Neurology Asia 2024; 29(1) : 201 – 206

Study of the association between anemia and prognosis of moderate-to-severe traumatic brain injury

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Abstract

Objective: To investigate the impact of admission anemia on the prognosis of patients with moderate-to-severe traumatic brain injury (TBI). *Methods:* The clinical data of patients with moderate-to-severe TBI treated in the Department of Intensive Care Unit in our hospital from January 2020 to September 2022 were retrospectively analyzed. The patients were divided into admission non-anemia group (Hb ≥ 100 g/L) and admission anemia group (Hb<100 g/L) based on hemoglobin (Hb) levels. The Glasgow Coma Scale (GCS) score, first blood analysis, arterial blood gas, blood pressure, injury mechanism, pupillary reflex at admission and others were compared, multivariate logistic was used to analyse independent risk factors for patient death. *Results:* One hundred and nine patients were included in the study, of which 17 died in the hospital and 52 had anemia at admission. Compared with patients in the admission non-anemia group, patients in the admission anemia group were younger, had lower admission GCS and trauma score (PTS) scores, higher mortality rates, and longer hospital stay (all *P*<0.05).Univariate analysis showed that moderate-to-severe TBI patients with admission anemia, admission hyperglycemia, GCS<8, PTS<8, abnormal pupillary reflex, and other organ injuries had higher mortality rates (all *P*<0.05) .Multivariate logistic regression analysis showed that admission anemia (OR=9.383, 95% CI=1.086~81.094, *P*=0.042), admission pupillary reflex abnormalities (OR=23.121,95% CI=3.680~145.270,P=0.001), and admission hyperglycemia (OR=15.181, 95% CI=2.019~114.160, P=0.008) are independent risk factors for death of Moderate-to-severe TBI patients. *Conclusions:* Admission anemia is an independent risk factor for death of moderate-to-severe TBI patients, and it can prolong the length of hospital stay for such patients.

Keywords: Anemia, traumatic brain injury (TBI), prognosis, retrospective cohort study

INTRODUCTION

Anaemia is defined by the World Health Organization (WHO) as a haemoglobin (Hb) concentration less than 130 g/L for men and less than 120 g/L for women.[1] The incidence of anemia before neurosurgery is 18%-30%.[2] Preoperative anemia can increase the demand for blood transfusion in patients undergoing non cardiac surgery, prolong the length of hospital stay, and increase postoperative mortality. It is an independent risk factor for postoperative infection.[3] The blood flow in the brain is abundant, and its blood supply accounts for 15% of the left cardiac output.[4] Traumatic brain injury (TBI) is not only related to metabolic changes, but also to an increase in acute and subacute energy demands.[5,6] For such patients, the primary issue is to provide sufficient oxygen for the damaged tissues.

Hemoglobin (Hb) is a key factor in the body's oxygen transports, and anemia can lead to reduced brain oxygen transports and secondary brain damages.[7] Previous studies have shown that acute anemia with Hb below 70 g/L can lead to memory and executive function damage.[8] Anemia can cause the decrease of oxygen saturation of internal jugular vein, while the decrease of oxygen saturation of internal jugular vein in TBI patients is related to the adverse outcome of nervous system.[9] Previous studies also suggests that anemia is associated with mortality in TBI patients.[10-13] Litofsky *et al*.[14] found a correlation between admission anemia and adverse Glasgow

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Date of Submission: 6 July 2023; Date of Acceptance: 6 January 2024

https://doi.org/10.54029/2024pda

Coma Scale (GCS) in TBI patients. GCS has been used mainly applied to stroke patients, post-traumatic brain surgery patients, and patients with varying degrees of coma caused by various reasons. This score can comprehensively reflect the current severity of consciousness disorders in patients.[14] However, some studies suggest that admission anemia (100 g/L) has an incidence of 9.8% in severe TBI patients and is not a risk factor for death in severe TBI patients.[15] Till to-date, there are few studies reporting on the relationship between anemia and the prognosis of TBI patients both in China and internationally.

