Abstract
This is a prospective, community based, single blind, monocentric, clinical study performed in a community based healthcare centre, Chatkhil, Noakhali for the period from June 23, 2006 to September 21, 2008. Patients of hypertension & IHD (chronic stable angina) were selected for study, age limit 20-80 years, both genders was included; sample size 507. The prime objective is to study the efficacy of amlodipine on left ventricular function on hypertension & ischaemic heart disease. Patients were evaluated clinically & then investigated by X-Ray, ECG, Echocardiography. Amlodipine therapies (5 mg daily) was given with or without other medications followed by echo-evaluation of LV function for 9-12 months LV-EF & LV mass/BSA were measured very accurately. Among 507, male 355 (70.01%) & female 152 (29.98%). 50-59 years age group was affected much (210 cases, 41.42%). Second affected age group is 60-69 years (107 cases, 21.10%). Service holders & businessmen were affected much (135 cases- 26.62%, 134 cases- 26.42%). Normal LV-EF was observed in 95 (18.73%) & 114 cases (23.26%) before & after drug therapy. Besides normal LV mass/BSA was observed in 50 (9.86%) & 67 (13.67%) cases respectively before & after treatment. So it is concluded that amlodipine, a third generation CCB effectively control BP, helps in regression of LV hypertrophy & thus improves LV function (LV-EF).

Key words
Amlodipine, LV function, echocardiography

Introduction
Calcium (Ca++) is required for contraction of cardiac & smooth muscle, also responsible for propagation of cardiac impulse; Calcium Channel Blockers (CCBs) block the influx of calcium into cells. This relaxes the muscles in the walls of arteries resulting in dilatation. This lowers the blood pressure and improves the blood supply to the heart muscle. All of these effects allow the heart to work with reduced blood supply together with relief of anginal pain.

Calcium Channel Blockers (CCBs) may be divided into benzothiazepine (diltiazem); phenylalkylamine (verapamil); and dihydropyridines (first generation: Nifedipine, nicardipine, felodipine, nisoldipine; second generation: isradipine, nimodipine; third generation: amlodipine, lacidipine etc).

Amlodipine is a third generation CCB with long half-life. It has interaction with specific high affinity binding sites in the calcium channel complex. It maintains therapeutic efficacy throughout 24 hours. It has less negative inotropic and chronotropic action, having lack of clinically, relevant increase in cardiac or peripheral sympathetic activity. It has higher lipophilicity; reflex tachycardia is minimal, relatively safe in heart failure.

The L-type calcium channel is the dominant type in cardiac & smooth muscle. The calcium channel blockers act from the inner side of the membrane and bind more effectively to channels in depolarizing membranes.

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In the cardiac myocyte, Ca\textsuperscript{++} binds to troponin and reduces inhibitory effects of troponin on contraction, favouring muscle contraction. CCBs reduce transmembrane movement of Ca\textsuperscript{++}, reduce the amount reaching intracellular sites and therefore reduce vascular smooth muscle tone.

Amlodipine has got minimal or no effect on AV conduction.

CCBs have direct negative inotropic effects and showed some benefits on haemodynamic parameters alone or in combination with ACE inhibitors. Amlodipine has got potentially beneficial effects on hypertension and coronary artery disease especially stable angina. But amlodipine showed minimal beneficial effects in patients with heart failure which was observed on large, randomized, placebo-controlled trials.

Aims and objectives

The objectives were-

i. To study the efficacy of amlodipine on left ventricular function in hypertension.

ii. To study the efficacy of amlodipine on left ventricular function in ischaemic heart disease (stable angina).

iii. To evaluate any side effects of amlodipine used for HTN & stable angina.

iv. Echocardiographic evaluation of LV functions after amlodipine therapy in HTN & IHD.

v. Finally to provide some new information on amlodipine therapy in this regard.

Materials and methods

It is a prospective, community based, single blind, mono-centric, clinical study performed in a Community Health Care Centre, Chatkhil, Noakhali from 23.06.2006 to 21.09.2008.

