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To Study The Relationship Between Blood Pressure Control And Cerebral Microbleeds In Acute Non Traumatic Supratentorial Intracerebral Haemorrhage In A Tertiary Care Centre : An Observational Prospective Study

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Abstract

Background: SICH is still a major source of morbidity and mortality around the world. It is the second most prevalent subtype of stroke, accounting for 4-14 percent of all strokes, with a greater reported incidence in Asian countries than in the West. The prevalence of SICH varies by country, psychological, ethnic, age, gender, and economic characteristics, and it is directly associated to the prevalence of arterial hypertension. Despite increased control of certain risk factors, the incidence of SICH is increasing. Chronic arterial hypertension is the most major modifiable risk factor in spontaneous ICH. The purpose of this study is to find the relationship between blood pressure control and Cerebral Microbleeds in acute non traumatic Supratentorial Intracerebral Hemorrhage.

Material and Methods: This study was a prospective, observational study which was carried out at Apollo Gleneagles Hospital, Kolkata during the period of one year during April 2021 to April 2022. A total of 48 patients were recruited in the study. Patients willing to provide consent, patients with spontaneous intracerebral hemorrhage presenting to the emergency within 24 hours of onset of symptoms, with age > 18 years and GCS > 8 were included in the study. Recruited patients were divided in to two groups, easy to control Blood Pressure and difficult to control Blood Pressure and then number and location of CMB were compared and analyzed between the two group along with the baseline data collection.

Results: Mean age of patients with acute non traumatic supratentorial Intracerebral Hemorrhage was 60.29±13.68 years which ranged from 37 to 79 years. Baseline ICH score was 0.85±0.54 which ranged from 0 to 2. Baseline GCS was 11.27±1.85 which ranged from 9 to 15. Mean NIHSS score was 6.85±4.79 which ranged from 1 to 16. Mean TFSO to Arrival to ED (min) was 739.90±224.84 which ranged from 128 to 937. Mean SBP at Median of 7 hours (mmHg) was 137.40±9.89 which ranged from 126 to 156. Mean number of CMB in deep and lobar location was 9.10±6.48 (ranged from 0 to 26) and 2.48±1.79 (ranged from 0 to 8) respectively.

Conclusion: Our study concluded that though there was significant difference in the systolic blood pressure in the patient with difficult and easy to control BP groups, there was no impact of difficulty in controlling the BP upon the overall number CMB, their locations being deep or lobar, ICH score, GCS score, mRS score or NIHSS.

Keywords: Blood pressure control, Cerebral microbleeds, SICH, CMB

Introduction

The term "spontaneous intracerebral hemorrhage (SICH)" refers to nontraumatic bleeding into the brain parenchyma, which may extend into the ventricles and subarachnoid space.[1] SICH is still a major source of morbidity and mortality around the world. It is the second most prevalent subtype of stroke, accounting for 4-14 percent of all strokes, with a greater reported incidence in Asian countries than in the West.[2] The prevalence of SICH varies by country, psychological, ethnic, age, gender, and economic characteristics, and it is directly associated to the prevalence of arterial hypertension. Despite increased control of certain risk factors, the incidence of SICH is increasing. SICH is twice as common in low- and middle-income nations as it is in high-income countries.[3] Chronic arterial hypertension is the most major modifiable risk factor in spontaneous ICH. The most prevalent sites for hypertensive bleeding are the deep perforator arteries in the pons, midbrain, thalamus, basal ganglia, and deep cerebellar nuclei, which have been persistently injured by hypertension. [4] Old age, male sex, ethnicity, chronic kidney disease, cerebral amyloid angiopathy (CAA), and cerebral microbleeds (CMB) are non-modifiable risk factors for SICH.[5]

