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Original Article

Serum albumin is a predictor for duration of weaning in patients with traumatic brain injury

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Abstract: Serum albumin is a widely used method of accessing nutritional and inflammation status in both acute and chronically ill patients. The aim of this study was to find out whether the serum albumin concentration could be a predictor for duration of weaning in patients with isolated traumatic brain injury. A retrospective study was conducted in the ICU of Huashan Hospital affiliated to Fudan University between January 2009 and June 2014. 104 patients suffering from traumatic brain injury were included. Serum albumin concentration, Motor GCS score and other clinical and laboratory data were collected and analyzed. Serum albumin concentration was associated with duration of weaning, patients with higher albumin levels had shorter duration of weaning, either at admission ($P = 0.002$) or at weaning ($P < 0.001$). Lower albumin levels appeared to be more frequent in patients with epidural hematoma ($P = 0.004$). Serum albumin level seems to be an independent predictor for duration of weaning in patients with isolated traumatic brain injury. Therefore it is advisable that albumin can be used for clinical instruction for weaning in patients with isolated brain injury.

Keywords: Serum albumin, brain injury, ventilator weaning, Glasgow Coma Scale

Introduction

Patients suffering from traumatic brain injury (TBI) often require mechanical ventilation (MV) as a component of their initial care in intensive care units (ICU) [1]. But clinical experience showed that endotracheal intubation with mechanical ventilation and ventilation circuits can lead to potential complication and some unfavorable physiologic effects especially in long-term ventilation patients [2]. It was reported that cumulative frequency of pneumonias is from 8.5% during first 3 days after beginning of ventilation, 21.1% during first 7 days, 32.4% to 14th day and 45.6% in cases with mechanical ventilation with duration over 14 days [3]. What's more, long-term mechanical patients account for an increase ICU costs > 37% [4]. The weaning process is a gradual decrease in ventilator setting that leads to termination of MV support [5]. But more than 40% of total duration of MV is spent enduring the weaning process [6]. So it is crucial to find some clinical assessment tools to instruct weaning from MV.

Serum albumin is a widely used method of accessing nutritional and inflammation status in both acute and chronically ill patients. Although many studies explored the relationship between serum albumin levels and the duration of weaning in patients with mechanical ventilation, but its effect on patients' outcome of weaning was still unknown. The aim of this study was to find the relationship between serum albumin and duration of weaning in patients with isolated TBI.

Methods and materials

Patient selection

One hundred and four patients have been included in our retrospective study from January 2009 to June 2014 in the ICU of Huashan Hospital affiliated to Fudan University, Shanghai, China. Patients with isolated traumatic brain injury received mechanical ventilation for more than 7 days and had successful weaning were entered into the study. To insure homogeneity of our cohort, patients were excluded if they

Table 1. Characteristic of the patients at baseline

Characteristic	Descriptive statistics (N = 104)
Age-years	
Median (Interquartile range)	52.5 (39-60)
Male sex-n (%)	88 (84.6)
Motor GCS score	
Median (Interquartile range)	7 (5-10)
Serum albumin (at admission)-g/liter	35.7±7.0*
Serum albumin (at weaning)-g/liter	31.8±5.1**
Intracranial lesion, n (%)	
Epidural hematoma	18 (17.3)
Subdural hematoma	44 (42.3)
Traumatic subarachnoid hemorrhage	65 (62.5)
Intra-cerebral mass lesion	69 (66.3)
Compressed/absent basal cisterns	2 (1.9)
Brainstem/cerebellar lesion	4 (3.8)
Diffuse axonal injury	12 (13.5)
Neurosurgical procedure, n (%)	
Craniotomy	59 (56.7)
ICP monitor insertion	77 (74.0)
Nonsurgical	12 (11.5)
Co-morbidities, n (%)	
Chronic obstructive pulmonary disease	9 (8.6)
Diabetes mellitus	15 (14.4)
Coronary artery disease	11 (10.6)
Congestive heart failure	9 (8.7)
Hypertension	20 (19.2)
Hypothyroidism	7 (6.7)

