

Effect of Blood Pressure Lowering Therapy in Stroke Patients

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ABSTRACT

Objective: The objective of the study is to assess the effect of blood pressure lowering with Candesartan in patients with stroke and elevated blood pressure admitted in this hospital.

Study Design: Prospective descriptive observational study.

Setting: Neurosurgery, Medical Emergency / OPD, Lady Reading Hospital, Peshawar.

Materials and Methods: This descriptive study was done at the Department of Medicine and Neurosurgery, Postgraduate Medical Institute, Lady Reading Hospital Peshawar from January 2013 to May 2014 (for One year and 5 months period) in a total of 357 patients. In this descriptive study, patients presenting to Emergency department or OPD with stroke and elevated blood pressure, presenting within 30 hours of symptom onset and with SBP \geq 140 mmHg, diastolic $>$ 90 mmHg, were eligible for inclusion. Exclusion criteria were contraindications to or ongoing treatment with an angiotensin receptor blocker, markedly reduced consciousness, patients with chronic heart failure and intolerance to ACE inhibitors, patient unavailability for follow-up and pregnancy or breast – feeding. The acute phase treatment was a fixed dose of 4 mg on day 1, 8 mg on day 2 and 16 mg on days 3 to 7. Blood pressure was measured daily with the patient in the supine position using a blood pressure monitor. All patients were follow-up on day 7 and at 1 and 6 months after discharged from hospital.

Results: Among 357 cases, 68.06% were males and 31.93% females. Majority (37.25%) belongs to age group of 61 – 70 years. Out of these, 66.10% patients were found to have ischemic and 33.89% patients had hemorrhagic stroke. Highest (40.05%) patients belonged to severe hypertensive group i.e. \geq 180/110 mmHg. Target was achieved in 75.91% patients.

Conclusions: Our data suggests that lowering BP in acute ICH is probably safe; however, it remains to be seen if this decreases hematoma expansion or improves outcome.

Key Words: Stroke; hypertension; Candesartan.

Abbreviations: TIA = Transient Ischemic Attack. INTERACT = Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial. SCAST = Scandinavian Candesartan Acute Stroke.

INTRODUCTION

Stroke is a leading cause of morbidity and mortality worldwide.^{1,2} The estimated annual incidence of stroke in Pakistan is 250 per 100,000 population, which is projected to an estimate of 350,000 new cases every year.³ A local study conducted in the urban slums of Karachi (the largest metropolitan city of Pakistan) estimated a 21.8% life – time prevalence of stroke and/or

transient ischemic attack (TIA) in individuals aged 35 years and older.⁴

Chronically elevated blood pressure (BP), so-called ‘hypertension’, is the predominant underlying risk factor for stroke.⁵

Its frequency varies across studies due to variability in patient characteristics, settings and criteria used to define hypertension, but a systematic review of

18 observational studies reported a 53% frequency of hypertension (systolic BP, 150 – 200 mmHg) in the setting of acute stroke.⁶ More impressive was a study which reported a 63% overall frequency of systolic BP >140 mmHg among 563,704 patients with acute stroke attending emergency departments across the United States.⁷

Up to 80% of patients have systolic blood pressure (SBP) \geq 140 mmHg at the time of hospital admission. A spontaneous fall is observed in most patients within 10 – 14 days.⁸⁻¹⁰

The angiotensin receptor type 1 blocker candesartan was used in the ACCESS study, including 339 hypertensive patients (BP > 200 systolic and/or > 110 diastolic pressure) within 30 hours (median) after stroke. Although no effect on death or disability (primary outcome) was seen, the number of deaths and vascular events at 1 year were significantly fewer among candesartan – treated patients.¹¹

The results of three large randomized clinical trials on blood pressure lowering in acute stroke-the Chinese Antihypertensive Trial in Acute Ischaemic Stroke,¹² the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT₂),¹³ and the Scandinavian Candesartan Acute Stroke Trial (SCAST) suggest that treatment should differ according to the type of stroke.¹⁴

The Scandinavian Candesartan Acute Stroke Trial (SCAST), which involved 2029 patients with acute stroke (IS and ICH) and a systolic BP > 140 mmHg within 30 hours (mean time 18 hours) of symptoms onset, randomly allocated to candesartan or placebo, achieved a modest mean systolic BP difference of 5 mmHg ($p < 0.0001$) between groups over 7 days but no difference in functional outcome or vascular events between groups at 6 months.¹⁴

The rationale of the study was to assess the effect of blood pressure lowering with Candesartan in patients with stroke and elevated blood pressure admitted in this hospital.

