Usefulness of Impedance Cardiography and Pulse Study for the Evaluation of the Pharmacological Action of the Depressants

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Purpose
Systolic and diastolic blood pressure (SBP and DBP) by the cuff measurement of the upper arm have been the markers of the effectiveness of the depressants. However, it has been reported SBP and DBP do not reflect the blood pressure of the ascending aorta, which is the true load of the heart1,2). More reliable and usable examinations than SBP & DBP are needed. These methods should be easy and noninvasive, and reflect the aortic pressure or peripheral circulation. The candidates for these methods are (1) late systolic shoulder of the peripheral artery. (2) parameter of the cardiac contractility from the impedence cardiography. In order to discuss the validity of these methods, we studied the pharmacological effects of vasodilator, Nifedipine.

Methods
Subjects were 6 healthy normotensive adults(33±8y. female 1, male 5). After signing informed consents, they took a Nifedipine soft capsule (Nifedipine 10 mg) through sublingual route, followed by radial artery pulse recording (Nippon Colin CBM2000) and Impedance cardiography (CIC:Nihon Denshi Coltd, Nicoview) at sitting position for 30 minutes. Control study were previous 30 minutes recording just before the experiment. Plasma Nifedipine concentration was determined every 5 minutes after taking Nifedipine capsule (HPLC method). Statistical analysis was according to paired t-test (significant level was p<0.05). Al (augmentation index of the radial pulse: Yt/Yt) was determined from an ensemble pulse of successive 20 pulses. Al (Yt/Ye) has been reported to be well correlated with the aortic impedance1,2). PEP/Ts obtained from CIC indicate the cardiac contractility. PEP is pre-ejection period and Ts is systolic time obtained from CIC. Originally CIC is for calculating cardiac output, however its validity has not yet fully ascertained. We used its orignal wave of impedance change, and gained PEP and Ts (Fig.1). PEP/Ts is well correlated with left enricular Ejection Fraction (r=0.90, p<0.01)3.

Results
No significant changes of SBP nor DBP occurred by Nifedipine for 30 minutes.

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In turn, BP increased after Nifedipine in some cases. Heart rate (HR) increased especially in the cases who showed BP increase, in general, HR increased. Al(Yt/Ye) decreased significantly after 30 minutes (p<0.05). PEP/Ts changed concomittantly with plasma Nifedipine, and decreased significantly (p<0.05). It indicates increased contractility. The correlation between SBP, DBP, MBP and plasma concentration were poor, however, Al(Yt/Ye) and PEP/Ts showed a good and significant correlation with plasma Nifedipine concentration (R²=0.81 & p=0.0014, R²=0.99 & p<0.0001 respectively). The correlation between HR change and concentration (R²=0.94, p=0.0014) was not so high as PEP/Ts ratio shown in Fig. 2.

**Discussion**

Nifedipine, a representative Ca antagonist, should decrease aortic impedance, which phenomenon was showed by the change of Al. As a result of decrease of peripheral impedance, cardiac contractility should secondarily increase (decrease of PEP/Ts). Our data was compatible with pharmacological effect of Nifedipine. HR increase should be a secondary change of depressant effect, however, in our result HR increased in cases with pressant effect, which indicate HR change may not be a primary indicator of Nifedipine. The changes of HR, Al and PEP/Ts may be the effect of adrenergic action of Nifedipine. Al is a rate dependnet parameter, may be changed by chronotropic changes after Nifedipine.

**Conclusion**

Without significant changes of SBP, MBP nor DBP, significant changes of Al(Yt/Ye), PEP/Ts and HR occured. These changes were well correlated with plasma Nifedipine concentration. These results support the validity and usefulness of Al or PEP/Ts for the evaluation of pharmacological effect of depressants. These methods are so easy and noninvasive that they may be usable for the evaluation and follow up of the patients in the outpatient clinic. Especially O'Rourke et al. reported that the radial arterial pulses are related with aortic pressure pulse by the generalized transfer function \(^{13}\), which indicate aortic pressure can be calculated by noninvasive radial pulse. So far, brachial SBP and DBP by the cuff methods, have been parameters of circulation. In the future, we should change this old pre-modern style, and use peripheral pulse shape analysis and impedance cardiography in the outpatient clinic or mass screening.

**References**