

· 临床研究 ·

应激性高血糖对重型颅脑损伤术后患者预后的影响

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【摘要】 目的 探讨重型颅脑损伤术后合并应激性高血糖对患者预后的影响。方法 采用回顾性研究方法, 选择2016年1月至2018年12月就诊于徐州医科大学附属医院、经影像学确诊、根据格拉斯哥昏迷(GCS)评分评为重型颅脑损伤(GCS评分为3~8分)、并行外科开颅血肿清除术治疗、术后入重症医学科进一步治疗的患者。将患者分为正常血糖组、应激性高血糖组和糖尿病组, 比较3组患者的28 d病死率、ICU住院时间及并发症。应用SPSS 16.0软件进行统计学分析。数据分别用均数±标准差($\bar{x} \pm s$)、中位数和四分位数间距 $[M(Q_1, Q_3)]$ 或例数(百分率)表示; 依据数据类型分别采用单因素方差分析、SNK-q检验、Kruskal-Wallis秩和检验、 χ^2 检验或Fisher确切概率法对数据进行比较。生存资料分析采用Kaplan-Meier方法绘制生存曲线, 组间生存率的比较采用Log-rank检验。采用Cox回归模型分析影响预后的危险因素。结果 共收集165例患者, 每组各55例。Kaplan-Meier生存分析显示, 应激性高血糖组28 d累积存活率较正常血糖组和糖尿病组明显下降。应激性高血糖组28 d病死率43.27%(26/55) > 糖尿病组23.64%(13/55) > 正常血糖组18.18%(10/55), 两两比较显示, 应激性高血糖组死亡率较正常血糖组及糖尿病组均明显升高(均 $P < 0.05$), 正常血糖组与糖尿病组相比, 差异无统计学意义($P > 0.05$)。3组患者4周内的并发症及ICU住院时间比较显示: 应激性高血糖组患者4周内肺部感染发生率显著高于正常血糖组[58.18%(32/55)和34.55%(19/55), $P < 0.05$], 而较糖尿病组[49.10%(27/55)]有所升高, 但差异无统计学意义($P > 0.05$); 3组之间颅内感染、继发脑梗死、下肢深静脉血栓形成、急性肾功能衰竭等并发症发生情况及ICU住院时间均无统计学差异($P > 0.05$)。多变量Cox比例风险回归模型分析显示, 应激性高血糖($HR = 1.16, 95\% CI 1.07 \sim 1.26$)是影响预后的危险因素之一。结论 合并应激性高血糖的重型颅脑损伤术后患者28 d病死率显著高于正常血糖及糖尿病史患者, 提示应激性高血糖是影响预后的危险因素。

【关键词】 重型颅脑损伤术后; 应激性高血糖; 糖尿病; 预后; 危险因素

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Effect of stress-induced hyperglycemia on prognosis in patients with severe brain injury

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【Abstract】 Objective To investigate the effect of stress-induced hyperglycemia on the prognosis of the patients after operation for severe craniocerebral injury. **Methods** A retrospective study was conducted on the patients with severe craniocerebral injury confirmed by radiological imaging and Glasgow Coma score (GCS score, 3 to 8 points), who were admitted to our hospital from January 2016 to December 2018. After surgical treatment, all the patients were transferred to the intensive care unit (ICU) for further treatment, and were divided into normoglycemia group, stress-induced hyperglycemia group and diabetes mellitus group. The 28-day mortality, length of ICU stay, and complications were compared among the three groups. SPSS statistics 16.0 was used to perform the statistical analysis. Data were expressed as mean ± standard deviation ($\bar{x} \pm s$), median and interquartile range $[M(Q_1, Q_3)]$, or number of cases (percentage). According to the data type, one-way analysis of variance, SNK-q test, Kruskal-Wallis rank sum test, Chi-square test or Fisher exact probability test were employed for comparison. Survival data were analyzed using Kaplan-Meier method to draw survival curves, and intergroup comparison of survival rates was performed using Log-rank test. Cox regression model was applied to analyze the risk factors affecting prognosis. **Results** A total of 165 patients were enrolled, with 55 in each group. Kaplan-Meier survival analysis showed that the 28-day cumulative survival rate was significantly lower in the stress-induced hyperglycemia group than the