TBI patients have severe illness and undergo rapid changes. If relevant indicators can be used to quickly evaluate their condition and prognosis upon admission, it may be helpful for resuscitation and treatment. Thus, this study aimed to analyze the relationship between admission anemia (100 g/L) and mortality, total hospital stay, and PICU hospital stay in patients with moderate-to-severe TBI.

METHODS

Data source

The clinical data of patients with moderate-to-severe TBI treated in the Department of Intensive Care Unit (ICU) in our hospital from January 2020 to September 2022 were retrospectively analyzed. A total of 109 patients were included as the study cohort. Inclusion criteria were: TBI patients with age ≥ 18 years old, admission GCS 3-14 points (for individuals with consciousness disorders). Exclusion criteria: surgery and blood transfusion before admission, diabetes, large dose of sugary solution infusion before and after admission, transport to our hospital more than 24 hours after trauma, hemophiliacs, patients receiving trauma surgery in other parts of body except the head.

It is found that the maximum vasodilation may occur when Hb is 80-90 g/L; Hb < 100 g/dl is related to mortality, severe disability, delayed cerebral ischemia, and others, which will lead to lower oxygen saturation indexes such as StO2, and Hb is often used as the threshold of blood transfusion in clinic.[16]Thus, define anemia as Hb <100 g/L in blood analysis upon admission[16,17]; hyperglycemia is defined as the value of blood sugar of admission artery>11.1 mmol/L; Unequal or dilated pupils at admission are fixed as abnormal pupils. Patients with TBI are given routine care, sedation and analgesia, and patients with intracranial hypertension are given 20% mannitol and/or 3% NaCl solution dehydration treatment. Patients with surgical indications shall be given relevant neurosurgery surgery.

Data collection

The following information were collected: Gender, weight, age, admission GCS score, first admission blood analysis, arterial blood gas, blood pressure, injury mechanism, pupillary reflex, whether there is other organ injury besides TBI, diagnosis, skull surgery methods, and others. The pediatric trauma score (PTS) is calculated based on weight, airway status, systolic blood pressure, consciousness level, fracture and wound condition scores[15,18], which can assess the severity of trauma in patients. The GCS scoring results are interpreted as follows: 15 points: clear consciousness; 12-14 points: Mild disturbance of consciousness; 9-11 points: moderate consciousness disorder; 3-8 points: Severe consciousness disorder. Hospital death is the primary end point indicator of this study. The secondary indicators were the length of stay in Intensive Care Unit and the total length of hospitalization.

Statistical analysis

SPSS 20.0 statistical software was used to analyse the dates. The measurement data is verified by Shapiro-Wilk test whether the data is normal distribution. The normal distribution data is represented by mean ± standard deviation ($x \pm s$), and the skewed distribution data is represented by M (P_{25}, P_{75}). If it is normal distribution, two independent samples t-test shall be used for inter group comparison; If the distribution is not normal distribution, the non parametric test method (Mann Whitney U test) shall be used for inter group comparison; The counting data was compared between groups using chi square test; Univariate and multivariate logistic regression analysis to investigate whether anemia is an independent risk factor for death. The α value is 0.05 as a standard test.

RESULTS

Comparison of clinical characteristics between non-anemia group and anemia group

A total of 109 patients with moderate-to-severe TBI were included in this study. The primary cause of moderate-to-severe TBI is motor vehicle accidents (41.3%). Fifty-two patients were admitted with Hb<100 g/L. 109 patients with moderate-to-severe TBI were divided into

non-anemia group (Hb≥100 g/L) and anemia group (Hb<100 g/L) based on their admission Hb levels. Through univariate analysis, it was found that compared with non-anemia patients, the anemia group had younger age, lighter weight, higher mortality rates; lower number of white blood cells (WBCs), lower GCS and PTS scores upon admission, and longer total hospital stay, all $P<0.05$. However, there was no statistically significant difference between the two groups in terms of comorbidities with other organ injuries, abnormal admission pupillary reflex, admission platelet counts (PLT), admission blood glucose levels, PICU (Postoperative Intensive Care Unit) hospitalization time, and injury mechanism (all $P>0.05$) (Table 1).

