Research Article

Comparative Study on Beneficial Effects of Calcium Channel Blockers and Beta Blockers in Post Stroke Patients

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ABSTRACT

The study was conducted to compare the effects of calcium channel blockers and beta blockers on reducing the blood pressure and in improving the neurological function. A prospective observational study was conducted in 89 stroke patients for a period of six months. Two antihypertensive drug classes were compared in post- stroke patients and the improvement in neurological function was estimated by using National Institute of Health Stroke Scale and Power of Limb. The reduction in the mean blood pressure among the groups showed that Calcium Channel Blockers has high Systolic Blood Pressure (20.29mmHg) and Diastolic Blood Pressure difference (9.71mmHg) when compared to Beta Blockers and Control group. A better improvement in neurological function was found in Calcium Channel Blockers Group by assessing the NIHSS score (7.88±2.45) and Power of limb. This study suggests Calcium channel blockers contribute a superior neuroprotective action than Beta blockers in post stroke patients.

Keywords: Stroke, Calcium Channel Blockers, Beta Blockers, Power of limb, NIHSS.

INTRODUCTION

One of the leading modifiable risk factor in both ischemic and hemorrhagic stroke is high blood pressure. 75% of acute stroke patients have increased blood pressure and 50% have a prior history of hypertension. Blood pressure falls spontaneously in two third of patients in the first week following stroke, one-third remain hypertensive with an increased risk of a poor outcome. The potential causes for the acute hypertensive response in stroke include fluctuations in pre-existing hypertension, infection, pain, stress related to hospitalization, cortisol activation, and raised intracranial pressure. Low blood pressure is far less common in acute stroke and is associated with a poor outcome.[1]

An increase in intraluminal pressure leads to alteration in endothelium and smooth muscle function in intracerebral arteries. This leads to an increased stress on the endothelium which increases the permeability over the blood brain barrier resulting in focal or multifocal brain edema. The endothelial damage can also lead to local thrombi formation and ischemic lesions. Degenerative changes in the smooth muscles and the endothelium of the cerebral arteries predisposes for ICH.

Hypertension can accelerate the atherosclerotic process, thereby increasing the chances for stenosis related cerebral lesions and embolism originating from large extra cranial vessels, the aortic arc and the heart.[2] Hypertension causes atheromatous deposits blocking or narrowing brain arteries, leading to local clot formation. Atheroma damages the cerebral arterioles and the brain tissue supplied by them. Infarcts are more common than cerebral hemorrhages. Previous ischemic vascular damage is usually followed by ICH as the high blood pressure cannot directly rupture the small intracerebral blood vessels. Lowering of blood pressure thus would reduce the risk and extend of bleeding into the brain once an arterial wall breaks. Induced hypotension prevents ischemic stroke by decreasing pressure induced or ischemia induced arteriolar spasms and by vasodilatation of some of the more ischemic territories. Hypertensive vascular lesions in the brain include increased formation of atheroma, lacunae, atherothrombotic brain infarction and vascular dementia.[3]

Under normal conditions, a constant cerebral blood flow in the capillary bed is maintained between 60 and 150mmHg by changes in precapillary arteriolar diameter. A fast response to changes in pressure pulsations is followed by a slow static response that restores the cerebral blood flow by myogenic and metabolic mechanisms. When BP increases, the progressive vasoconstriction of the arterioles occurs until BP exceeds the upper limit of auto regulation, followed by breakthrough vasodilatation, increase in cerebral blood flow, blood brain barrier disruption and cerebral edema. In case of chronic hypertension the lower end of the auto regulatory curve is shifted towards high blood pressure (because of thickening of the vessel walls and narrowing of lumen). In acute stroke, dilation of cerebral resistance vessel to increase the blood flow to the ischemic tissue may cause impaired auto regulation in region surrounding the acute lesion. Auto regulation is impaired for rapid changes in systemic BP.

Conditions such as cerebral vasospasm in SAH causes arteriolar constriction, shifting the auto regulatory range towards higher values. As the ICP increases the pressure to > 60mmHg, it will be inadequate to maintain constant cerebral blood flow. In stroke patients the brain trauma foundation recommends a cerebral perfusion pressure of

>70mmHg to enhance perfusion to areas of traumatic injury.[4]

An excessive calcium influx into depolarised neurons causes necrosis of neurons in ischemic area. CCBs block the neuronal calcium influx and reduces ischemic injury. Randomised clinical trials show that CCBs are able to interfere with preclinical neuronal dysfunction in patients with an increased risk of stroke. They also prevent progression of carotid atherosclerosis on carotid intema-media.[5] β-blockers such as propranolol reduce the metabolic demand in the ischemic brain and have shown neuroprotective effect. They limit the neurologic damage mediated by catecholamines in patients with subarachnoid hemorrhage.[6] Hence this study helps in overweighing Calcium channel blockers from Beta blockers in improvement in neurological function after stroke.