Univariate analyses were used to estimate the association between duration of weaning and variables. *$P < 0.05$, **$P < 0.001$.

had severe injuries with Abbreviated Injury Scale (AIS) score > 2 in any other body region, penetrating TBI, died in the ICU, postoperative status of pulmonary resection, administration of albumin before admission, previous advanced directives to withhold life-sustaining interventions and age younger than 16 years old. And all patients had no acute liver disease or chronic active liver disease. No patents received albumin during the study period. The principle was carried for definitive withdrawal of mechanical ventilation, weaning was considered successful if the patients were able to breathe spontaneously without ventilator support for more than 24 h [7-10]. This study was approved by the ethics committees of Huashan hospital, Fudan University, China.

Data collection

All patients had no acute liver disease or chronic active liver disease. Serum albumin was always measured by means of the bromocresol purple method using automated equipments. These reagents and equipments were convenience-validated and standardized in our central clinical laboratory. The data of serum albumin concentration at admission within 3 days after traumatic brain injury and at the beginning of weaning were collected.

Some patients with severe TBI underwent early tracheostomy or PEG placement, and other patients underwent tracheostomy after long-term (7 days) ventilation through endotracheal intubation. Our ICU regularly follows a weaning protocol. When the following criteria are fulfilled, we try to preceding the beginning of weaning: Improvement or resolution of the underlying causes of respiratory failure, PaO2/FIO2 of > 200 mm Hg with positive end-expiratory pressure (PEEP) of ≤ 8 cm H_2O, hemoglobin level of > 8 g/dL, cardiovascular stability, and adequate level of consciousness. Therefore, if pressure support is ≤ 10 cm H_2O, FIO2 is ≤ 0.4, and PEEP is ≤ 8 cm H_2O, with spontaneous breathing, a spontaneous breathing trial (PEEP of 5 cm H_2O and pressure support of 6 cm H_2O) for 30 min is undertaken. If the respiratory rate/tidal volume ratio stays < 100 and there is no clinical evidence of respiratory distress, extubation or disconnection from ventilator is performed. The spontaneous breathing trial is repeated only once a day for those patients who failed [11]. Sedation and analgesia during mechanical ventilation were obtained through continuous intravenous midazolam and fentanyl, adjusted to a Ramsay scale from 3 to 4.

The primary end point was the duration of weaning, length of mechanical ventilation and length of stay in the ICU. Weaning duration was defined as the time between the beginning of weaning until successful extubation. It was categorized into three periods as follows: early (< 5 days), moderate (5 days to 8 days) and late (> 8 days). ICU days and ventilation days were also divided into 3 levels. The other parameters included: age, sex, injury severity (as measured by motor Glasgow Coma Scale (GCS) score), type of intracranial lesion, Neurosurgical procedure (craniotomy and intracranial pressure [ICP] monitor insertion) and comorbidities.