Comparison of clinical characteristics between survival group and death group

Ninety-two patients improved and survived after treatment, while 17 patients died in the hospital who had failure to treatment, and the mortality rate was 15.6%. There was no statistically significant difference between the survival group and the death group in terms of age, weight, admission white blood cells, platelets, and injury mechanism ($P>0.05$). The differences in admission GCS scores, admission PTS scores, admission pupillary reflex abnormalities, TBI combined with other organ injuries, admission hyperglycemia, and admission Hb between the survival and death groups were statistically significant, indicating that these factors are related to mortality in patients with moderate-to-severe TBI (Table 2).

Logistic regression analysis of related factors of death from brain injury in patients

This study established a multivariate logistic regression model using indicators such as admission hyperglycemia, GCS<8, PTS<8, admission abnormal pupillary reflex, presence or absence of other organ damage, and Hb<100 g/L to explore the impact of these factors on mortality in moderate-to-severe TBI patients. The relevant factors and assigned values of death in severe TBI are shown in Table 3. The admission hyperglycemia (OR=15.181, 95% CI=2.019-114.160, $P=0.008$), admission pupillary reflex abnormalities (OR=23.121, 95% CI=3.680-145.270, $P=0.001$), and admission anemia (OR=9.383, 95% CI=1.086-81.094, $P=0.042$) were independent risk factors for death in patients with moderate-to-severe TBI, while concomitant other organ injuries (OR=3.257, 95% CI=0.360-

Table 1: Comparison of clinical characteristics between non-anemia group and anemia group

Clinical characteristics	Hb≥100g/Lgroup (n=57)	Hb<100g/Lgroup (n=52)	Z/χ^2/t value	*P* value
Age[M (P_{25}, P_{75}) years]	35.0 (21.0, 76.5)	34.0(23.0, 74.8)	-4.966	0.000
Male gender (n, %)	49(85)	47(82)	0.264	0.627
Weight[M (P_{25}, P_{75}) kg]	60.0 (55.5, 73.5)	55.0(53.0, 74.0)	-5.540	0.000
Mortality (n, %)	4	13	6.680[a]	0.010
Admission GCS scores M (P_{25}, P_{75})	9.0 (7.0, 12.0)	7.5(5.0, 10.75)	-2.314	0.021
Admission PTS scores M (P_{25}, P_{75})	7.0 (5.5, 8.0)	6.0(3.0, 8.0)	-2.193	0.028
Admission abnormal pupillary reflex (n, %)	8	14	2.804[a]	0.094
PLT (x±s, $\times10^9$/L)	269.9 ±79.6	258.0 ±103.8	0.675[b]	0.501
WBC (x±s, $\times10^9$/L)	19.2 (13.4, 24.5)	14.4 (11.8, 19.8)	-2.490	0.013
Admission blood glucose (mmol/L)	6.0 (5.1, 8.4)	6.3 (5.2, 10.3)	-0.631	0.528
Combined organ damage (n, %)	26	26	0.210	0.647
PICU hospitalization time [M (P_{25}, P_{75}), d]	1 (1, 3.5)	1 (1, 3)	-0.361	0.718
Hospital stay[M (P_{25}, P_{75}), d]	20 (11.5, 28.0)	15.5 (8.0, 24.5)	-2.107	0.035
Cause of injury (n, %)			3.309[a]	0.191
Traffic accident	27	18		
High crash	22	20		
Others	8	14		

a: χ^2value: b: tvalue

Table 2: Comparison of clinical characteristics between survival group and death group