MATERIALS AND METHODS

The study was a Prospective Observational Study conducted at Vivekanandha Medical Care Hospital, Elayampalayam, Tiruchengode with the approval of the Institutional Ethical Committee (Ref.No.: SVCP/IEC/JAN/2019/01 dated 03/01/2019) after obtaining prior consent from the study participants for a period of 6 months (January 2019- June 2019).

Study Population

A total of 102 stroke patients were screened from General Medicine and Neurology Departments and 89 patients both male and female, above the age of 18 years, confirmed with stroke by radiological studies and undergoing antihypertensive therapy were included in the study. Patients suffering brain tumor and receiving multiple antihypertensive drugs were excluded along with the Pregnant and lactating women.

Information such as demographic details, past medical and medication history was collected by chart review. The blood Pressure, power of limb was measured and NIHSS score was calculated at the time of admission, during discharge and follow up. Based on the antihypertensive therapy 27 were grouped into control group (subjects under irregular therapy of antihypertensives excluding CCBs and Beta Blockers), 33 into Group A (subjects under calcium channel blocker treatment) and 29 into Group B (subjects under beta blocker treatment).

Study Tools

1. NIHSS

It includes 13 questions, each of which is given a score between 0 and 4. A lower score indicates a reduced neurological impairment. The maximum total possible score is 42 which is indicates an untreatable score and the minimum being 0 in case of mild stroke.

2. Power of Limb

It is a score (on 5), given by the physician on assessment of muscle power. It was given for all the four limbs.

3. Blood Pressure

The blood pressure was recorded at the time of admission, discharge and during follow up to evaluate which agent exhibits better control over hypertension.

RESULTS

The demographic characteristics of the study subjects are provided in Table 1. Among 37 females and 52 males a 41.57% came with complaints of left sided weakness and 58.42% with right sided weakness. The prevalence of hypertension was found to be 87.64%. The mean BP of patients during admission was found to be 158/87mmHg.

Table 1: Baseline Characteristics

Variable	Control Mean ± SD	Group A Mean ± SD	Group B Mean ± SD
Age (Years)	61.07±8.20	66.03±12.79	58.37±14.63
Systolic BP (mmHg)			
Admission	158.52±9.49	159.09±11.82	154.48±16.38
Discharge	148.89±7.51	139.09±10.42	143.45±10.78
Diastolic BP (mmHg)			
Admission	87.04±6.09	88.79±8.20	79.31±8.44
Discharge	81.11±6.41	78.79±4.85	89.31±6.51
Smoking/ Non-smoking (%)	88.88/11.11	69.69/30.30	80.69±5.30
Previous history of stroke/ no history (%)	11.11/88.88	39.39/60.60	24.13/75.86
Previous history of SHT/ no history (%)	88.88/11.11	81.81/18.18	93.10/6.89

Comparison between the treatment groups based on Mean Difference in NIHSS Score

A better improvement is shown by the Calcium channel blocker treated group as depicted in figure 1.

Statistical analyses were done using One-way ANOVA followed by t-Test. Data was expressed as mean± SD. Here, mean indicates difference between NIHS score before and after treatment. Superscript a, b and c denotes significance at $P < 0.05$, $P < 0.01$ and $P < 0.001$ versus Group B; Superscript x, y and z denotes significance at $P < 0.05$, $P < 0.01$ and $P < 0.001$ versus Control group.