Table 2. The association between characteristics and serum albumin level

Variable		Number of patients stratified by serum albumin level, g/l (at admission)				Number of patients stratified by serum albumin level, g/l (at weaning)			
		< 31	31-35	> 35	*P*	< 31	31-35	> 35	*P*
Age	≤ 65	19	26	40	0.938	32	33	20	0.527
	> 65	2	9	8		7	11	1	
Sex	Male	18	29	41	0.927	35	37	16	0.049
	Female	3	6	7		4	7	5	
Motor GCS score	≤ 8	14	31	28	0.098	27	29	17	0.549
	> 8	7	4	20		12	15	4	
Duration of ICU	< 20	7	13	18	0.645	14	16	8	0.880
	20-30	10	17	15		18	16	8	
	> 30	4	5	15		7	12	5	
Duration of ventilation	< 10	8	7	17	0.417	11	14	7	0.097
	10-18	10	23	25		22	23	13	
	> 18	3	5	6		6	7	1	
Duration of weaning	< 5	5	13	27	0.022	12	18	15	< 0.001
	5-8	8	18	16		15	21	6	
	> 8	8	4	5		12	5	0	
Intracranial lesion	Epidural hematoma	8	6	4	0.004	11	3	4	0.590
	Subdural hematoma	11	13	20	0.422	20	16	8	0.150
	Traumatic subarachnoid hemorrhage	11	22	32	0.303	18	35	12	0.069
	Intra-cerebral mass lesion	14	22	33	0.664	21	31	17	0.239
	Compressed/absent basal cisterns	1	0	1	0.732	0	2	0	0.686
	Brainstem/cerebral lesion	1	3	0	0.135	0	3	1	0.240
	Diffuse axonal injury	2	5	5	0.909	5	3	4	0.803
Co-morbidities	Chronic obstructive pulmonary disease	3	4	2	0.126	2	5	2	0.489
	Diabetes mellitus	5	6	4	0.077	5	7	3	0.890
	Coronary artery disease	3	6	2	0.088	4	4	3	0.795
	Congestive heart failure	4	2	3	0.174	4	2	3	0.931
	Hypertension	5	7	8	0.489	4	8	8	0.020
	Hypothyroidism	2	2	3	0.717	3	3	1	0.638
Neurosurgical Procedure	ICP monitor	18	21	20	0.407	25	22	12	0.770
	Craniotomy	14	26	37	0.001	28	34	15	0.105
	Nonsurgical	3	1	8	0.627	5	4	3	0.487

GCS = Glasgow Coma Scale. ICP = craniotomy and intracranial pressure. ICU = Intensive Care Units.

Data analysis

The result are reported as median (range) or as mean ± standard deviation (SD) as appropriate. Univariate analyses were used to estimate the association between duration of weaning and variables: age, sex, serum albumin (at weaning and admission), intracranial lesion, neurosurgical procedure and comorbidities. Spearman rank order correlation coefficient (Spearman's rho, rs) for nonparametric data was used to study the association between serum albumin level and variables: age, sex, motor GCS score, duration of ICU, duration of ventilation, duration of weaning, intracranial lesion, comorbidities and neurosurgical procedure. The statistical analysis was performed with SPSS 16.0. And a *P* value of 0.05 was considered statistically significant.

Results

Baseline characteristics, correlation of clinical variables and serum albumin

The details of the 104 patients were compared in **Table 1**. Correlations of serum albumin concentration with weaning days, GCS, ventilation days, ICU days and other clinical variables were shown in **Table 2**. Respectively, serum albumin concentration was associated with duration of weaning (**Figure 1**), patients with higher albu-

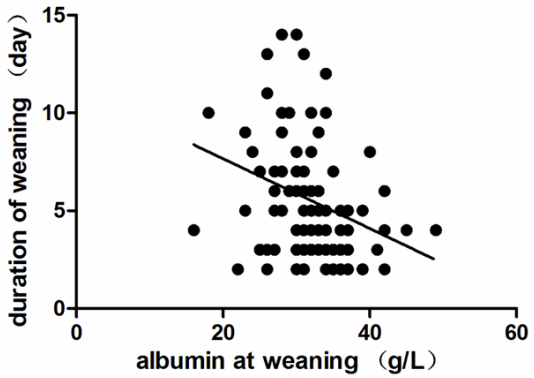

Figure 1. The relationship between albumin and duration of weaning.

min levels had shorter duration of weaning, either at admission (P = 0.002) or at weaning (P < 0.001). We also found lower albumin levels appeared to be more frequent in patients with epidural hematoma (P = 0.004).

Discussion

The goal of this study was to determine whether the serum albumin concentration could be a predictor of duration of weaning. Our study demonstrated that the serum albumin level was an independent predictor of the duration of weaning in patients with isolated TBI and identified that patients suffering from epidural hematoma had lower albumin levels.