A larger geographical area of Noakhali district i.e. Chatkhil, Sonaimuri, Begumgonj and part of Lakhipur and Comilla districts were fairly covered in this study.

All patients attending the OPD were screened. Patients of hypertension & IHD (stable angina) were selected for study. Age limit was 20-80 years; no gender variation; associated heart failure was not a contraindication for inclusion. Consent was taken from all patients or relatives prior entry to study.

After clinical case selection, patients were investigated by X-ray, ECG, Echo, blood glucose and lipid profile. Then amlodipine therapy (5 mg daily) was given with other medications followed by echocardiographic evaluation of LV function every 2-3 months interval.

For 2D & M-mode echocardiography we used ALOKA SSD-1100 equipment. Left ventricular function was evaluated by the following parameters: wall thickness, chamber dimension, wall motion abnormality, ejection fraction, stroke index, LV mass/BSA etc.

Some LV parameters

<table>
<thead>
<tr>
<th>A. Stroke Volume (SV)</th>
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<tbody>
<tr>
<td>SV</td>
</tr>
<tr>
<td>Vold</td>
</tr>
<tr>
<td>Vold</td>
</tr>
<tr>
<td>End diastolic volume in ml</td>
</tr>
<tr>
<td>Vols</td>
</tr>
<tr>
<td>End systolic volume in ml</td>
</tr>
<tr>
<td>LVEDV</td>
</tr>
<tr>
<td>90-140 ml</td>
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<tr>
<td>LVESV</td>
</tr>
<tr>
<td>27-85 ml</td>
</tr>
<tr>
<td>SV</td>
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<tr>
<td>50-100 ml</td>
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</table>

<table>
<thead>
<tr>
<th>B. Stroke Index in ml/m\textsuperscript{2}(SI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.I.</td>
</tr>
<tr>
<td>SV/BSA</td>
</tr>
<tr>
<td>Stroke volume in ml</td>
</tr>
<tr>
<td>BSA</td>
</tr>
<tr>
<td>Body Surface Area in m\textsuperscript{2}</td>
</tr>
<tr>
<td>Example</td>
</tr>
<tr>
<td>SV-75 ml; BSA- 1.5 m\textsuperscript{2}</td>
</tr>
<tr>
<td>So, S.I.=75/1.5 = 50 ml/m\textsuperscript{2}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Cardiac Index in L/min/m\textsuperscript{2}(CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.I.</td>
</tr>
<tr>
<td>CO/BSA</td>
</tr>
<tr>
<td>Cardiac output in L/min</td>
</tr>
<tr>
<td>BSA</td>
</tr>
<tr>
<td>Body Surface Area in m\textsuperscript{2}</td>
</tr>
<tr>
<td>Example</td>
</tr>
<tr>
<td>CO-5 L/min; BSA- 1.5 m\textsuperscript{2}</td>
</tr>
<tr>
<td>So, C.I.=5/1.5 =3.3 L/min/m\textsuperscript{2}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D. LV mass- cube (gm) = 1.04 [(IVS+LVID+PW)\textsuperscript{3}-(LVID)\textsuperscript{3}]</th>
</tr>
</thead>
<tbody>
<tr>
<td>(measurement in cm)</td>
</tr>
<tr>
<td>Example</td>
</tr>
<tr>
<td>IVS-1.0 cm; LVID- 4.5 cm</td>
</tr>
<tr>
<td>PW-1.0 cm</td>
</tr>
<tr>
<td>So, LV mass-cube=190.84 gm</td>
</tr>
</tbody>
</table>

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E. LV mass = 0.80 (LV mass cube) + 0.60 (ASE convention)  
American Society of Echocardiography  
Example, LV mass cube 190.84 gm  
So, LV mass = 153.27 gm

F. LV mass (Penn Convention) = (LV mass cube) – 14  
G. LV mass/BSA : 125–150 gm/m2  
H. Ejection fraction in percent (EF)  
EF = 100 \times \frac{\text{Vold} - \text{Vols}}{\text{Vold}}  
\text{Vold}  
End diastolic volume in cm³  
\text{Vols}  
End systolic volume in cm³

Results
Various data obtained from the study were presented below using various tables, figures and graphs.