Clinical characteristics	Total (n=109)	Survival group (n=92)	Death group (n=17)	Z/χ^2/t value	*P* value
Age[M (P_{25}, P_{75}) years]	54.0 (22.0~74.5)	37.5 (23.0, 70.5)	44.3 (22.6, 74.8)	-0.530	0.596
Weight[M (P_{25}, P_{75}) kg]	60.0 (57.4~74.3)	59.0 (56.5, 72.5)	63.0 (52.4, 73.0)	-0.410	0.682
Admission abnormal pupillary reflex (n, %))	22 (20.2)	7 (7.6)	15 (88.2)	57.900[a]	0.000
WBC (x±s, $\times10^9$/L)	16.6 (12.2, 22.2)	17.0 (12.1, 21.7)	15.9 (13.3, 23.1)	-0.464	0.643
PLT (x±s, $\times10^9$/L)	264.2±91.7	268.6±91.9	240.5±89.5	1.164[b]	0.247
Hb (x±s, g/L)	99.4±19.6	101.7±18.9	87.4±19.3	2.861[b]	0.005
Hb<100 g/L (n, %)	52 (44.7)	39 (40.4)	13 (76.5)	6.680[a]	0.010
Admission GCS<8 (n, %)	48 (44.0)	33 (35.7)	15 (88.2)	15.966[a]	0.000
Admission PTS<8 (n, %)	68 (62.4)	53 (48.6)	15 (88.2)	5.735[a]	0.017
Admission blood glucose >11.1 mmol/L (n, %)	21 (19.3)	10 (10.9)	11 (64.7)	26.737[a]	0.000
Combined organ damage (n, %)	52 (47.7)	39 (42.4)	13 (76.5)	6.680[a]	0.010
Cause of injury (n, %)				0.285[a]	0.867
Traffic accident	45 (41.3)	38 (41.3)	7 (41.2)		
High crash	42 (38.5)	33 (30.3)	7 (41.2)		
Others	22 (20.2)	21 (19.3)	3 (17.6)		

a: χ^2value; b: tvalue

29.501, *P*=0.294), admission PTS<8 (OR=1.958, 95% CI=0.151-25.315, *P*=0.607) and admission GCS<8 (OR=3.892, 95% CI=0.373-40.595, *P*=0.256) were not independent risk factors for death in moderate-to-severe TBI patients, as shown in Table 3.

DISCUSSION

Anemia is the most common blood system disease of surgical patients, which is often a symptom of a potential disease, or may affect the results of surgery under some conditions.[19] Among patients undergoing various neurosurgery operations, anemia has been identified as an independent factor affecting the outcome of patients.[20-22] Liu *et al*.[23] retrospectively analyzed the incidence of preoperative anemia in 8,275 patients undergoing elective neurosurgery and found the incidence to be 19.94%. The anemia frequency of patients with different types of surgery was different, and the anemia frequency of patients undergoing cerebrovascular resection and brain tumor resection was relatively high. The blood flow in the brain is more abundant and has a higher demand for oxygen compared to other organs. In addition to metabolic changes, TBI is also

Table 3: Logistic regression analysis of related factors of death from brain injury in patients

Risk factors	*B*	*SE*	*Wald* χ^2	*P*	OR	OR (95%*CI*)
Constant term	-18.818	4.909	14.697	0.000		
Admission hyperglycemia	2.720	1.029	6.982	0.008	15.181	2.019~114.160
Admission GCS<8	1.359	1.196	1.290	0.256	3.892	0.373~40.595
Admission PTS<8	0.672	1.306	0.265	0.607	1.958	0.151~25.315
Admission anemia	2.239	1.100	4.140	0.042	9.383	1.086~81.094
Combined organ damage	1.181	1.124	1.103	0.294	3.257	0.360~29.501
Abnormal pupillary reflex	3.141	0.938	11.218	0.001	23.121	3.680~145.270

associated with an increase in acute and subacute energy demand.[5,6] It is thus critical to provide sufficient oxygen for the damaged cerebral tissue.