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normoglycemia group and the diabetes mellitus group. The 28-day mortality rate was obviously higher in the stress-induced hyperglycemia group [43.27%, (26/55)] followed by the diabetes mellitus group [23.64%, (13/55)] and the normoglycemia group [18.18%, (10/55)] sequentially. The mortality of the stress-induced hyperglycemia group was significantly higher than those of the other 2 groups (both $P < 0.05$). But no such difference was seen between the normoglycemia group and the diabetes mellitus group ($P > 0.05$). The incidence of pulmonary infection within 4 weeks were notably higher in the stress-induced hyperglycemia group than the normoglycemia group [58.18% (32/55) vs 34.55% (19/55), $P < 0.05$], and was higher than the diabetes mellitus group [49.10% (27/55)], but the difference was not statistically significant ($P > 0.05$). There were no remarkable differences in the incidences of complications, such as intracranial infection, secondary cerebral infarction, deep venous thrombosis of the lower extremity, acute renal failure and ICU stay length among the 3 groups ($P > 0.05$). Multivariate Cox proportional hazard regression analysis showed that stress-induced hyperglycemia was one of the risk factors affecting prognosis ($HR = 1.16$, 95% CI : 1.07–1.26). **Conclusion** The 28-day mortality rate is significantly higher in the patients with severe craniocerebral injury complicated with stress-induced hyperglycemia than those with normoglycemia and diabetes history, suggesting that stress-induced hyperglycemia is a risk factor for prognosis.

【Key words】 severe brain injury; stress-induced hyperglycemia; diabetes mellitus; prognosis; risk factors

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颅脑损伤是指头部受到打击,引起脑组织结构破坏和神经功能紊乱的疾病,随着经济和交通的发展,近年来其发病率呈逐年上升趋势,目前已成为全身创伤发生率的第二位,且致残率和死亡率居于首位^[1],给社会和家庭带来了沉重的打击和经济负担。重型颅脑损伤诊断的标准为格拉斯哥昏迷评分(Glasgow Coma Scale, GCS)3~8分、伤后昏迷6h以上,或在伤后24h内意识情况恶化、再次昏迷6h以上者。重型颅脑损伤发病率占所有颅脑损伤的10%~20%。与颅脑损伤相关的应激反应可诱发一种短期的以高血糖为特征的糖代谢紊乱,即应激性高血糖(stress-induced hyperglycemia, SIH),这种并发症通常也发生于患有烧伤、心肌梗死、中风等严重疾病患者^[2]。许多研究表明,入院时高血糖可通过多种机制损害机体,与创伤性脑损伤患者的发病率和死亡率相关^[3]。入院时高血糖可能发生于SIH患者,也可能发生于糖尿病(diabetes mellitus, DM)患者,然而很少有研究评估SIH和DM对创伤人群结局的不同影响。本研究回顾性分析165名重型颅脑损伤术后患者,从应激性高血糖的角度,通过与正常血糖及糖尿病患者的比较,分析不同血糖水平对预后的影响。

1 对象与方法

1.1 研究对象

本研究为回顾性队列研究。选择2016年1月至2018年12月入住徐州医科大学附属医院重症监护室(intensive care unit, ICU)的重型颅脑损伤术后患者。纳入标准:(1)明确急性颅脑损伤病史,均行CT检查明确诊断;(2)入院时GCS 3~8分,伤后昏

迷或再昏迷6h以上;(3)颅脑外伤后24h内在我院行初次手术治疗并入住ICU;(4)年龄 ≥ 18 岁。排除标准:(1)既往有脑出血、脑梗死等神经系统疾病;(2)伴有其他部位严重创伤致失血性休克;(3)入ICU前输注含糖液体;(4)住院时间 < 3 d;(5)规律使用可引起血糖升高的药物;(6)甲亢、内分泌肿瘤、急性胰腺炎等可引起血糖升高的疾病;(7)妊娠期妇女。剔除标准:(1)患者中途放弃治疗;(2)资料不全,28d内随访失败患者。

1.2 临床资料

收集165例重型颅脑损伤术后患者的基线资料:性别,年龄,入院时GCS评分,平均动脉压,颅脑损伤类型,合并脑疝及疾病(高血压、糖尿病、冠心病)情况,手术时间等临床资料。