The second most prevalent risk factor is CAA, which is a disease that worsens with age. Lobar ICH is commonly caused by cerebral amyloid angiopathy, which is more common in the elderly. Amyloid protein deposition in cortical arterioles causes this disease; amyloid protein accumulation in the basal ganglia and brain stem is uncommon. ICH can be caused by coagulopathies and systemic illnesses like thrombocytopenia.[6] Patients with higher systolic blood pressure (SBP) or diastolic blood pressure (DBP) have 5.5 times increased rate of SICH, compared with normotensive patients.[7] CMB are an accumulation of tiny blood products in the brain tissue that occurs over time. CMB are small hypointense foci discovered using susceptibility-weighted (SW) magnetic resonance imaging (MRI) with a maximum size of 5 mm or even 10 mm.[8] CMB are common in ICH patients and have evolved as radiological markers of underlying cerebral small vessel disease (CSVD), most notably hypertensive arteriopathy (arteriolosclerosis) (deep CMB) or CAA (strictly lobar CMB).[9] The purpose of this study is to find the relationship between blood pressure control and Cerebral Microbleeds in acute non traumatic supratentorial Intracerebral Hemorrhage.

Objectives:

To study the relationship between blood pressure control and Cerebral Microbleeds in acute non traumatic supratentorial Intracerebral Hemorrhage.

Material and Methods: A prospective observational study was conducted 48 patients at Apollo Gleneagles Hospital, Kolkata from April 2021 to April 2022. Patients selected on the basis of inclusion and exclusion criteria, NCCT Brain, MRI Brain, predesigned proforma for data collection.

Inclusion Criteria:

1. All patients with spontaneous intracerebral hemorrhage presenting to the emergency within 24 hours of onset of symptoms.

2. Age >18 years.

3. Glasgow Coma Scale >8.

4. Willing to participate in the study

Exclusion Criteria:

1. Patients with onset of symptoms beyond 24 hours at the time of presentation or whose time of onset of symptoms unknown.

2. Primary intraventricular hemorrhage.

3. Post thrombolysis or mechanical thrombectomy bleeding in acute ischemic stroke patients.

4. Post traumatic intracerebral hemorrhage.

5. Patients those requiring emergency surgical interventions like hemicraniectomy or hematoma evacuation over the next 24 hours of study period as a part of life saving procedures.

6. Pregnancy.

7. Any contraindications for MRI.

8. Refusal to give informed consent

Sample Size Calculation:

The formula used to calculate the sample size was as follows-

$n = (z2pq)/d2$

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Where n = sample size, z = the standard normal deviate, which is 1.96 at 95% confidence interval, p = prevalence in the population of the factor under study

Here we take p = 8.65% = 0.0865 (from previous study)

q =1-p = 0.9135

d = Absolute precision

Thus using the formula n = = , we get n> 47, So we have to take at least 48 patients.

Methodoloy:

This study was a prospective, observational study which was carried out at Apollo Gleneagles Hospital, Kolkata during the period of one year during April 2021 to April 2022. A total of 48 patients were recruited in the study. Patients willing to provide consent, patients with spontaneous intracerebral hemorrhage presenting to the emergency within 24 hours of onset of symptoms, with age > 18 years and GCS > 8 were included in the study. Patients with onset of symptoms beyond 24 hours at the time of presentation or whose time of onset of symptoms unknown, primary intraventricular haemorrhage, post thrombolysis or mechanical thrombectomy bleeding in acute ischemic stroke patients, Post traumatic intracerebral hemorrhage and pregnancy were excluded from trial. Recruited patients were divided in to two groups, easy to control Blood Pressure and difficult to control Blood Pressure and then number and location of CMB were compared and analyzed between the two group along with the baseline data collection. All the statistical data were entered in icrosoft excel sheet 2007 and analysed by performing using IBM SPSS ver. 20 software. P value of <0.05 was considered as significant.