MATERIALS AND METHODS

This descriptive study was done at the Department of Medicine and Neurosurgery, Postgraduate Medical Institute, Lady Reading Hospital Peshawar from January 2013 to May 2014 (for One year and 5 months period) in a total of 357 patients.

Inclusion Criteria

All patients presenting to Emergency department or

OPD with acute stroke and elevated blood pressure, aged 21 years or older, with a clinical diagnosis of stroke (ischemic or hemorrhagic), presenting within 30 hours of symptom onset and with SBP \geq 140 mmHg, diastolic > 90 mmHg, were eligible for inclusion.

Exclusion Criteria

1. Contraindications to or ongoing treatment with an angiotensin receptor blocker
2. Markedly reduced consciousness
3. Patients with chronic heart failure and
4. Intolerance to ACE inhibitors,
5. Patient unavailability for follow-up and
6. Pregnancy or breast – feeding. Written, informed consent was sought from all patients or their relatives.

Procedure

The acute phase treatment was a fixed dose of 4 mg on day 1, 8 mg on day 2 and 16 mg on days 3 to 7. Patient's compliance was assessed by frequent daily recordings of the doses that the patients received. Blood pressure was measured frequently daily during the morning round with the patient in the supine position using a blood pressure monitor. Dose adjustments were made if SBP was below 120 mmHg or when clinically indicated. All patients received standard treatment, and therapeutic agents other than angiotensin receptor blockers could be administered at investigators' discretion, including additional anti-hypertensive drugs in case of severe and sustained hypertension. All patients were advised to visits in the follow-up period on day 7 and at 1 and 6 months after discharge from hospital. All these information and bio – data including age, gender, hospital course and follow up was recorded.

Statistical Analysis

All the qualitative variables like history of hypertension, drug, and death, were analyzed for descriptive statistics. The frequencies / percentages of these variables were calculated. For quantitative variables for example age, BP levels at various occasions, mean \pm standard deviation was calculated. For sex distribution, male to female ratio was calculated. All the data was analyzed in computer program SPSS version 12 for windows.

RESULTS

Sex Incidence

A total of 357 patients including 68.06% males and 31.93% females were studied according to age, type of stroke, and level of blood pressure. Maximum number of patients (37.25%) belongs to age group of 61 – 70 years with mean age of 65 years (Table 1).

Clinical Presentation

On the basis of type of stroke, 66.10% patients were found to have ischemic and 33.89% patients had hemorrhagic stroke.

Blood Pressure

The patients were divided into five categories according to level of blood pressure and highest number of patients (40.05%) belonged to severe hypertensive group i.e. $\geq 180/110$ mmHg. Out of 357 hypertensive patients with stroke, target was achieved in 75.91% patients (Table 2).

DISCUSSION

Hypertension is common immediately after acute ischemic stroke mainly due to altered brain auto regulation. In Pakistan, evidence based paradigm is still in its infancy and most of the hospitals do not have stroke protocols or clinical care pathways for acute stroke management. Moreover, the choice of antihypertensive therapy for both primary and secondary prevention of stroke may lack the necessary evidence base.^{15,16}

A study highlighted the enormous burden of hypertension in the country. Twenty – two percent of the urban Pakistani population over the age of 15 years, and a third of those aged 45 years and above, had hypertension.¹⁷ The National Health Survey of Pakistan (NHSP) (1990-4) also showed that > 70% of all hypertensive patients (85% in rural areas) in Pakistan are unaware of their disease, despite the fact that the average number of annual visits to the healthcare provider is 5.8 for women and 4.9 for men. This suggests that factors other than poor access to healthcare providers contribute to the lack of awareness and lack of control of hypertension in Pakistan.¹⁸

In a recent study the mean age was 62.0 years; 64.0% of participants were men, 49.1% were taking antihypertensive medication at admission, and 77.9%

Table 1: Various Characteristics of Patients (n = 357).