1.3 资料分组

入ICU后收集采用试纸法首次测得的随机血糖信息,按糖尿病诊疗指南,依据糖尿病史、随机血糖测试(random blood glucose, RBG)及糖化血红蛋白(glycosylated hemoglobin A1c, HbA1c)水平,将患者分为正常血糖组($RBG < 11.1$ mmol/L, $HbA1c < 6.5\%$,无糖尿病史)、糖尿病组($RBG \geq 11.1$ mmol/L, $HbA1c \geq 6.5\%$,有糖尿病史)以及应激性高血糖组($RBG \geq 11.1$ mmol/L, $HbA1c < 6.5\%$,无糖尿病史)。入ICU后3组患者均依据第4版《重型颅脑损伤救治指南》^[4]予脱水降颅压、营养脑神经、镇痛镇静、亚低温、预防感染、预防深静脉血栓等治疗。

1.4 观察指标

收集患者入ICU首次血糖值、24h动脉血乳酸值,第一天患者的血常规(hemoglobin, Hb)、白蛋白(albumin, ALB)、肝功能[天冬氨酸转氨酶(aspartate

aminotransferase, AST)、丙氨酸转氨酶 (alanine aminotransferase, ALT)]、肾功能 [血肌酐 (serum creatinine, SCr)]、凝血功能等指标。收集 3 组患者 ICU 住院时间及住院 28 d 时死亡率,入 ICU 后 4 周内继发院内感染、脑梗死、下肢深静脉血栓形成、急性肾功能衰竭等情况。(1)肺部感染以痰培养、血培养出病原菌阳性,结合胸片或胸部 CT 为标准;颅内感染以脑脊液生化、常规、培养结果为标准,血行感染以血培养为标准。(2)外伤性脑梗死 CT 诊断标准:有明确的头部外伤史;伤后出现脑梗死症状;CT 检查表现脑实质内低密度灶。(3)下肢深静脉血栓形成:以彩超报告为准,每周 2 次下肢静脉彩超检查,记录 1、2、4 周患者有无下肢深静脉血栓。(4)急性肾功能衰竭 (acute kidney injury, AKI) 定义:48 h 内 SCr 上升 $\geq 26.5 \mu\text{mol/L}$ ($\geq 0.3 \text{ mg/dl}$), 或 7 d 内 SCr 升至 ≥ 1.5 倍基线值,或连续 6 h 尿量 $< 0.5 \text{ ml}/(\text{kg} \cdot \text{h})$ 。

1.5 统计学处理

数据采用 SPSS 16.0 软件进行统计学分析。使用 Kolmogorov-Smirnov 检验判断连续型数据是否服从正态分布。服从正态分布的连续型数据用均数 \pm 标准差 ($\bar{x} \pm s$) 表示;组间同一时间点比较采用单因素方差分析,两两比较采用 SNK-*q* 检验;非正态分布的定量资料采用中位数和四分位数间距 [$M(Q_1, Q_3)$] 表示;组间同一时间点比较采用

Kruskal-Wallis 秩和检验,两两比较采用 SNK-*q* 检验。定性资料用率表示,多组率的比较采用卡方检验或 Fisher 确切概率法。生存资料分析采用 Kaplan-meier 方法绘制生存曲线,组间生存率的比较采用 Log-rank 检验。采用 Cox 回归模型分析影响预后的危险因素。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 3 组患者基线资料比较

每组纳入 55 人,共 165 人。糖尿病患者多合并高血压病史;3 组患者在性别构成比、年龄、合并脑疝、入院平均动脉压、GCS 评分、手术时间等方面差异无统计学意义 (表 1)。

2.2 3 组患者入 ICU 后 24 h 内实验室指标比较

3 组血糖水平不同,差异有统计学意义;3 组 24 h 乳酸水平有统计学差异,第一天 3 组血红蛋白、白细胞、凝血功能及肝肾功情况无统计学意义,实验室指标较均衡 (表 2)。

