, this digital blood pressure monitor for medical use, called Pasesa, displays numbers indicating maximum and minimum blood pressure, pulse, pulse pressure, and the extent of blood vessel elasticity. (Photo courtesy of Shisei Datum Co., Ltd., with the collaboration of RIKEN and the National Institute of Advanced Industrial Science and Technology)

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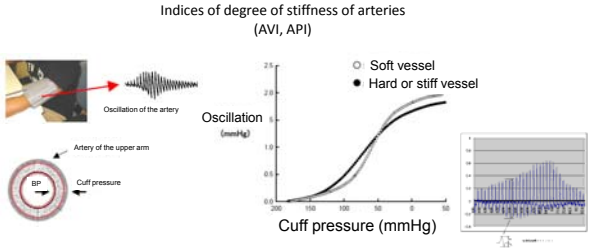

Under high cuff pressure, an arterial vessel is suppressed and the volume of the artery becomes smaller. According to the release of the pressure, the volume of the artery which reflects oscillation becomes larger.

AVI: Vr/Vf

Vr: velocity of release, Vf: velocity of fastened

API: $\alpha * \arctan(\beta * X + \gamma) + \delta$, API=1/β

X is cuff pressure, and α, β, γ, δ are parameters.

RESULTS

	before	after	P value vs before
n (M/F)	26 (16/10)		
age (y.o.)	68.3 ± 10.9		
duration of diabetes (y)	12.3 ± 11.8		
BMI (kg/m^2)	23.6 ± 4.0	23.2 ± 4.1	0.22
HbA1c (%)	7.8 ± 1.4	7.4 ± 1.4	0.04
systolic BP (mmHg)	134 ± 20	136 ± 21	0.63
diastolic BP (mmHg)	73 ± 15	71 ± 15	0.16
PR (/min)	75 ± 20	79 ± 13	0.44
AVI	23.6 ± 8.4	22.6 ± 6.6	0.54
API	31.7 ± 8.2	33.2 ± 8.9	0.49
LDL-C (mg/dL)	94.5 ± 21.3	102.6 ± 31.4	0.49
HDL-C (mg/dL)	43.3 ± 12.0	48.4 ± 15.8	0.48
TG (mg/dL)	146 ± 84	131 ± 61	0.75

On average, linagliptin was used for 11.9 ± 9.3 months.
Use of anti-diabetic agents: insulin 10 (bolus 15.6, basal 16.1 units/day), glimepiride 1, repaglinide 4, mitiglinide 2, pioglitazone 5, metformin 3.
Use of anti-hypertensive agents: ARB 9, ACEI 1, Ca blocker 7, beta blocker 1, diuretics 2.
Use of lipid-lowering agents: statins 9, fibrate 2, ezetimibe 1.
LDL cholesterol levels are calculated by the Friedewald equation.

SUMMARY

Twenty six diabetic patients (M/F=16/10, age: 68±11y.o., duration of diabetes: 12±11yrs, HbA1c: 7.8±1.4% , BMI: 24±4kg/m^2, BP: 134±20 / 73±15mmHg) received linagliptin 5mg qd for 11.9 months on average. Although BP at the observation (135±21/70±14mmHg) was not different from the base line, HbA1c was reduced to 7.4±1.6% ($p<0.05$). AVI (from 23.6±8.4 to 22.6±6.6) and API (from 31.7±8.2 to 33.2±8.9) were not different significantly. While HDL-C was increased from 43±12 to 48±16 mg/dL, LDL-C was not decreased (from 95±21 to 102±31 mg/dL).

CONCLUSIONS

CAROLINA (CARdiovascular Outcome Study of LINAgliptin Versus Glimepiride in Early Type 2 Diabetes) study has been conducted to investigate the long term impact of linagliptin on cardiovascular morbidity and mortality. However the result will not be available until 2018. Our data indicate that there were not any deteriorate effects on AVI, API, and lipid profiles by linagliptin. Since glucose control has been improved it may be possible to expect some beneficial effects by this drug.

The Japan Diabetes Society
COI Disclosure

Anna Sakashita

The author have no financial conflicts of interest to disclose concerning the presentation.

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