Table 1: Gender distribution of patients (n=507)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>355</td>
<td>70.01</td>
</tr>
<tr>
<td>Female</td>
<td>152</td>
<td>29.98</td>
</tr>
</tbody>
</table>

Table 2: Age distribution of patients

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>05</td>
<td>0.98</td>
</tr>
<tr>
<td>30-39</td>
<td>45</td>
<td>8.87</td>
</tr>
<tr>
<td>40-49</td>
<td>97</td>
<td>19.13</td>
</tr>
<tr>
<td>50-59</td>
<td>210</td>
<td>41.42</td>
</tr>
<tr>
<td>60-69</td>
<td>107</td>
<td>21.10</td>
</tr>
<tr>
<td>70-79</td>
<td>43</td>
<td>8.48</td>
</tr>
</tbody>
</table>

Table 3: Occupation of patients (n=507)

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer</td>
<td>02</td>
<td>0.39</td>
</tr>
<tr>
<td>Day labourer</td>
<td>31</td>
<td>6.11</td>
</tr>
<tr>
<td>Service holder</td>
<td>135</td>
<td>26.62</td>
</tr>
<tr>
<td>Teachers</td>
<td>96</td>
<td>18.93</td>
</tr>
<tr>
<td>Fishermen</td>
<td>37</td>
<td>7.29</td>
</tr>
</tbody>
</table>

Table 4: Disease profile in study subjects (n=507)

<table>
<thead>
<tr>
<th>Disease profile</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>249</td>
<td>49.11</td>
</tr>
<tr>
<td>IHD (Stable angina)</td>
<td>162</td>
<td>31.95</td>
</tr>
<tr>
<td>HTN + IHD (Co-exist)</td>
<td>96</td>
<td>18.93</td>
</tr>
</tbody>
</table>

Table 5: Gradings of hypertension (n=345)

<table>
<thead>
<tr>
<th>Gradings</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>84</td>
<td>24.34</td>
</tr>
<tr>
<td>Moderate</td>
<td>157</td>
<td>45.50</td>
</tr>
<tr>
<td>Severe</td>
<td>104</td>
<td>30.14</td>
</tr>
</tbody>
</table>

Table 6: Echo-evaluation of LV-EF before treatment (n=507)

<table>
<thead>
<tr>
<th>LV</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (60-75%)</td>
<td>95</td>
<td>18.73</td>
</tr>
<tr>
<td>Mild dysfunction (50-59%)</td>
<td>102</td>
<td>20.11</td>
</tr>
<tr>
<td>Moderate dysfunction (40-49%)</td>
<td>109</td>
<td>21.49</td>
</tr>
<tr>
<td>Severe dysfunction (30-39%)</td>
<td>114</td>
<td>22.48</td>
</tr>
<tr>
<td>Very severe dysfunction (&lt;30%)</td>
<td>87</td>
<td>17.15</td>
</tr>
</tbody>
</table>

Table 7: Echo-evaluation of LV-EF after treatment (n=490)

<table>
<thead>
<tr>
<th>LVEF</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>114</td>
<td>23.26</td>
</tr>
<tr>
<td>Mild dysfunction</td>
<td>110</td>
<td>22.44</td>
</tr>
<tr>
<td>Moderate dysfunction</td>
<td>90</td>
<td>18.36</td>
</tr>
<tr>
<td>Severe dysfunction</td>
<td>99</td>
<td>20.20</td>
</tr>
<tr>
<td>Very severe dysfunction</td>
<td>77</td>
<td>15.71</td>
</tr>
<tr>
<td>Drop out</td>
<td>17</td>
<td>3.35</td>
</tr>
</tbody>
</table>

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Discussion

For hypertensive patients, one should select the appropriate medication to control hypertension. Hypertension is one of the most prevalent risk factors for cardiovascular disease, affecting as many as 800 million people worldwide.