2.3 3 组患者 28 d 病死率的生存分析

应激性高血糖组 28 d 病死率 $>$ 糖尿病组 $>$ 正常血糖组 ($\chi^2 = 12.599, P = 0.002$)。两两比较应激性高血糖组死亡率较正常血糖组及糖尿病组均明显升高 (均 $P < 0.05$),正常血糖组与糖尿病组相比,差异无统计学意义 ($P > 0.05$; 表 3, 图 1)。

表 1 3 组患者基线资料比较

Table 1 Comparison of baseline data among three groups

($n = 55$)

Group	Gender (male/female, n)	Age (years, $\bar{x} \pm s$)	MAP (mmHg, $\bar{x} \pm s$)	GCS [score, $M(Q_1, Q_3)$]	Combined with hypertension [$n(\%)$]	Combined with cerebral palsy [$n(\%)$]	Operation time (min, $\bar{x} \pm s$)
N	(38/17)	60.2 \pm 8.7	95.5 \pm 19.3	6.0(4.0,7.0)	9(16.4)	15(27.3)	257.1 \pm 25.0
SIH	(34/21)	61.6 \pm 8.4	91.8 \pm 20.4	5.0(4.0,7.0)	11(20.0)	12(21.8)	263.2 \pm 24.6
DM	(37/18)	61.1 \pm 7.2	89.6 \pm 13.5	6.0(5.0,7.0)	20(36.4)	10(18.2)	266.6 \pm 28.4
<i>P</i> value	0.704	0.663	0.231	0.371	0.033	0.516	0.156

N: normoglycemia; SIH: stress-induced hyperglycemia; DM: diabetes mellitus; MAP: mean arterial pressure; GCS: Glasgow Coma Score. 1 mmHg = 0.133 kPa.

表 2 3 组患者入 ICU 后 24 h 内临床指标比较

Table 2 Comparison of clinical indices within 24 hours after entering the ICU among three groups

($n = 55$)

Group	Initial blood glucose (mmol/L, $\bar{x} \pm s$)	Lactate (mmol/L, $\bar{x} \pm s$)	Oxygenation index (mmHg, $\bar{x} \pm s$)	Hb (g/L, $\bar{x} \pm s$)	WBC ($\times 10^9/L$, $\bar{x} \pm s$)	Coagulation dysfunction [$n(\%)$]	Hepatic dysfunction [$n(\%)$]	Renal dysfunction [$n(\%)$]
N	7.9 \pm 1.2	2.5 \pm 1.4	285.2 \pm 55.5	112.1 \pm 26.5	10.1 \pm 4.3	16(29.1)	3(5.5)	5(9.1)
SIH	13.5 \pm 1.6	2.9 \pm 1.2	277.5 \pm 38.8	102.9 \pm 21.9	9.6 \pm 2.9	19(34.5)	9(16.4)	8(14.5)
DM	15.5 \pm 1.7	2.3 \pm 1.1	294.4 \pm 31.0	106.3 \pm 16.8	10.0 \pm 3.3	15(27.3)	5(9.1)	12(21.8)
<i>P</i> value	< 0.001	0.025	0.045	0.148	0.739	0.689	0.159	0.175

ICU: intensive care unit; N: normoglycemia; SIH: stress-induced hyperglycemia; DM: diabetes mellitus; Hb: hemoglobin; WBC: white blood cell. 1 mmHg = 0.133 kPa.

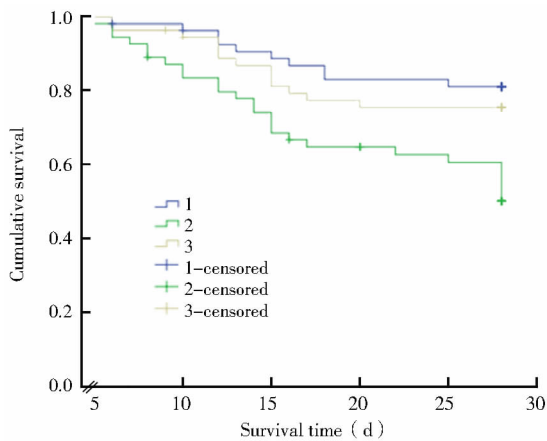


图1 3组患者Kaplan-Meier生存曲线比较

Figure 1 Comparison of Kaplan-Meier survival curves among three groups

1: normoglycemia group; 2: stress-induced hyperglycemia group; 3: diabetes mellitus group.