Observation and Results:

Table:1 Characteristics of the study population

Descriptive Statistics					
	N	Minimum	Maximum	Mean	SD
Baseline ICH Score	48	0	2	.85	.545
Baseline GCS	48	9	15	11.27	1.854
mRS Score	48	2	5	4.69	.657
NIHSS	48	1	16	6.85	4.794
TFSO to Arrival to ED (min)	48	128	937	739.90	224.844
Age (years)	48	37	79	60.29	13.686
SBP at Median of 7 hours (mmHg)	48	126	156	137.40	9.892
Mean SBP at 24 Hours (mmHg)	48	116	146	127.40	9.892
No of CMB in Deep location	48	0	26	9.10	6.482
No of CMB in Lobar location	48	0	8	2.48	1.798

Above table shows the baseline characteristics of the patients with acute non traumatic supratentorial Intracerebral Hemorrhage. Mean age of patients with acute non traumatic supratentorial Intracerebral Hemorrhage was 60.29±13.68 years which ranged from 37 to 79 years. Baseline ICH score was 0.85±0.54

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which ranged from 0 to 2. Baseline GCS was 11.27±1.85 which ranged from 9 to 15. Mean NIHSS score was 6.85±4.79 which ranged from 1 to 16. Mean TFSO to Arrival to ED (min) was 739.90±224.84 which ranged from 128 to 937. Mean SBP at Median of 7 hours (mmHg) was 137.40±9.89 which ranged from 126 to 156 whereas mean SBP at 24 Hours (mmHg) was 127.40±9.89 which ranged from 116 to 146. Mean number of CMB in deep and lobar location was 9.10±6.48 (ranged from 0 to 26) and 2.48±1.79 (ranged from 0 to 8) respectively.

Table 2: Comparing clinical parameters between groups

Parameters	Group				P value
	D		E		
	Mean	SD	Mean	SD	
AGE (years)	64.38	11.826	57.11	14.388	0.067
Mean SBP at 24 hours (mmHg)	137.81	4.423	119.3	2.478	<0.001
No of CMB in Deep location	9	6.95	9.19	6.227	0.923
No of CMB in lobar location	2.9	2.022	2.15	1.562	0.15
Baseline ICH Score	0.76	0.539	0.93	0.55	0.306
Baseline GCS	11.38	2.061	11.19	1.711	0.721
mRS Score	4.62	0.59	4.74	0.712	0.53
NIHSS	6.86	4.575	6.85	5.044	0.997
TFSO to arrival to ED	619.19	295.704	833.78	56.613	0.001

Above table shows the comparison of clinical parameters between groups. Mean age of difficult to control patients was higher (64.38±11.82 years) than easy to control patients (57.11±14.38 years), however it was insignificant with p value of 0.067. Mean SBP at 24 hours (mmHg) was significantly (p<0.001) higher in difficult to control patients (137.81±4.43) than easy to control patients (119.30±2.47). No significant difference was obtained between difficult and easy to control patients in terms of no of CMB in deep (p=0.923) and lobar (p=0.150) location, baseline ICH score (p=0.306), baseline GCS (p=0.721), mRS score (p=0.530) and NIHSS

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(p=0.997). TFSO to arrival to ED was significantly earlier in difficult to control patients (619.19±295.704) compared to easy to control patients (833.78±56.613) with p value 0.001.

Table:3 Distribution of location of CMB between groups

Location of CMB	GROUP		Total	P value
	D	E		
Deep	4	8	12	0.726
Lobar	4	5	9	
Predominantly deep	15	19	34	
Predominantly lobar	1	0	1	

