Effective High Dose Multi-Drug Treatment Regimen Favours Event Free Survival Rate in DCMP Patients.

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ABSTRACT

Background: To study the effect of multidrug treatment regimen in the patient of DCMP (Dilated cardiomyopathy) compared to single drug/low dose multi drug regimen. Methods: A total of 40 patients diagnosed with DCMP (both ischemic and non-ischemic) in the last 5 years attending to Cardiology OPD/Inpatients in National Institute of Medical sciences, Jaipur were enrolled in the study. Out of 40 patients, 20 were kept on routine treatment regimens like diuretics, beta-blockers, angiotensinogen converting enzyme inhibitor/ Angiotensin receptor blockers (ACEI/ARB), either of them or all three of them in low dose. The other 20 patients were started on mineralocorticoid receptor antagonists (MRA’s), beta-blockers, ACEI all together with gradual increments of doses to a higher level. Both these groups were followed for 2 years and we found that patient groups with effective high dose multi drug regimen has good event free survival rate compared to traditional single drug/low dose multiple regimen. Tests of statistical significance were done using Chi-square Test. Results: Out of 20 patients in normal (routine treatment regimen) 12 patients presented with congestive cardiac failure (CCF), 15 with dyselectrolemia. 10 with hypotensive episodes and 6 deaths were seen compared to 5 patients with CCF, 5 with dyselectrolemia, 8 with hypotension and 2 deaths were seen in high dose multi drug regimen. Out of this episodes of CCF (p=0.002), dyselectrolemia (p=0.001) are statistically significant. Conclusion: High dose MDR is preferable for event free survival rate in patients of DCMP.

Keywords: Eplerenone, Dilated Cardiomyopathy, Multi drug regimen.

INTRODUCTION

Cardiomyopathy has been described as a “heterogenous group” of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes-frequently genetic, either confined to the heart or are a part of a generalized systemic disorder often leading to cardiovascular death or progressive heart failure related disability.[1] Based on phenotypic and genotypic information, cardiomyopathies are classified into various types.[2,3]

Table 1: Types of cardiomyopathies.

<table>
<thead>
<tr>
<th>Cardiomyopathy</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated cardiomyopathy</td>
<td>Left ventricular Non-compaction</td>
</tr>
<tr>
<td>Restrictive cardiomyopathy</td>
<td>Infiltrative</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Ischemic</td>
</tr>
<tr>
<td>Arrhythmogenic cardiomyopathy</td>
<td>Inflammatory</td>
</tr>
<tr>
<td>Left ventricular cardiomyopathy</td>
<td>Infectious</td>
</tr>
</tbody>
</table>

DCM is characterized by a dilated left ventricle with systolic dysfunction that is not caused by ischemic or valvular heart disease, whose cause is generally genetic or idiopathic.[4] However, the most common cause ischemic injury (here the term DCM is used generally to describe the morphology and function of left ventricle regardless of etiology) caused by CAD or prior myocardial infarction.[5,6] Patients with DCM are at risk of sudden cardiac death and dangerous ventricular arrhythmias.[4]

Most patients present between the age of 20-60 years, but DCM can occur in children and older adults.[7] Affected patient present with symptoms of heart failure (progressive dyspnea, impaired exercise capacity, orthopnea, paroxysmal nocturnal dyspnea and peripheral edema) are most common. Other presentation include the incidental detection of asymptomatic cardiomegaly and symptoms related to co-existing arrhythmia, conduction disturbance, thromboembolic complication or sudden death.[8]

Diagnosis of DCM requires evidence of dilatation and impaired contraction of the left ventricle or both ventricles (eg. LVEF < 40% or fractional shortening less than 25%).[5,6] primarily by 2D-Echocardiography/ clinical features along with history of coronary artery disease, alcoholism, infections (Chagas disease), amyloidosis, etc.. Differentiation between ischemic and non-ischemic is made by coronary angiography, based on which treatment regimen differ.[9] Management[4] of ischemic DCM includes Anti-platelets, Percutaneous transluminal coronary angioplasty, coronary bypass grafting in addition to beta-blockers, ACEI/ARB’s, Diuretics.
Drugs like Ivabradine and devices like CRT (cardiac resynchronization therapy), ICD (intra cardiac defibrillators) have also been suggested. Heart transplantation is the ultimate modality. Current study is focused on treatment regimen favouring event free survival rate.