2.4 3组患者4周内的并发症及ICU住院时间比较

应激性高血糖组患者4周内肺部感染发生率显著高于正常血糖组($P < 0.05$),而较糖尿病组有所升高,但差异无统计学意义($P > 0.05$)。3组之间颅内感染、继发脑梗死、下肢深静脉血栓形成、急性肾功能衰竭等并发症发生情况无统计学差异,3组ICU住院时间比较也无统计学差异($P > 0.05$,表3)。

2.5 影响重型颅脑损伤术后患者28d预后的多因素Cox比例风险回归模型分析

经校正年龄,GCS评分,入院平均动脉压,是否合并脑疝,入院24h乳酸值,初次血糖值,第一天血

红蛋白、氧合指数、白细胞计数后,多变量Cox比例风险回归模型分析结果显示,年龄($HR = 1.039$, $95\%CI = 1.004 \sim 1.076$)、合并脑疝($HR = 5.999$, $95\%CI = 3.140 \sim 11.461$)、乳酸水平($HR = 1.301$, $95\%CI = 1.054 \sim 1.606$)、高血糖($HR = 1.159$, $95\%CI = 1.070 \sim 1.256$)、氧合指数($HR = 0.989$, $95\%CI = 0.980 \sim 0.998$)及白细胞计数($HR = 1.135$, $95\%CI = 1.047 \sim 1.231$)是影响重型颅脑损伤术后患者的独立因素(表4)。

3 讨论

入住ICU患者常因大手术、各种创伤、心脑血管意外等导致机体发生应激反应。应激性高血糖是指机体在急性疾病强烈刺激下,神经-内分泌系统发生应激性紊乱和全身炎性介质过度释放,造成机体能量和物质代谢异常,出现以高血糖为特征的糖代谢紊乱,可作为危重症患者监测应激反应的标志^[5,6]。据文献报道,ICU应激性高血糖的发生率约为43%~50%^[7]。

有研究表明,应激性高血糖可通过使无氧酵解增加引起脑组织乳酸堆积、降低免疫功能、电解质紊乱等途径影响患者的预后。目前有许多动物实验及临床研究均已证实颅脑损伤后可有不同程度的高血糖,而且血糖的水平与颅脑损伤的严重程度及预后密切相关。瑞典一项包含267名中重度颅脑损伤患者(GCS评分3~12分)的前瞻性研究发现,颅脑损伤后高血糖的发生率可高达87%,且与损伤程度相

表3 3组患者4周内并发症情况及ICU住院时间与28d病死率比较

Table 3 Comparison of complications within 4 weeks, length of ICU stay and 28-day mortality among three groups (n = 55)

Group	Nosocomial infection [n(%)]		Secondary	Lower extremity deep	Acute renal	Length of	28-day
	Pulmonary infection	Intracranial infection	cerebral infarction [n(%)]	vein thrombosis [n(%)]	failure [n(%)]	ICU stay (d, $\bar{x} \pm s$)	mortality [n(%)]
N	19(34.5)	1(1.8)	7(12.7)	2(3.6)	1(1.8)	12.1 ± 3.9	10(18.2)
SIH	32(58.2)	4(7.1)	13(23.6)	4(7.3)	3(5.5)	14.0 ± 5.3	26(47.3)
DM	27(49.1)	0(0.0)	10(17.5)	1(1.8)	7(12.7)	13.0 ± 3.8	13(23.6)
P value	0.043	0.128	0.333	0.506	0.084	0.087	0.002

ICU: intensive care unit; N: normoglycemia; SIH: stress-induced hyperglycemia; DM: diabetes mellitus.

表4 影响重型颅脑损伤术后患者28d预后的多因素Cox回归分析

Table 4 Multivariate Cox regression analysis on 28-day prognosis of patients with severe brain injury

Factor	B	SE	Wald	HR(95%CI)	P value
Age	0.038	0.018	4.667	1.039(1.004-1.706)	0.031
Combined with hernia	1.792	0.330	29.412	5.999(3.140-11.461)	0.000
Lactate	0.263	0.107	6.003	1.301(1.054-1.606)	0.014
Initial blood glucose	0.148	0.041	13.033	1.159(1.070-1.256)	0.000
Oxygenation index	-0.110	0.004	5.987	0.989(0.980-0.998)	0.014
WBC	0.127	0.041	9.485	1.135(1.047-1.231)	0.002

WBC: white blood cell.

