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Original Article

Effect of preload reduction by haemodialysis on doppler indices of diastolic function in patients with end-stage renal disease

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Abstract
Objective: To assess the influence of preload reduction by haemodialysis on Doppler echocardiographic indices of cardiac diastolic function.
Methodology: Parameters of left ventricular diastolic function were measured in patients with end-stage renal disease before and after a single session of haemodialysis. Patients with valvular heart disease, coronary artery disease, cardiomyopathies, pericardial disease and those not in sinus rhythm were excluded from the study.
Results: Seventeen subjects (12 males and 5 females, mean age 48 ± 16 years) were studied. Over the duration of 3.7 ± 0.6 hours of haemodialysis, 2.6 ± 1.3 litres of ultrafiltrate was removed. The comparison of pre and post haemodialysis peak mitral E and A velocities showed a decrease in E velocity ($p < 0.01$) whereas the change in A velocity was not significant. The E/A ratio decreased significantly ($p < 0.05$).The decrease in E velocity correlated well with the amount of ultrafiltrate ($r = 0.653$, $p < 0.01$). There was a significant increase in isovolumetric relaxation time ($p< 0.05$) whereas deceleration time did not change ($p =0.3$).
Conclusion: Ultrafiltration during haemodialysis causes a rapid reduction in preload. It results in decreased early left ventricular diastolic filling without a change in the atrial phase of filling, hence causing a decrease in calculated E/A ratio.

Key words: Doppler indices, echocardiography, diastolic function, end-stage renal disease, BPKIHS

Doppler echocardiographic examination is increasingly being used in the evaluation of diastolic dysfunction. There are well defined filling patterns that occur in abnormalities of left ventricular (LV) diastolic filling[1,2]. However, these patterns based on Doppler indices of transmitral velocities are also affected by factors other than the cardiac diastolic function. In particular, intravascular volume excess can confound interpretation of transmitral flow variables by causing pseudonormalization of the flow pattern despite the presence of diastolic dysfunction[3]. Studies of the influence of fluid removal on the parameters of LV diastolic function have shown conflicting results[4,5,6,7,8]. The present study aims at evaluating the alterations in Doppler parameters of transmitral flow velocities and intervals induced by a rapid preload reduction after a single haemodialysis session.

Materials and methods

After signing an informed consent, thirty one end-stage renal disease (ESRD) patients on maintenance haemodialysis (HD) at the Nephrology unit of our institute were selected to take part in the study. These patients had been receiving 8 hours a week maintenance HD for at least one month. The inclusion criteria were presence of sinus rhythm, no history suggestive of coronary artery disease, absence of significant valvular heart disease and pericardial disease including effusion, no clinical evidence of congestive heart failure (CHF) and absence of regional wall motion abnormality on 2- dimensional (2D) echo. Blood pressure, pulse, weight and blood urea were measured before and after dialysis. The amount of ultrafiltrate to be removed was determined as per the dialysis prescription. Haemodialysis machine used was Althim system 1000 (TINA) in all cases.

All patients underwent 2-D, colour, continuous-wave and pulsed Doppler echocardiographic examinations, immediately before and one hour after the completion of HD session. In all examinations, the machine used was Hewlett Packard SONOS 1800.

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The investigator doing echocardiography was blinded to the fluid removal data and the measurements were done in accordance to the guidelines of the American Society of Echocardiography[9]. Pulsed Doppler measurements were obtained with the sample volume positioned at the tips of mitral valve leaflets.

The peak of E velocity representing the early rapid filling phase, the peak of A velocity representing the late filling contributed by atrial contraction, deceleration time (DT) and isovolumetric relaxation time (IVRT) were measured by Doppler examination in apical four chamber view. LV diastolic dysfunction was categorized into four grades based on Doppler examination of mitral inflow; grade 0: normal; grade 1: abnormal relaxation with E/A ratio < 1; grade 2: pseudonormal; and grade 3: restrictive with E/A ratio > 2[1]. To distinguish between the normal and pseudonormal pattern, measurements were repeated after a Valsalva maneuver.

Statistical analysis was done using SPSS 11.5 for windows software with the significance level set at 0.05. Data consisting of continuous variables were reported as mean ± standard deviation. Categorical variables were expressed in percentage. A paired Student's t test was employed to assess the significance of differences between measurements obtained before and after HD.

Results

Seventeen patients completed the study. Out of fourteen patients excluded, six had significant valvular lesions, four had regional wall motion abnormality, three patients were in congestive heart failure and one patient was in atrial fibrillation. Table 1 shows frequency distribution of clinical parameters including the aetiology of ESRD and the antihypertensive medications used by the subjects.

Recording of the transmitral velocities before HD showed grade 1 diastolic dysfunction (abnormal relaxation) in ten subjects whereas grade 3 (restrictive) pattern was seen in one. Four patients out of seven who underwent Valsalva maneuver showed a grade 2 pattern (pseudonormal) and the remaining three had grade 0 (normal) pattern. Table 2 shows the comparison of Doppler indices of diastolic function before and after HD in our subjects. There was a significant correlation between the amount of ultrafiltrate and the change in E velocity following HD ($r = 0.653$, $p = 0.004$). The change in E velocity, however, did not show any significant correlation with the reduction in blood urea level ($r = 0.16$, $p = 0.5$).