MATERIALS AND METHODS

A total of 40 patients diagnosed with DCMP (both ischemic and non-ischemic) in the last 5 years attending to Cardiology OPD/ Inpatients in National Institute of Medical sciences, Jaipur were enrolled in the study. Out of 40 patients, 20 were kept on routine treatment regimens like diuretics, beta-blockers, angiotensin converting enzyme inhibitor/Angiotensin receptor blockers (ACEI/ARB), either of them or all three of them in low dose. The other 20 patients were started on mineralocorticoid receptor antagonists (MRA’s), beta-blockers, ACEI all together with gradual increments of doses to a higher level. Both these groups were followed for 2 years and various complications in DCMP patients are noted like congestive cardiac failure, dyselectrolemia, hypotensive/shock episodes and ultimately deaths. We found that patient groups with effective, high dose multi drug regimen has less complications compared to traditional single drug /low dose multiple regimen. The data obtained were analyzed using Excel sheet/SPSS software. Tests of significance were done using the Chi - square test at 95% confidence interval.

RESULTS

Out of 20 patients in normal (routine treatment regimen) 12 patients presented with congestive cardiac failure (CCF), 15 with dyselectrolemia, 10 with hypotensive episodes and 6 deaths were seen compared to 5 patients with CCF, 5 with dyselectrolemia, 8 with hypotension and 2 deaths were seen in high dose multi drug regimen.

N stands for normal / conventional low dose combination therapy or single dose diuretic therapy.

MDR stands for high dose multi drug regimen.

Table 2: CCF (Congestive Cardiac Failure).

<table>
<thead>
<tr>
<th></th>
<th>CCF episodes</th>
<th>No CCF episodes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>12</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>MDR</td>
<td>5</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>23</td>
<td>40</td>
</tr>
</tbody>
</table>

For observed value (O) of 12, expected value (E) is 8.5 (20 x 17 / 40), $X^2 = 1.441$

For O= 5, E= 8.5 (20 x 17 / 40), $X^2 = 1.441$

For O= 8, E= 11.5 (20 x 23 / 40), $X^2 = 1.06$

For O= 15, E= 11.5 (20 x 23 / 40), $X^2 = 1.06$

Total $X^2 = 1.441+1.441+1.06+1.06 = 5.002$

For $X^2=5.002$, p value is 0.02 which is significant.

Table 3: Dyselectrolemia.

<table>
<thead>
<tr>
<th></th>
<th>Dyselectrolemia episodes</th>
<th>No Dyselectrolemia episodes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>15 ($X^2 = 2.5$)</td>
<td>5 ($X^2 = 2.5$)</td>
<td>20</td>
</tr>
<tr>
<td>MDR</td>
<td>5 ($X^2 = 2.5$)</td>
<td>15 ($X^2 = 2.5$)</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>20</td>
<td>40</td>
</tr>
</tbody>
</table>

Total $X^2 = 10$

For $X^2=10$, p value is 0.001 which is highly significant.
DISCUSSION

DCM is a disease of high incidence and has a great social impact on patients. The main cause for the development of DCM is an ischemic heart disease which is thought to be responsible for ventricular dilatation in more than 60% cases of DCM. DCM carries a poor prognosis with 5 year survival rate is around 50%. In developing countries like India, it is unlikely for patients in developing nations to opt for ICD, CRT, and cardiac transplantation due to high cost. Hence, to prolong event free survival rate with good efficiency, proper medical management approach is necessary. Our study reveals that high dose multi drug regimen has shown promising results rather than conventional single drug diuretic or combination low dose regimen.

CONCLUSION

DCM is disease of high social impact on patients. It incapacitates patients performing routine activities, limiting them to household activities, which shows great impact of survival in developing nations like India. It is unlikely for patients in developing nations to opt for ICD, CRT, and cardiac transplantation due to high cost. Hence, to prolong event free survival rate with good efficiency, proper medical management approach is necessary. Our study reveals that high dose multi drug regimen has shown promising results rather than conventional single drug diuretic or combination low dose regimen.

LIMITATIONS: - Patient diagnosed with DCM in last 5 years were taken into study. Before coming to us, patient would have already taken various treatment regimens, which determine ventricular modification process unknown to us, thus altering the findings in our study. It would have been better if DCM was first diagnosed and followed with different regimens but the rarity of this disease forced us to take previously diagnosed patient into study to increase sample size.

REFERENCES


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