Amlodipine effectively reduces the cardiovascular risk factors related to hypertension.

Table 1 shows the gender distribution of patients (n=507); male- 355 (70.01%), female- 152 (29.98%). We have observed prevalence of hypertension and coronary artery disease much more in males rather than females; which was supported by Scandinavian research group in 2007.6

Table 2 shows age distribution of patients. Maximum affected age group in 50-59 years (210 cases, 41.42%); next common affected group in 60-69 years (107 cases, 21.10%). Malhotra and Co-workers7 also found the similar incidence in European Community; 50-59 years, 43.42% & 60-69 years age group 23.25% respectively.7

Various occupations of patients were showed in table 3. Maximum incidence was observed in service holders (135 cases, 26.62%) & businessmen (134 cases, 26.42%). Other researchers also observed the same phenomena in white, as well as black races.8

Table 4 narrated the disease profile in study subjects (n=507) i.e. only hypertension-249 cases (49.11%), only IHD (stable angina)-162 cases (31.95%) & associated HTN plus IHD- 96 cases (18.93%).

Gradings of hypertension were done on 345 cases:

a) Mild- 84 cases (24.34%)

b) Moderate- 157 cases (45.50%)

c) Severe- 104 cases (30.14%).

In our community population prevalence of moderate hypertension is higher, which was...
supported by Kamango, Picarno & other Co-workers in 2006.

Left ventricular function of the study-subjects suffering from hypertension & chronic stable angina (n=507) was evaluated by echocardiography. Though various methods of calculation are available, simplest formula of calculating LV-EF through POMBO method was adopted.

Table 6 & 7 showed the comparative study of echo-evaluation of LV-EF before & after amlodipine treatment. Before treatment normal LV-EF was observed on 95 cases (18.73%). After treatment it has become 114 cases (23.26%). This rise of 19 cases (4.51%) is due to control of BP resulting from amlodipine therapy. Before treatment severe dysfunction was observed in 114 cases (22.48%); but after treatment it has come down to 99 cases (20.20%). This reduction (2.28%) of LV systolic dysfunction is due to drug therapy. It was observed by Panthorian and Co-workers in 2007 i.e. 3.31%.

Table 8 & 9 showed the comparative study of LV mass/BSA in study subjects just before & after amlodipine therapy. Suggested cut off point for LVH is 125g/BSA.

Table 8 showed different gradings of LV hypertrophy where grade-I: LVH- 107 cases (21.10%), grade-II: LVH- 193 cases (38.06%), grade-III: LVH- 157 cases (30.96%).

Despite drop out of 17 cases (3.35%), the scenario has been changed after control of BP with amlodipine with or without other medications i.e. grade-I: LVH- 101 cases (20.61%), grade-II: LVH- 184 cases (37.55%), grade-III: LVH- 138 cases (28.16%).

Reduction of LV mass/BSA index was observed in the study groups- Quinkibay and Co-worker in 2006. Ducketty & Pathania in 2007 and also in LV mass/BSA trial in Scandanavian population in 2008.

Conclusion
Amlodipine is a third generation calcium channel blocker with favourable pharmacokinetic profile. For its much higher affinity for vascular calcium channels, it is particularly useful in treating hypertension. Due to its intrinsic natriuretic effect, it is proven effective for mild, moderate & severe hypertension. It provides 24 hours angina protection including morning hours. It is also effective in variant angina. From various studies it was proved that amlodipine is efficacious in improving left ventricular function in hypertensive and ischaemic heart. So adjunct to other usual medications we shall suggest to add low dose CCB i.e. amlodipine with a view to improve left ventricular function, unless contraindicated; though it invites more research work worldwide.

Acknowledgement
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References