The oxygen delivery of the body mainly depends on three factors: Hb concentration, cardiac output and oxygen saturation. When the patient's anemia level exceeds the body's compensatory capacity, their blood oxygen carrying capacity decreases and causes varying degrees of harm to the body. A meta-analysis study found that preoperative anemia (Hb<120 g/L in male patients) is associated with poor postoperative prognosis in surgical patients, and preoperative anemia increases patient mortality (OR=2.90, 95% CI=2.30-3.68, I2=97%, *P*=0.000).[24]

The harm of anemia to TBI should not be ignored. After TBI, due to factors such as anemia, hypoxia, and reduced cerebral blood perfusion, the transport of oxygen and metabolic substances in brain tissue is reduced, and the clearance of metabolic waste and toxins is reduced, resulting in secondary brain damage. Hare *et al*.[11] found in a TBI rat model that anemia can expand the brain contusion area and increase brain cell apoptosis, exacerbating secondary brain damage. Previous studies have also shown that a decrease in hematocrit is associated with a decrease in the prognosis score of TBI patients upon discharge.[25] Hb ≤ 100 g/L can reduce brain oxygen and increase the risk of poor prognosis in TBI patients.[12] Red blood cell transfusion can increase brain tissue oxygen metabolism in TBI patients.[26,27]

This study found that the incidence of admission anemia (Hb<100 g/L) in patients with moderate-to-severe TBI was about 50%, indicating that anemia at admission is more common in patients with moderate-to-severe TBI. Yang *et al*.[16] found that the incidence of anemia in the emergency room upon admission (Hb<100 g/L) in patients with severe TBI was higher in the mortality group than in the survival group (13.2% vs. 5.7%), but the difference was not statistically significant. However, our study found that the incidence of admission anemia in the death group was significantly higher than that in the survival group (76.5% vs. 40.4%), with statistically significant differences, indicating a correlation between anemia and mortality in patients with moderate-to-severe TBI.

Without considering the influence of blood transfusion factors, anemia (Hb ≤90g/L) occurring within the first 7 days of hospitalization is an independent factor in the death of TBI patients.[13] Studies have shown that an average Hb concentration of<90 g/L within the first 7 days of hospitalization is an independent factor in the mortality of patients with severe TBI.[10] This study found in multivariate logistic regression analysis that admission anemia (Hb<100 g/L) to be an independent risk factor for death in patients with moderate-to-severe TBI.

Litofsky *et al*.[14] found that the lower the admission Hb of TBI patients, the lower their GCS score. This study also found that in patients with moderate-to-severe TBI, the admission GCS and PTS scores of the anemia group were lower than those of the non-anemia group. In addition, admission anemia was associated with prolonged total hospital stay of patients. PTS is an important indicator for evaluating the severity of a patient's post-traumatic condition. Studies have shown that in patients with severe TBI (GCS≤8), the mortality rate of patients with PTS≤3 is five times higher than that of patients with PTS>3 (P=0.000).[16] However, this study found through multivariate logistic regression analysis that PTS<8 is not an independent risk factor for death in patients with moderate-to-severe TBI.

This study also has the following limitations. First, only the data of moderate and severe TBI patients at admission were recruited to analyze the influence of anemia on the death of patients. The number of patients included in the study was too small, and the anemia criteria of male and female were not considered to be different. In the future, we should continue to collect further data and analyze different genders. Secondly, the influence of the change of Hb level on the prognosis of TBI patients during hospitalization needs further study and exploration.

In conclusion, admission anemia (Hb<100 g/L) is common in patients with moderate-to-severe TBI. Admission anemia is associated with mortality in patients with moderate-to-severe TBI and is an independent risk factor for mortality in such patients. In addition, admission anemia is associated with prolonged hospitalization of patients with moderate-to-severe TBI.

DISCLOSURE

Ethics: This study was approved by the Medical Ethics Committee of Jiaozhou Central Hospital of Qingdao (2023-01-008).

Data availability: All data generated or analyzed during this study are included in the published article.

Financial support: None

Conflicts of interest: None

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