A hyper catabolic state is usually observed in TBI patients with long-term ventilationin intensive care units. Hyper-metabolism may last for several weeks after TBI is healed [12]. A state of hyper-metabolism is created by anorexia, muscle protein breakdown, body weight loss and hypoalbuminaemia [13]. As there is no stored reservoir of albumin, the serum concentration depends upon the balance between albumin synthes is in the liver and albumin metabolism. Previous studies showed that infections, traumatic events andother clinical conditions activating an inflammatory process may repress synthesis of albumin [14-17]. Hypoalbuminaemia may be considered the result of a decrease in its absolute content, altered metabolism, the redistribution from the intravascular to the interstitial space [18] and the alteration of volaemia [19]. The hypoalbuminemia following head injury probably be mediated by IL-1 or other toxins such as neutrophil-derived toxic oxygen radicals. The increase in endothelial permeability in response to inflammatory can lead to the loss of albumin [20]. But the reason why patients with epidural hematoma had significantly lower albumin levels, compared with other types of intracranial lesion, was still unknown.

The important physiologic roles for serum albumin include avidly binds free fatty acids, scavenges oxygen radicals and mental ions, and interrupts damaging oxidative processes in both intravascular and extravascular space [21]. Albumin may also bind the lysophosphatidic acid released from platelets and prevent pathologic platelet aggregation [22, 23]. Whether the alteration of serum albumin has an impact on the outcomes of TBI patientshas received increasing attention in recent years. Francis and coworkers [24] examined 138 patients with TBI and found that patients with albumin remained < 25 g/L had an unfavorable outcome. A meta-analysis of cohort studies showed significantly raised odds of mortality and morbidity in patients with each decrease of 10 g/L in serum albumin concentration [25]. So the maintenance of the serum albumin concentration within normal ranges is crucial [19]. Organ function and the Sequential Organ Failure Assessment score may be improved with treating intensive care patients with albumin [26]. Controversially, a prospective, randomized, double-blind study showed that higher mortality rate has been detected in traumatic patients, especially after head injury, when treated with albumin [27]. Another study also found that in TBI patients, resuscitation with isotonic albumin solution was associated with higher mortality when compared with saline [28]. However, markedly neuro-protective has been proved when administered in a high concentration human serum albumin in models of TBI and the improvement of neurological score and reduction of histological damage were found [29], but the neuro-protective mechanisms of high-concentration albumin requires further study.

Serum albumin, as acommon used predictor of non-pulmonary factor, had been proved to be a predictor of weaning [3, 30-33]. In our study, all patients suffered from isolated TBI and we found the increase of serum albumin levels by each 5 g/L may potentially provide a beneficial impact on patients' outcome of weaning significantly. Serum albumin has been recognized

as an indicator of both the nutritional and inflammation status. There were reports demonstrated that malnutrition caused muscle mass decrease, muscle dysfunction and fiber type percentages change [34, 35]. The consequences of muscle dysfunction can result in difficulty of the weaning process [36, 37]. The close relationship between weaning and systemic inflammatory response has received more attention in recent researches [38]. Systemic inflammatory response is a risk factor ofweaning failure. Serum albumin, as the indicator of inflammation status can provide clinical instruction for weaning. The measure of serum albumin has the advantages of its accuracy, simplicity, cheap and could be continually measured in intensive care units. So the assessment of nutritional and inflammation status using serum albumin should therefore be carried out very carefully.

This study has several limitations. First, it was a retrospective study and the sample size is not large because of the strict criteria. Second, the number of female was less than male in our study, which may cause deviation of result. Third, as the duration of admission and weaning were not same, we cannot show how albumin levels changed over the time in patients with different type intracranial lesion.

Conclusion

Serum albumin is a good predictor for duration of weaning in isolated TBI patients with long-term mechanical ventilation. As a potentially modifiable risk factor shown to influence outcome, each increase of 5 mg/l has a potentially beneficial impact on the duration of weaning from MV.

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Disclosure of conflict of interest

None.

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