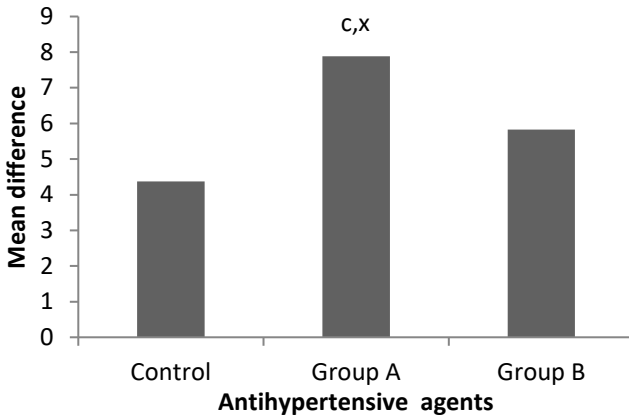

Figure 1: Mean difference in NIHSS score during admission and reviewSuperscript "c" denotes significance of CCB at p<0.001 versus BB; superscript "x" denotes significance of CCB at p<0.05 versus Control group.

CCBs significantly improve the NIHSS Score with respect to LOC compared to Control (P < 0.05) and BB (P < 0.05). There was a significant improvement in the LOC Commands and Motor function of the leg when CCBs was compared with Control (P < 0.001) and BB (P < 0.05). The NIHSS Score of Visual was improved significantly when compared to control group (P < 0.05), Best Gaze and Motor function of the arm improved significantly when compared to control group (P < 0.01). CCBs also significantly improved the Limb Ataxia when compared to control group (P < 0.01) and Beta blockers (P < 0.01). Facial Palsy was significantly improved by calcium channel blockers when compared to Control (P < 0.001). This is represented in Table 2.

Table 2: Difference in NIHSS among the three treatment groups.

Parameters	Control	Group A	Group B
LOC	0.37±0.49	$0.70±0.59^{a,x}$	0.41±0.50
LOC questions	0.56±0.51	0.76±0.56	0.66±0.48
LOC commands	0.30±0.47	$0.82±0.58^{c,x}$	0.52±0.51
Best Gaze	0.07±0.27	$0.36±0.49^{b}$	0.24±0.44
Visual	0.04±0.19	$0.24±0.44^{a}$	0.01±0.31
Facial Palsy	0.26±0.45	$0.76±0.61^{c}$	0.48±0.51
Motor function (Arm)	0.73±0.53	$1.21±0.55^{b}$	1.03±0.57
Motor function (Leg)	0.77±0.43	$1.15±0.36^{c,x}$	0.75±0.75
Limb ataxia	0.22±0.42	$0.58±0.50^{b,y}$	0.24±0.44
Sensory	0.22±0.42	0.33±0.48	0.24±0.44
Language	0.33±0.48	0.42±0.50	0.34±0.48
Articulation	0.19±0.40	0.27±0.45	0.38±0.49
Extinction and inattention	0.15±0.36	0.15±0.36	0.24±0.44

LOC- Level of Consciousness; Superscript a, b and c denotes significance at P < 0.05, P < 0.01 and P < 0.001 versus Group B; Superscript x, y and z denotes significance at P < 0.05, P < 0.01 and P < 0.001 versus Control group.

Comparison of the treatment groups based on difference in Power of limb during admission and follow up

Calcium channel blockers showed significant improvement of power in Right lower limb compared to control group (P < 0.05) and Beta blockers (P < 0.05). Improvement of power in left upper limb showed significance when CCBs were compared to Beta blockers (P < 0.05) and left lower limb showed significance when CCBs were compared to Beta blockers (P < 0.05) and control group (P < 0.05). This is represented in Figure 2.

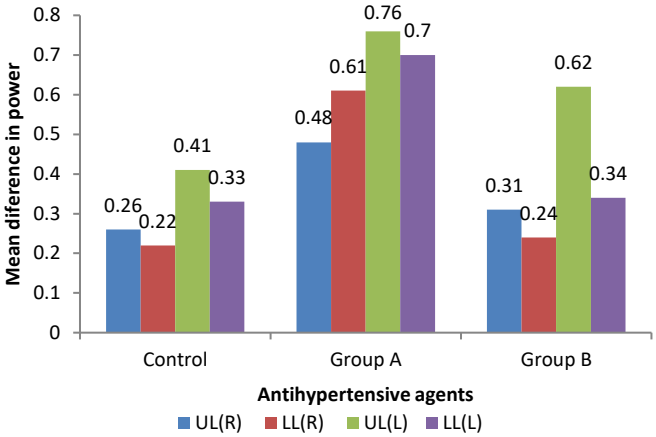

Figure 2: Mean difference in improvement in power of limb between admission and follow up.

