Manipal Journal of Medical Sciences

Volume 3 | Issue 2 Article 3

12-1-2018

Haemoglobin: An amenable outcome factor of acute ischemic stroke after thrombolysis

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Original Article

Haemoglobin: An amenable outcome factor of acute ischemic stroke after thrombolysis

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Abstract

Objective: To study the role of haemoglobin in outcome of thrombolysis after stroke. **Material and method:** Our observational study was conducted over five years at KMC Hospital, Mangalore from July 2011 to July 2016. All patients above the age of 18 years presenting to the hospital within 4.5 hours of onset of stroke were included into the study. The patients' stroke severity was calculated by National Institute of Health Stroke Scale (NIHSS) score, while the outcome was measured by Modified Rankin Scale (mRS) score. The patients were divided into good outcome, poor outcome and expired group of patients depending on the mRS score (<3, ≥3 but <6 and 6 respectively). The blood investigation haemoglobin was measured and recorded in all our patients. At the end of the study, the significance was calculated by standard statistical methods. **Result:** 71.9% patients were found to have good outcome, 24.2% patients had poor outcome and rest were in the expired group of patients. Mean haemoglobin in the good outcome group amongst patients with thrombolysis was 12.8±1.3 gm/dl, while that of poor outcome group was 12±1.2gm/dl. The haemoglobin of expired patients was 14.8±0 gm/dl (p value- 0.0001). **Conclusion:** Our results suggest that haemoglobin levels need to be maintained in patients of stroke treated with thrombolysis. Normal haemoglobin levels may have a neuroprotective action and may predict a good outcome. On the other hand, high haemoglobin levels may lead to a poor outcome.

Key words: Blood transfusion, haemoglobin, hemodilution, mRS, neuroprotection, NIHSS, outcome of stroke, polycythemia, stroke, thrombolysis

Introduction

Tissue surrounding the core infarct area is ischemic but salvageable. This area is known as ischemic penumbra and is the target of most of the therapies for acute ischemic stroke. If blood flow is not compromised, oxygen therapy might protect the penumbra by preventing hypoxia that may expand the stroke volume. Hypoxia (defined as sPO2<95%) has previously been known to cause harm in patients of stroke. This warranted the use of oxygen among patients presented with acute stroke and had hypoxia.[1] We studied whether the low oxygen carrying capacity caused by low haemoglobin can affect the outcome as well, in the Indian scenario.

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Manuscript received : 19/3/2018
Revision accepted : 14/9/18

Materials and methods

Our observational study was conducted over five years at KMC Hospital, Mangalore from July 2011 to July 2016. All patients above the age of 18 years presenting to the hospital within 4.5 hours of onset of stroke were included in the study. The stroke severity was calculated by National Institute of Health Stroke Scale (NIHSS) score. The patients were divided into three categories - good outcome, poor outcome and expired, based on the Modified Rankin Scale (mRS) score (<3, ≥3 but <6 and 6 respectively). The haemoglobin level was recorded at the time of admission and these were correlated with the outcome.

How to cite this article: Mittal SH. Rakshith KC, Misri ZK, Pai S. Haemoglobin: An amenable outcome factor of acute ischemic stroke after thrombolysis. *MJMS*. 2018; 3(2): 4-7.

Results

We were able to include 128 patients in our study. The mean age of our patients was 62.5±13 years. A slight male preponderance was noted in our patients with 68 of the 128 (53.1%) patients being males. A majority of our patients 114 of 128 (89.1%) were found to have Middle Cerebral Artery territory stroke, followed by Posterior Cerebral Artery stroke (8.6%) and Anterior Cerebral Artery stroke. The mean time of presentation to our hospital was 120±55 minutes with a door to needle time of 17±4 minutes (table 1).

Table 1: Basic Details of Patients

Mean Age (years)	62.5±13
Male: Female	17:15
Mean time to presentation (min)	120±55
Door to needle time (min)	17±4
Mean NIHSS	22±7
ACA Stroke	2.30%
MCA Stroke	89.10%
PCA Stroke	8.60%

After analysis of thrombolysis by National Institute of Neurological Disease and Stroke criteria of 1995, 92 of the 128 (71.9%) patients were found to have a good outcome, 31(24.2%) patients had poor outcome and five patients were in the expired group. The mean NIHSS amongst our patients was 22±7 (table 2).

Table 2: Outcome and Haemoglobin in our Patients

	Good outcome mRS<3	Poor outcome mRS ≥3 but <6	Expired mRS=6	p value
Percentage patients in each group	71.90%	24.20%	3.90%	
No. of Patients	92 of 128	31 of 128	5 of 128	
Haemoglobin (gm%)	12.8±1.3	12.1±1.2	14.8±0	0.0001

By the WHO's criteria, 19 males and 22 females had normal haemoglobin; 17 males and 5 females had mild anaemia; and 1 male and 4 female had moderate anaemia. None of our patients had severe anaemia or polycythemia (table 3). In our study, mean haemoglobin in the good outcome group amongst patients with thrombolysis was 12.8±1.3 gm/dl, while that of poor outcome group was 12±1.2gm/dl. The haemoglobin of expired patients was 14.8±0 gm/dl (p value- 0.0001).

