between benfluorex and valve regurgitations was based on small observational studies and retrospective estimations. We therefore designed an echocardiography-based multicenter study to compare the frequency of left heart valve regurgitations in diabetic patients exposed to benfluorex for at least three months and in diabetic controls never exposed to the drug.

Methods: This reader-blinded controlled study conducted in ten centres in France included prospectively between November 2009 and September 2011 393 consecutive diabetic subjects previously exposed to benfluorex referred by primary care physicians for echocardiography screening and 393 diabetic controls. Using propensity scores, 303 patients and 303 controls were matched for age, gender, body mass index, smoking, dyslipidemia, hypertension, coronary artery disease, and previous use of other drugs associated with valve lesions. The main outcome measure was the frequency of mild or greater left heart valve regurgitations.

Findings: In the matched sample, the frequency and relative risk (OR) of mild or greater left heart valve regurgitations were significantly increased in benfluorex patients compared to controls: 30·0% vs. 13·5% (OR 2·96[1·94-4·53]) for aortic and/or mitral regurgitation; 21·1% vs. 5·0% (OR 5·63[3·08-10·3]) for aortic regurgitation, and 17·2% vs. 10·2% (OR 1·99[1·22-3·25]) for mitral regurgitation. The frequency of moderate left heart valve regurgitations was also increased among benfluorex patients vs. controls (7·3% vs. 0·7%; OR 13·9[3·21-60·7]).

Interpretation: Our results indicate that use of benfluorex is associated with significant increase in the frequency of left heart valve regurgitations. The natural history of benfluorex-induced valve abnormalities needs further research.

Methods: 156 patients, 79 men and 77 women, mean age 41±14 years, at the inclusion, were recruited for a MD. Patients were asymptomatic at the inclusion. The following studies were performed at the inclusion and repeated 4.5±3.5 years later in 124 of them. Recording of 24 hour Holter monitoring and measurement of HRV in the time domain was calculated every 5 minutes with the Elatec system; standard deviation of the mean RR intervals (SDNN) (ms) was determined. Left ventricular ejection fraction (LVEF) was evaluated at the same time by 2D echocardiography.

Results: LVEF decreased significantly from 62±8 to 58±11% (p< 0.03). None of them had sustained ventricular tachycardia. 19 patients died (12%) during the follow-up generally from cardiac and respiratory failure. Mean values of SDNN did not change significantly between first inclusion (126±42.5 ms) and last study (126±47 ms). At inclusion, SDNN was significantly shorter in patients who died than in alive patients (109±50 msec vs 128±41) (p <0.025). Among the patients who died, initial SDNN was missing in 6 patients, less than 100 msec in 10 patients and more than 100 msec in only 3 patients. Among total population only 40 patients had an initial SDNN <100 msec and 10 died (25%). Remaining patients had a SDNN >100 msec and only 3 patients died (3%) (p<0.0001).

Conclusions: The modifications of HRV during the follow-up were not useful for the prediction of the occurrence of dilated cardiomyopathy or of life-threatening arrhythmias in myotropic dystrophy, although LVEF decreased with time. However, a low HRV (<100msec) at the first evaluation was predictive of increasing mortality from 3 to 25%.

143

Clinical and echographic characteristics of patients exposed to fenfluramine derivatives:

Results of a prospective, monocenter observational study

David Cambon, Marion Berous, Kamila Solecki, Christelle Robert, Florence Leclercq
Hôpital Arnaud De Villeneuve, Cardiologie Nord, Pr F Leclercq, Montpellier Cedex 5, France

Objectives: Fenfluramine derivatives have been associated with significant risk of developing cardiac valvulopathy. This prospective study evaluated characteristics of patients hospitalized in cardiology and who have been exposed to these drugs.

Methods: Between July 2011 and February 2012, patients admitted in the cardiology department, University Center of Montpellier, France, were questioned about past exposition to fenfluramine derivatives. In case of positive response, a questionnaire assessing prescribing patterns and previous medical history was proposed and echocardiography was performed. All usual echocardiographic parameters were analysed. We applied criteria from the French multicenter registry for diagnosis of drug-induced valvulopathy.

Results: Ninety patients exposed to the drugs were included. Sixty-seven percent were women (n=60). Fifty-three percent had diabete (n=47). Ninety percent were exposed to benfluorex (n=81). Mean treatment duration was 48 months (IC95%; 36,5-60,2). Valvular regurgitations were observed in 62,2% of patients (n=51) while 19% of patients (n=15) had pulmonary hypertension. Distribution of valvulopathies is summarized in table 1. Highly probable induced valvulopathies were mild to moderate in all except 3 cases.

Conclusion: In absence of definite knowledge about evolution of drug-induced valve disease, systematic questioning concerning fenfluramine derivatives use could be recommended in hospitalized patients.

Table 1 – Distribution of regurgitations

<table>
<thead>
<tr>
<th>Patients</th>
<th>Mitral R</th>
<th>Aortic R</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP</td>
<td>16 (20.3%)</td>
<td>8 (10.7%)</td>
</tr>
<tr>
<td>PI</td>
<td>28 (34.1%)</td>
<td>20 (24.4%)</td>
</tr>
<tr>
<td>UI</td>
<td>22 (26.8%)</td>
<td>15 (18.3%)</td>
</tr>
</tbody>
</table>

(HP: highly probable induced regurgitations; PI: possibly induced regurgitations; UI: unlikely induced regurgitations; R: regurgitation)

© Elsevier Masson SAS. All rights reserved.