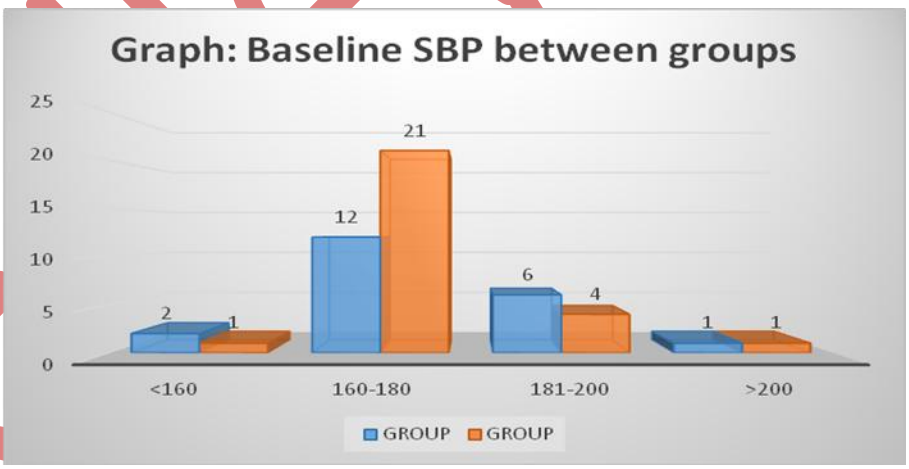
Above table shows the distribution of location of CMB between groups. No significant difference in terms of location of CMB was observed between difficult to control and easy to control patients with p value of 0.726.

Table:4 Distribution of shape of ICH between groups

Shape of ICH	GROUP		Total	P value
	D	E		
Irregular	8	12	20	0.658
Ovoid	13	15	28	
Total	21	27	48	

Above table shows the distribution of shape of ICH between groups. No significant difference in terms of shape of ICH was observed between difficult to control and easy to control patients with p value of 0.658.

Figure:1 Baseline SBP between groups



Graph 1 shows the baseline SBP between groups. No significant difference in terms Baseline SBP was observed between difficult to control and easy to control patients with p value of 0.480.

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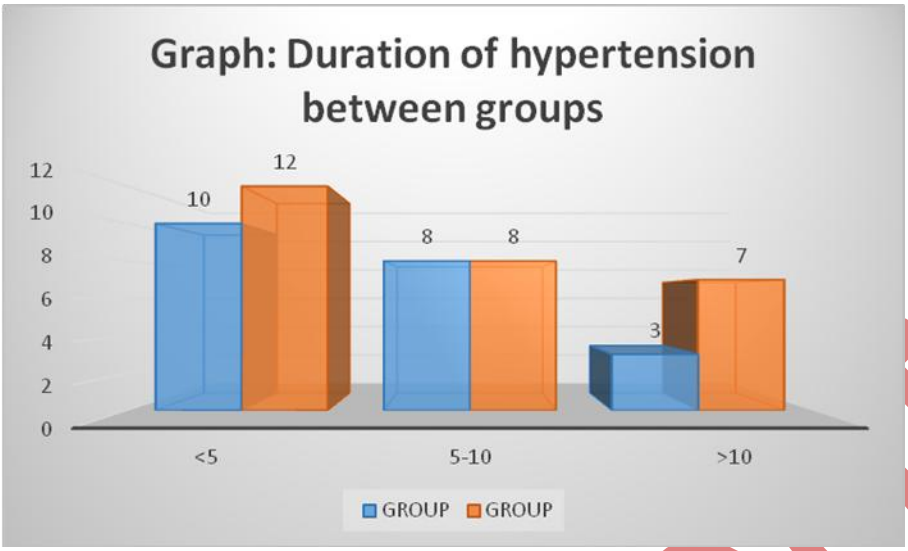
Figure:2 Duration of hypertension between groups



Graph 2 shows the duration of hypertension between groups. No significant difference in terms duration of hypertension was observed between difficult to control and easy to control patients with p value of 0.592.

