Assessing the Effect of Low Dose Dobutamine on Various Diastolic Function Indexes

Düşük Doz Dobutaminin Değişik Diyastolik Fonksiyon Parametreleri Üzerine Etkilerinin Değerlendirilmesi

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ABSTRACT

Objective: The aim of this study was to evaluate the effect of low dose dobutamine (LDD) on various diastolic function parameters in patients without wall motion abnormality.

Methods: Thirty-one volunteer patients who had no regional wall motion abnormality were included in the study. Echocardiographic measurements were taken both at pre-dobutamine and during LDD infusion. The peak E velocity, A velocity, the E/A ratio, deceleration time (DT), isovolumetric relaxation time (IVRT), myocardial performance index (MPI) and flow propagation velocity (FPV) were assessed as left ventricular diastolic function parameters. Tissue Doppler velocities were also obtained in order to calculate the E/Em and Em/Am ratios.

Results: No significant changes were observed in heart rate, E velocity, A velocity, E/A ratio, E/Em ratio, Em/Am ratio, systolic and diastolic blood pressure with LDD. With LDD, DT (239±40 msec vs. 201±31 msec, p<0.001), IVRT (109±12 msec vs. 94±11 msec, p<0.001) and MPI (0.57±0.15 vs. 0.44±0.22 p<0.001) were found to be decreased, while there was an increase in FPV (45±8 cm/s vs. 59±10 cm/s, p<0.001) and ejection fraction (64±6% vs. 66±7%, p<0.05).

Conclusion: Low dose dobutamine (5mcg/kg of body weight) improves left ventricular relaxation in patients with normal wall motion, while it has no effect on left ventricular filling pressure index. *(Anadolu Kardiyol Derg 2004; 4: 227-30)*

Key words: Low dose dobutamine, diastolic function indexes

ÖZET

Amaç: Çalışmanın amacı düşük doz dobutaminin (DDD) duvar hareket bozukluğu olmayan hastalarda değişik sol ventrikül diyastolik fonksiyon parametreleri üzerine olan etkilerini incelemektir.

Yöntem: Çalışmaya duvar hareket bozukluğu olmayan gönüllü 31 hasta dahil edildi. Ekokardiyografik ölçümler DDD öncesi ve DDD infüzyonu esnasında yapıldı. Sol ventrikül diyastolik fonksiyon parametreleri olarak pik E, A velositeleri, E/A oranı, deselerasyon zamanı (DT), izovolumetrik gevşeme zamanı (IVRT), miyokardiyal performans indeksi (MPI) ve akım yayılma hızı (FPV) alındı. Ayrıca E/Em ve Em/Am oranlarının hesabı için doku Doppler velositeleri de alındı.

Bulgular: Düşük doz dolbutamin ile kalp hızı, E,A velositesi, E/A oranı, E/Em oranı, Em/Am oranı, sistolik ve diyastolik kan basıncı değişkenlerinde değişiklik gözlenmedi. Deselerasyon zamanı (239±40 msn karşı 201±31 msn, p<0.001), IVRT (109±12 msn karşı 94±11 msn, p<0.001) ve MPI (0.57±0.15 karşı. 0.44±0.22 p<0.001) DDD infüzyonu sonrası azalırken FPV (45±8 cm/s karşı 59±10 cm/s, p<0.001) ve ejeksiyon fraksiyonu (64±6% karşı 66±7%, p<0.05) artmış olarak bulundu.

Sonuç: Düşük doz dobutamin (5mcg/kg/dk) duvar hareket bozukluğu olmayan hastalarda sol ventrikül relaksasyonunu iyileştirirken, sol ventrikül doluş basıncı parametresi üzerine etkisi yoktur. *(Anadolu Kardiyol Derg 2004; 4: 227-30)*

Anahtar kelimeler: Düşük doz dobutamin, diyastolik fonksiyon parametreleri

Introduction

In the most studies the diagnosis of viability or ischemia is based on dobutamine-induced wall motion abnormalities (1-3). Although dobutamine stress echocardiography (DSE) is a noninvasive and relatively safe test (4), its major drawback is that the assessment of regional wall motion may be highly subjective. Therefore, previous attempts to document ischemic diastolic dysfunction with Doppler parameters have been made suggesting a potential to provide diagnostic information that supplement wall motion analysis (5,6).

Dobutamine has certain effects at low dose and high dose

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on ventricular diastolic function parameters. Different diastolic function parameters have been used in evaluating diastolic function during DSE (7,8). In one study isovolumetric relaxation time (IVRT) was found to be significantly longer at high dose dobutamine in patients with residual ischemia after early myocardial infarction (7). Another study suggested that myocardial ischemia provokes an increase in E wave deceleration time at high dose dobutamine (8). We also know that evaluation of diastolic function by measuring noninvasive Doppler left ventricular filling parameters certainly has its limitation because this is influenced by heart rate (9). During low dose dobutamine infusion (LDD) echocardiographic recordings are usually done at 10mcg/kg of body weight which causes slight increase in heart rate.