Table 3: Haemoglobin (Hb) Profile in our Patients

	Male	Female
Normal Hb	19	22
Mild Anemia	17	5
Moderate Anemia	1	4
Severe Anemia	0	0
Polycythemia	0	0

Discussion

In our study, lower haemoglobin was associated with poorer outcome of thrombolysis. The patients also showed a U-shaped response curve. The low haemoglobin and high haemoglobin were both related to poor outcome.

In Lars Kellert et al., the baseline haemoglobin in patients with good outcome was 14.1±1.4 gm/dl while that in the poor outcome was 13.6±1.6 gm/dl and this was found to be significant (p value- 0.016). The fate of the tissue after a stroke depends upon timely reperfusion of the tissue. Therefore, the oxygen carrying capacity of the blood, that is haemoglobin, may play a decisive role in penumbral destiny.[2] It has been previously concluded that supplemental oxygen therapy was beneficial for patients of acute stroke, if the patient has associated hypoxia.[1, 3] Barlas et al. in their registry based in UK also concluded that low haemoglobin adversely affects the outcome in stroke. They also noted that high haemoglobin was associated with a higher mortality, especially within the first month of stroke.[4] A U-shaped relationship has been demonstrated - a poor outcome is expected with low as well as high haemoglobin.[2]

The possible pathology that may explain the association of anaemia with poor outcome have been hypothesized. Lower haemoglobin due to anaemia may cause a lower oxygen carrying capacity. This lowered oxygen carrying capacity would lead to a lower oxygen yield. This may therefore intensify the

ischemia at the stroke site and contribute to hypoxia within the penumbra.[4,5,6] Besides, due to anaemia, the cerebral auto regulation may be compromised. There is an altered delivery of oxygen to the brain. This may lead to a more turbulent flow to brain. This may further trigger a migration of the thrombus or cause atherothromboembolism. The hyper dynamic circulation may also lead to increased expression on adhesion molecules on the vascular endothelial cells. This leads to a further brain damage during ischemia due to up regulated production of inducible nitric oxide synthase and CXC chemokine receptor.[4, 7-13]

Anaemia is common in India. It affects the outcome and stay in the hospital in many conditions, including stroke, where it is found in as many as 20% patients. Anaemia has been defined as haemoglobin < 12 and less than 13, in females and males respectively by WHO.[2] The WHO staging of anaemia is different from that provided by ICMR for Indians. As per WHO, haemoglobin in males and females above 13 and 12 gm/dl respectively, is normal. The mild anaemia is haemoglobin of 11-12.9 and 11-11.9 in males and females respectively. Moderate anaemia was categorized as haemoglobin of 8-10.9 gm/dl and severe anaemia was defined as less than 8 gm/dl in both males and females.[14] On the other hand, as per ICMR, haemoglobin above 11 is normal. Anaemia is classified as mild with haemoglobin of 10-10.9 gm/dl, moderate with haemoglobin as 7-10 gm/dl, severe with haemoglobin of < 7gm/dl and very severe with haemoglobin < 4gm/dl.[15] Polycythemia has been known as haemoglobin of more than 18 gm/dl in males and more than 16 gm/dl in females.[16]

The haemoglobin in our patients was lower than that in the study conducted previously. However, the Caucasian population is known to have higher haemoglobin compared to Indian population. This is evident as the differences noted in grades of anaemia in WHO and ICMR criteria. Similarly, our study showed lower haemoglobin compared to the Caucasian population studied, for example the study by Kellert et al. [2]

Raised haemoglobin has been found to have a poor outcome in stroke. In fact, polycythemia is known to present with a stroke. The raised haemoglobin is postulated to increase the blood viscosity. With higher viscosity, the cerebral blood flow may decrease. With reduced flow, platelet marginalization increases further fulfilling the Virchow's triad. This mechanism has been accepted as a cause of thrombosis causing stroke. A similar mechanism may be the cause for the poor response seen in patients with high haemoglobin. Polycythemia is treated with hemodilution usually.[17] The Multicenter Austrian Hemodilution Stroke Trial has shown that hemodilution does not influence death and outcome.[18]

Conclusion

We conclude that in patients undergoing thrombolysis, haemoglobin levels need to be well maintained. It can significantly affect the outcome of stroke in patients undergoing thrombolysis. We found that in Indian population also, low haemoglobin as well as high haemoglobin may adversely affect the outcome of thrombolysis. The haemoglobin between 12 and 13 gm/dl in Indian population yielded best results of thrombolysis in patients who suffered stroke.

To the best of our knowledge, no study has been performed on the effect of haemoglobin on thrombolysis in stroke patients in India. Also, we found no study that suggested a range of haemoglobin that would suitably affect the outcomes of thrombolysis in stroke. Patients with myocardial infarction have shown improvement in outcomes with correction of haemoglobin using packed red cells.[19] However, to the best of our knowledge; no study or guidelines have been yet published regarding the correction of haemoglobin in thrombolysis for acute stroke.

Conclusions of our study suggest that guidelines regarding maintenance of haemoglobin levels are needed. The intervention and treatment of haemoglobin abnormalities may result in improved outcomes of stroke post thrombolysis and this may be an adjunctive therapy.

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