Discussion:

In the present study, the mean age of patients with acute non traumatic supratentorial intracerebral haemorrhage was 60.29 years which ranged from 37 to 79 years. Baseline ICH score was 0.85 ranging from 0 to 2. Baseline GCS was 11.27 (9 – 15) and mean NIHSS score was 6.85 (1 – 16). Mean TFSO to arrival to ED (min) was 739.90 which ranged from 128 to 937. Mean SBP at Median of 7 hours (mmHg) was 137.40 which ranged from 126 - 156 whereas mean SBP at 24 Hours (mmHg) was 127.40 which ranged from 116 - 146. Khurana D et al observed in their patient population that median time from symptom onset (TFSO) at presentation was 11.15 hrs. 68% patients presented after 12 hours of onset. 88% patients were hypertensives most (81.8%) being poorly compliant to treatment. Baseline Mean GCS was 12; Systolic BP:187.76; Diastolic BP:110. Most patients (56%) had basal ganglia haemorrhage and 24% had midline shift. 80% had CMB on SWI-MRI: 90% predominantly deep, 5% infratentorial and 5% lobar.[10] We observed in the present study that mean number of CMB in deep and lobar location was 9.10 (0 - 26) and 2.48 (0 - 8) respectively. Lee JS et al (2017) observed in their study that CMB were detected in 66% (62 out of 94). The number of CMB per patient ranged from 0 to 121 (median 4.0). Among 958 CMB, 341 (36%) were located in the thalamus, 298 (31%) were lobar, 106 (11%) in the basal ganglia, 83 (9%) in the brainstem, 42 (4%) in cerebellum, 39 (4%) in deep periventricular white matter, 28 (3%) in internal capsule, and 21 (2%) in external capsule. Among the patients with CMB, 3% had strictly lobar CMB, 15% strictly deep CMB, and 2% strictly infratentorial CMB, whereas 80% had mixed CMB.[11]

We observed in the present study that mean age of difficult to control patients was higher (64.38 years) than easy to control patients (57.11 years) and mean SBP at 24 hours (mmHg) was significantly ($p<0.001$) higher in difficult to control patients (137.81) than easy to control patients (119.30). No significant difference was obtained between difficult and easy to control patients in terms of no of CMB in deep ($p=0.923$) and lobar ($p=0.150$) location, baseline ICH score ($p=0.306$), baseline GCS ($p=0.721$), mRS score ($p=0.530$) and NIHSS ($p=0.997$). TFSO to arrival to ED was significantly earlier in difficult to control patients (619.19±295.704) compared to easy to control patients (833.78±56.613) with p value 0.001. **Khurana D et al** observed in their study that easy to control BP group (E) had 52% while rest were in difficult to control BP group (D). "D" patients were likely to be smokers, had higher mortality at 1 month($p=0.052$), had greater number of deep CMB ($p<0.001$).[10] In the present study we found no significant difference in terms of sex distribution between difficult to control and easy to control patients with p value of 0.658. Similar results were reported by Shoamanesh A et al (2018) in their

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study.[12] We studied the location of CMB in all the patients and classified the locations in to main 4 groups namely deep, lobar, predominantly deep and predominantly lobar. Majority of the patients in either group presented with predominantly deep CMB. We didn't observe any difference between the two groups in terms of the location of the CMB. The results of the present study was contradictory to the findings of Khurana D et al. They reported that difficult to control BP patients were more likely to have greater number of deep CMB. Also they suggested that deep CMB were significantly associated with poor BP control.[10] We observed in the present study that all 8 patients who had TFSO ≤360 were difficult to control whereas out of 40 patients with TFSO > 720 min, majority were easy to control (n=27) than the 13 patients who were difficult to control ($p<0.001$). Khurana D et al reported that median time from symptom onset (TFSO) at presentation was 11.15 hrs. 68% patients presented after 12 hours of onset.[10]

Conclusion:

We studied the association of blood pressure control and cerebral microbleeds. It was concluded in the present study that though there was significant difference in the systolic blood pressure in the patient with difficult and easy to control BP groups, there was no impact of difficulty in controlling the BP upon the overall number CMB, their locations being deep or lobar, ICH score, GCS score, mRS score or NIHSS. However, we did observe that patients in whom the control of the BP was easier had longer time from onset of symptom onset. We also didn't find any difference between the two groups in terms of any gender preponderance, symptoms, distribution of risk factors, shape of ICH as well as midline shift. Thus it was concluded that CMB do not impose any influence on BP control in acute ICH.

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