Multiple case-control studies and case series suggested that low dose dobutamine improved functional capacity in patients with dilated cardiomyopathy (10-12). It has also been known that LDD improves diastolic function parameters in patients with wall motion abnormalities (13). In a different study, we indicated that the improvement in myocardial performance index (MPI) with LDD predicts the outcome of revascularization in patients with previous myocardial infarction (14). Since MPI is an index incorporating both systolic and diastolic functions, it was not clear whether this improvement with LDD occurred through diastolic or systolic function or both (14). Furthermore, despite the well-known effect of LDD in patients with left ventricular dysfunction, its effect on various diastolic function parameters in patients with normal wall motion remains unclear. Therefore, the aim of this study was to evaluate the effect of dobutamine infusion at a dosage of 5 μg/kg of body weight, which usually does not increase the heart rate, on various diastolic function parameters.

Material and Methods

Thirty-one volunteer patients who had no regional wall motion abnormality were included in the study. There were 16 (51%) men and 15 (49%) women, ranging in age from 31 to 76 years (mean 53 ± 12 years). Among these patients, 2 had diabetes mellitus, 5 had coronary artery disease and 13 had hypertension. Coronary artery disease was diagnosed by coronary angiography in two patients and by exercise test in three patients. The remaining 13 participants were healthy individuals with no apparent cardiac disease. The exclusion criteria of the study were: (1) regional wall motion abnormality, (2) valvular heart disease including any kind of mild valvular regurgitation (3) an ejection fraction less than 55 %, (4) a summation of the E and A velocity (5) poor echocardiographic visualization. All patients had normal sinus rhythm without changes in PR interval or conduction abnormalities during the study.

The study protocol was in accordance with the ethical standards of the Helsinki declaration of 1983. All patients gave informed consent for participation in the study.

Study Protocol: Transthoracic echocardiography was performed by one of the authors, using a System-Five Performance machine (General Electric, Vingmed) with a 2.5 MHz phased-array transducer. Echocardiographic measurements were taken both at pre-dobutamine and during LDD, which was started at a dosage of 5 μg/kg of body weight per minute. The second echocardiographic examination was initiated at least 5 minutes after the infusion was started. The dobutamine infusion lasted until the second echocardiographic examination was done. The right brachial artery systolic and diastolic pressures were taken before and at the end of the dobutamine infusion.

Echocardiographic measurements: Recordings were taken from patients placed in the left lateral decubitus position. The M-mode traces were recorded at a speed of 50 mm/sec and the Doppler signals were recorded at a speed of 100 mm/sec. Simultaneous electrocardiographic recordings were also taken. The average of 3 consecutive cycles was calculated for every parameter. Measurements of the left ventricle diameters and the left atrium systolic diameter were obtained according to the established standards (15). Left ventricular ejection fraction (EF) was calculated with the modified Simpson's method (16).

The peak E velocity (peak early transmitral filling velocity during early diastole), the peak A velocity (peak transmitral atrial filling velocity during late diastole), the deceleration time (DT-time elapsed between peak E velocity and the point where the extrapolation of the deceleration slope of the E velocity crosses the zero baseline) and the isovolumetric relaxation time (IVRT= the interval from aortic valve closure to mitral valve opening) were obtained in a standard fashion. The transmitral diastolic flow Doppler tracing was imaged in the apical 4 chamber view, using pulsed Doppler echocardiography with the sample volume sited at the tip of the mitral leaflets. The IVRT was measured on Doppler tracing obtained from the apical five-chamber view with the sample volume placed at the left ventricular outflow tract.

The mitral closure-to-opening interval (a) was the time from cessation to the onset of mitral inflow. The left ventricular ejection time (ET) was measured as the duration of the left ventricular outflow (b). Myocardial performance index MPI was calculated as: MPI=a-b/b (17).

Color M-mode of mitral inflow was also obtained to determine flow propagation velocity (FPV) in the left ventricle (18).

The echocardiography device was arranged so that tissue Doppler velocities could be obtained. The sample volume was placed on the lateral side of the mitral annulus in order to obtain early (Em) and late (Am) diastolic mitral annulus tissue Doppler velocities. Recordings of the mitral annular Em and Am velocities were made with pulsed wave Doppler.

Statistics: Data are expressed as mean ± 1 SD. For comparisons of variables before and after LDD Student's paired t test was used. A p value < 0.05 was considered statistically significant. The SPSS 7.5 program for Windows was utilized for the entire statistical work-up.

Results

The left ventricular diastolic diameter (LVDD), left ventricular systolic diameter (LVSD), thickness of the interventricular septum and posterior wall of the whole study population were 4.95±0.52 cm, 3.17±0.40 cm, 1.05±0.13 cm and 1.04±0.15 em, respectively.