Table 3 shows the change in various clinical parameters after the HD session that lasted for a mean of 3.7 hours (SD 0.6). The mean weight reduction was 2 kg (SD 0.98). The observed significant change in diastolic blood pressure, however, did not show any correlation with the reduction in weight ($r = 0.14$, $p = 0.6$).

Table 1: Clinical characteristics of the population (n = 17)

Parameters	
Age (years)	48 (21-78)
Male / Female	12 / 5
Time on dialysis (months)	3 (1-7)
Haemoglobin (gm/dL)	7.7 (5.8-10)
Aetiology	
Chronic renal parenchymal diseases*	8 (47%)
Diabetic nephropathy	5 (29%)
Hypertensive glomerulosclerosis	4 (24%)
Antihypertensive drugs	
Calcium channel blocker	16 (94%)
Beta blocker	9 (53%)
Prazosin	6 (35%)
Clonidine	1 (6%)

*Includes chronic glomerulonephritis and chronic interstitial nephritis.
For the continuous variables, values are expressed as mean (range). Categorical data are given in percentage.

Table 2: Doppler indices of diastolic function before and after haemodialysis (HD)

Parameters	Pre-HD	Post-HD	P value
E (cm/s)	77 ± 21	67 ± 24	< 0.01
A (cm/s)	81 ± 22	82 ± 18	0.7
E/A ratio	1.05 ± 0.5	0.82 ± 0.3	< 0.05
DT (ms)	255 ± 92	265 ± 78	0.3
IVRT (ms)	93 ± 24	101 ± 21	<0.01

E, mitral early diastolic velocity; A, mitral late diastolic velocity; DT, deceleration time; IVRT, isovolumetric relaxation time. All data are expressed as mean ± standard deviation.

Table 3: Effects of preload reduction by haemodialysis (HD) on selected measurements

Parameters	Pre-HD	Post-HD	P value
Systolic BP (mmHg)	157 ± 24	151 ± 24	0.2
Diastolic BP (mmHg)	90 ± 12	85 ± 7	<0.05
Mean BP (mmHg)	113 ± 14	107 ± 11	<0.05
Pulse (beats/min)	84 ± 16	82 ± 13	0.1
Body weight (Kg)	56 ± 7	54 ± 7	<0.001
Blood urea (mg/dL)	109 ± 40	42 ± 21	<0.001

All data are expressed as mean ± standard deviation.

Discussion

B.P. Koirala Institute of Health Sciences (BPKIHS) is the only centre in the eastern Nepal, which has been catering maintenance HD services to patients with ESRD. The data obtained from the dialysis unit shows a major bulk of patients had chronic renal parenchymal disease (55.5%) as the aetiology of ESRD followed by diabetes mellitus (30%)[10]. The same pattern of etiological distribution was seen in our subjects (Table 1).

LV filling in diastole, particularly, the early rapid phase depends on its diastolic function and preload. In subjects with reduced LV compliance or abnormal relaxation, a compensatory increase in late atrial phase of LV filling (A wave) occurs resulting in reduced E/A ratio. However, an increase in preload in these subjects elevates the left atrial pressure which eventually increases the early part of LV filling (E wave) and thus resulting in restoration of the E/A ratio back to normal or even to an increased value despite the presence of diastolic dysfunction. This change in Doppler pattern is called pseudonormalization[3]. Conversely, a reduction in preload should unmask the pre-existing diastolic dysfunction in such patients[4,5,6]. Indeed, studies using nitroglycerine to induce a reduction in preload have shown striking decrease in the early transmitral filling velocity independent of changes in the diastolic properties[11]. The selected patients in the present study had both increased preload due to intravascular fluid retention and diastolic dysfunction and thus served as an excellent study group to evaluate our objective.

The change in E velocity following fluid removal in our study is in congruence with most of other similar studies. This change is pathophysiologically consistent with reduced left atrial pressure caused by intravascular volume loss. Furthermore, the present study shows a significant correlation between the change in E velocity and the amount of ultrafiltrate. Dialysis without ultrafiltration doesn't show any significant change in E velocity[12]. In the present study we have demonstrated that there is no statistically significant correlation between the urea reduction rate and the change in E velocity. Even though the present study did not show any significant change in A velocity, Graham et al have reported a significant reduction in A velocity following preload reduction[8]. However, the reduction in A velocity in their study is in a much lesser extent than that of E velocity, causing the E/A ratio to fall significantly, thus still supporting the hypothesis that preload reduction can unmask the diastolic dysfunction in such patients. However, many other studies concur with the present study in demonstrating that the change that occurs in A velocity is not significant[4,5,6]. This is due to the fact that A velocity does not increase as a compensation after preload reduction in patients with diastolic relaxation abnormality[12]. A significant increase in IVRT without an increase in DT is probably the result of reduced LA pressure.

The demonstrated changes in the haemodynamic parameters in the present study are in congruence with similar studies[8,12].

Conclusion

Preload dependence is a limitation of Doppler indices in assessing diastolic function. Therefore, the finding "A more than E" shouldn't be used as a pathognomonic feature of diastolic dysfunction. An understanding of the hemodynamic effect of intravascular volume excess on these parameters along with a complete clinical and echocardiographic evaluation is mandatory to establish the diagnosis of heart failure.

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