Demographic Data	No. of Cases	Percentage
Gender Distribution:		
Male	243	68.06%
Female	114	31.93%
Age:		
21 – 30 years	11	03.08%
31 – 40 years	23	06.44%
41 – 50 years	37	10.36%
51 – 60 years	44	12.32%
61 – 70 years	133	37.25%
71 – 80 years	68	19.04%
81 – 90 years	41	11.48%

Table 2: Types of Stroke, Blood Pressure Levels, and Effect of Therapy in Patients (n = 357).

Findings	No. of Cases	Percentage
Type of Stroke:		
Ischemic	268	75.07%
Hemorrhagic	89	24.93%
Blood Pressure Levels:		
Normal < 130/85	25	07.00%
Prehypertension-130-139/85-89	64	17.92%
Stage I-140-159/90-99	77	21.56%
[Moderate 160-179/100-109	48	13.44%
Stage II < [Severe > 180 / > 110	143	40.05%
Effect of Drug:		
Successful criteria	271	75.91%
Un-successful criteria	86	24.08%

had strokes of thrombotic subtype.¹⁹ In our study patients’ mean age was 65 years and majority (68.06%) of patients were males. The male preponderance have also been reported in many local and international studies, which may be due to the reason that in this male oriented society females are not given preference to get medical treatment from male doctors even though they may die in homes untreated.

Hypertension is the single most important modifi-

able risk factors for both ischemic and hemorrhagic strokes. In one local study majority (66.10%) of patients had ischemic stroke. In another local study ischemic stroke constituted 44 (50%), intra-cerebral hemorrhage 26 (29.5%) and subarachnoid hemorrhage 10 (11.3%) cases.²⁰ Similarly in our study majority patients (68.06%) had ischemic stroke and 31.93% had hemorrhagic stroke which are in accordance with the above cited local studies.

In our study we have included all (100%) stroke patients with hypertension while in one local study, hypertension was the most common risk factor for stroke. Majority (75%) stroke patients were hypertensive.²⁰

Hypertension is recognized as the most common risk factor of stroke in one study. Out of 50 cases, 39 cases (78%) were hypertensive.²¹ The findings of hypertension in the above cited local study replicate the findings of hypertension in a study conducted in Karachi by Taj F et al,²² and also these values regarding hypertension is in near range of studies.^{23,24}

A large case – control study evaluating risk factors for stroke was conducted in Beijing China, has shown that 10 risk factors are associated with 90% of the risk of stroke and, of these modifiable risk factors, hypertension is the most important for all stroke sub types and is a particularly dangerous risk factor for intracerebral hemorrhage.²⁵ This study showed that many strokes can be predicted and that relatively simple measures, such as blood pressure control, could reduce the burden of disease. It can be modified with generic medications, and it can also be modified at the population level by implementing such policies as those aimed at reducing salt intake, losing weight and encouraging exercise.

Both ischemic and hemorrhagic stroke has strong gradients with blood pressure. For each rise of 20 mm-Hg in systolic blood pressure, the relative risk of ischemic and hemorrhagic stroke increases 2.23 and 3.18 times, respectively. Fall in blood pressure observed over the 20th century may lead to bigger reduction in the incidence of hemorrhagic stroke compared with ischemic stroke.²⁶ In our study we found that majority of our patients with stroke were in the severe blood pressure level group i.e. $\geq 180/\geq 110$ mmHg.

In this study we treated our hypertensive patients with stroke with Candesartan and it was found successful in majority (75.91%) patients which are in contrast to a study which found that the overall result of SCAST was neutral, and they found no **beneficial** effect of blood pressure lowering treatment with the

angiotensin receptor blocker candesartan in patients with acute stroke and elevated blood pressure.

A meta – analysis of randomized – controlled trials with more than 100 patients which have assessed the effect of blood pressure lowering treatment in acute stroke on death or **dependency**. The addition of the SCAST data did not materially alter the results of the meta-analysis and overall, there was no evidence of a beneficial treatment effect on functional outcome.²⁷ These results are also in line with the results of the latest Cochrane review.²⁸ Contrary results to our study could be due to varied study's designs and sample size selection in the above cited studies.

CONCLUSIONS

The management of hypertension in the setting of stroke is a clinical problem. Our data suggests that lowering BP in acute ICH is probably safe; however, it remains to be seen if this decreases hematoma expansion or improves outcome. As blood pressure management in acute ischemic stroke remains problematic and it should be decided timely as when to start antihypertensives and by how much to reduce BP. Lowering BP is effective for recurrent stroke prevention.

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