No significant changes were observed in heart rate, E velocity, A velocity, E/A ratio, E/Em ratio, Em/Am ratio, systolic and diastolic blood pressure with LDD (5μg/kg of body weight per minute) (Table I). With LDD, DT (239±40 msec vs. 201±31 msec, $p<0.001$), IVRT (109±12 msec vs 94±11 msec, $p<0.001$) and MPI (0.57±0.15 vs. 0.44±0.22 $p<0.001$) were found to be decreased, while there was an increase in FPV (45±8 cm/s vs 59±10 cm/s, $p<0.001$) and EF (64±6 vs. 66±7, $p<0.05$).

Discussin

Low dose dobutamine improves systolic and diastolic functions in patients with normal wall motion even at a dosage in which heart rate usually does not increase. In order to ascertain the LDD effect on systolic and diastolic functions we used conventional methods and new techniques like MPI, FPV and tissue Doppler imaging.

In the present study, no changes were observed in E, A wave velocities and E/A ratio with low dose dobutamine. These variables are highly influenced by heart rate (9). We used 5 μg/kg dobutamine, which doesn't increase the heart rate. It is therefore not surprising that we found no changes in these variables. These results were also in agreement with those of Edner et al (19). In a different study, A velocity was observed to be increased in patients with low ejection fraction while there was no change in E velocity and E/A ratio (13). Likewise, in patients with EF <50%, myocardial stiffness correlated with the peak atrial filling velocity (20). The increase in A velocity is highly influenced by heart rate (21). Even in a study of normal men during exercise, the late phase of diastole increased more than the early passive filling phase indicating that sympathetic drive would augment atrial contractility (22). As our dobutamine dose had no influence on heart rate, we found no significant alterations in these variables. This dose of dobutamine had also no influence on the left ventricular filling pressure since we found no alterations in E/Em ratio.

In the present study, DT and IVRT were found to be decreased with LDD indicating an improvement in diastolic function. It is interesting that these indexes were altered while the inflow velocities remained unchanged. The inflow velocities are mainly influenced by heart rate and the loading conditions (9). Deceleration time is less influenced by loading conditions (5,21,23-25). Taking into account that the heart rate didn't change after LDD and no alteration in mitral inflow velocities were found, the observed changes in DT and IVRT may result from direct myocardial relaxation due to beta-receptor stimulation. May be this very low dose dobutamine acts primarily on the cardiac tissue without demonstrating overt vasodilatory properties in the periphery.

Table 1. Baseline parameters and their changes with low dose dobutamine infusion

	Basal	Dobutamine	P
HR, beats/min	69±11	70±11	NS
EF, (%)	64±6	66±7	<0.05
E, cm/s	77±14	81±15	NS
A, cm/s	76±15	76±17	NS
E/A	1.06±0.29	1.10±0.28	NS
DT, msec	239±40	201±31	<0.001
IVRT, msec	109±12	94±11	<0.001
E/Em	8.09±2.74	8.47±2.83	NS
Em/Am	1.14±0.44	1.11±0.45	NS
FPV, cm/s	45±8	59±10	<0.001
MPI	0.57±0.15	0.44±0.22	<0.001
Ps, mmHg	118±17	120±15	NS
Pd, mmHg	76±10	79±14	NS

Abbreviations: A; mitral diastolic late flow velocity, DT; mitral E peak flow velocity deceleration time, HR- heart rate, E; mitral diastolic early flow velocity, E/A; mitral diastolic early and late flow velocity ratio, E/Em; mitral leaflet early diastolic flow velocity and late diastolic tissue Doppler velocity ratio, EF; ejection fraction, Em/Am; mitral annulus early and late diastolic tissue Doppler velocity ratio, FPV; flow propagation velocity, IVRT; isovolumetric relaxation time, MPI; myocardial performance index, NS; not significant, Pd; diastolic blood pressure, Ps; systolic blood pressure.

The increase in FPV with LDD was another finding of our study. Explanation for this phenomenon could be as follows: the FPV reflects the inflow conditions in a little earlier diastolic phase than a peak E velocity. In this setting, relaxation improvement may cause the inflow towards apex faster without real changes in maximal early interventricular gradients responsible for E velocity. Therefore FPV may reflect aspects of LV diastolic function other than the mitral inflow profile.

Myocardial performance index is an index that incorporates both systolic and diastolic functions. It was improved with LDD. Since improvement was observed in IVRT and EF with LDD, it is therefore not surprising that this index also improves. Previously, we indicated that the improvement in myocardial performance index with LDD predicts the improvement in wall motion after revascularization in patients with prior myocardial infarction (14). It was not clear, however, whether this improvement with LDD occurred through diastolic or systolic function or both (14). Our study showed that the improvement in MPI occurred due to the improvement of both systolic and diastolic functions.

Limitation: The lack of homogeneity of the study population may act as a limitation. However, the main goal of this study was to assess the effect of LDD on various diastolic function indexes in patients without wall motion abnormality rather than assessing a certain group with homogenous features.

Conclusion: Low dose dobutamine improves systolic function and left ventricular relaxation in patients with normal wall motion even at a dosage in which heart rate usually does not increase, while it has no effect on left ventricular filling pressure index.

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