Mean Blood Pressure reduction among different treatment groups:

The mean reduction in SBP was significant with respect to CCBs compared to control group (P < 0.001) and Beta blockers (P < 0.001). The mean reduction in DBP was significant with respect to CCBs compared to control group (P < 0.05) and Beta blockers (P < 0.05). This is presented in Table 3.

Table 3: Mean difference in blood pressure reduction between admission and follow up.

Groups	Mean reduction in SBP (mmHg)	Mean reduction in DBP (mmHg)
Control	9.63±5.18	5.93±5.78
Group A	20.29±9.68	9.71±6.61
Group B	11.03±10.47	8.28±3.90

DISCUSSION

Stroke is a condition where the oxygen carrying blood vessels to the brain get either blocked or ruptured leading to the irreversible damage of the neuronal tissue. Major types of stroke include ischemic and hemorrhagic stroke. Ischemic stroke occurs when a clot obstructs the blood flow to the brain, whereas hemorrhagic stroke results from rupture of blood vessels in brain. Transient Ischemic Attack (also known as mini stroke) occurs as a result of a temporary clot blocking the vascular supply. Risk factors of stroke can be classified as fixed (age, gender, heredity, previous vascular events) and modifiable (blood pressure, smoking, alcohol, hyperlipidemia, diabetes mellitus, lifestyle factors). Emergency care and management can improve the recovery rate in stroke survivors.

The study started off with screening of 102 patients, out of which 98 patients were included in the study and only 89 patients came for the follow-up. Patients were categorized into three groups based on their antihypertensive therapy.

33 patients (37.07%) were included in Group A (under regular treatment of Calcium channel blockers), 29 patients (32.58%) in Group B (under regular Beta blocker therapy) and 27 patients (30.33%) in Control group (under irregular anti hypertensive therapy excluding CCBs or Beta Blockers).

In the current study, stroke incidence was higher in males (58.42%) than females (41.57%) in accordance with the study that was conducted by Jeyaraj Durai Pandian et al.,.[7] Patients were categorized into age groups from less than 40 to above 80. Based on the age distribution, patients who were under the age group of 51 – 60 was predominant (37.07% of patients) than other age groups. The baseline characteristics in the study were evaluated in the three groups from admission to discharge and during follow up.

A total of 87.64% patients who enrolled in the study had a history of systemic hypertension. 25.84% were enrolled with history of CVA and 24.71% had a history of both hypertension and CVA. 4.49% of the patients had no previous medical history. The observation made in this study was similar to that conducted by Cairu Li et al., where more than 90% of stroke patients had a history of hypertension.[8]

The mean blood pressures of patients at the time of admission were 157.41±12.93 mmHg (Systolic Blood Pressure) and 88.47±7.95mmHg (Diastolic Blood Pressure).

Out of 89 patients, 67 were smokers and this was found to be greater than any other social habits. This states that smoking is one of the major risk factor for stroke, which was supported by the study conducted by Jingjing Chen et al,.[9]

Stroke may affect either left hemisphere or right hemisphere. If stroke affects the left hemisphere then the deficits will appear in the right side of the body and the stroke in right hemisphere will show left sided weakness. 58.42% of the patients enrolled in the study had right sided hemiparesis. The study focused on assessing the improvement in neurological function using NIHSS score and Power of limb. A mean difference of 7.88±2.45 was observed in NIHSS score of Calcium channel blocker users before and after therapy in comparison with Beta blockers (5.83±1.95) and Control Group (4.37±1.46).

In assessing the difference in power of limb during admission and follow-up, Calcium channel blockers showed a significant improvement in power of limb of right and left lower limb and left upper limb ($P<0.05$), when compared with Beta blocker and control group.

In total reduction of mean blood pressure among the treatment groups, Calcium channel blockers significantly reduced the blood pressure (SBP 20.29±9.68 and DBP 9.71±6.61) than Beta blockers (SBP 11.03±10.47 and DBP 8.28±3.90) and Control group (SBP 9.63±5.18 and DBP 5.93±5.78). This result is in accordance with the study conducted by Emma L. Heeley et al.,[10] and Paolo Verdecchia et al.,[11] concluding that Calcium channel blockers reduce the risk of stroke by reducing the blood pressure than other antihypertensive agents.

CONCLUSION

Our study concluded that Calcium channel blockers were superior to Beta blockers in post stroke patients. It shows significant improvement in neurological functions as assessed by using NIHSS score and an improvement in motor activity as suggested by Power of limb. Calcium channel blockers also provide a better control of Blood pressure.

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