关,预后不良的患者血糖水平明显高于预后较好的患者,在较严重的颅脑损伤患者中,血糖水平高于200 mg/dl 的患者预后较差^[8]。本研究结果显示,应激性高血糖组的患者较正常血糖组患者28 d病死率及并发症发生率高,可证实应激性高血糖对重型颅脑损伤患者的预后不良影响。

近年来有研究提示,同样是高血糖状态,单纯应激性高血糖患者较糖尿病患者死亡风险更高。一项关于脓毒症患者的meta分析显示,即使血糖水平无差异,无糖尿病病史的应激性高血糖患者几乎为糖尿病患者的2倍^[9]。国内也有类似的研究,一项对重症脑血管病患者的回顾性研究结果表明,应激性高血糖患者死亡率约是正常血糖患者的5倍,糖尿病患者的2倍,并发症也较其他2组较高^[10],可见单纯应激性高血糖患者的预后更差。既往关于应激性高血糖对重型颅脑损伤术后患者的影响多是只比较应激性高血糖患者与正常血糖患者的预后,而本研究从应激性高血糖的角度,回顾性分析正常血糖、糖尿病及应激性高血糖3种不同血糖水平的颅脑损伤患者的预后,结果显示SIH组28 d病死率较糖尿病组患者高,肺部并发症发生率也较糖尿病组高,但差异无统计学意义,这一结果考虑可能与样本量较小有关。有关糖尿病对危重疾病的“保护”作用,有人认为是由于糖尿病患者在长期慢性高血糖状态下适应性增强,对高水平的血糖状态耐受性更强,也更能适应血糖在较高范围内的波动^[11],但有关的病理生理机制仍需进一步探索。

本研究的多变量Cox比例风险回归模型分析结果显示,年龄、合并脑疝、乳酸水平、应激性高血糖、氧合指数及白细胞计数是影响重型颅脑损伤术后患者的独立危险因素,其结果与大量研究相符合^[12-14],也可进一步证实应激性高血糖是影响颅脑损伤术后患者预后的危险因素。

综上所述,颅脑损伤术后患者出现应激性高血糖是预后不良的重要信号,需引起临床医师的注意。颅脑损伤后患者除常规治疗外,应注意监测血糖,将血糖维持在适当的水平。而有关应激性高血糖及糖尿病对颅脑损伤术后患者预后影响的不同,需要进行大样本量的研究,以期得出疾病规律,指导临床实践,改善颅脑损伤术后患者的预后。

【参考文献】

- [1] Roozenbeek B, Maas AI, Menon DK. Changing patterns in the epidemiology of traumatic brain injury [J]. *Nat Rev Neurol*, 2013, 9(4): 231-236. DOI: 10.1038/nrneurol.2013.22.
- [2] Zygun DA, Steiner LA, Johnston AJ, et al. Hyperglycemia and brain tissue pH after traumatic brain injury [J]. *Neurosurgery*, 2004, 55(4): 877-881, 882. DOI: 10.1227/01.neu.00001-37658.14906.e4.
- [3] Rau CS, Wu SC, Chen YC, et al. Stress-induced hyperglycemia, but not diabetic hyperglycemia, is associated with higher mortality in patients with isolated moderate and severe traumatic brain injury: analysis of a propensity score-matched population [J]. *Int J Environ Res Public Health*, 2017, 14(11): pii: E1340. DOI: 10.3390/ijerph14111340.
- [4] Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury (Fourth Edition) [J]. *Neurosurgery*, 2017, 80(1): 6-15. DOI: 10.1227/NEU.0000-0000-00001432.
- [5] Chen QY, Zhang DH, Zhang XF, et al. The relationship between the levels and variability of blood glucose and the prognosis of massive cerebral infarction [J]. *Chin Crit Care Med*, 2013, 25(12): 749-753. DOI: 10.3760/cma.j.issn.2095-4352.2013.12.013.
- [6] 谭敏, 卢小岚, 段军伟, 等. 益生菌对重型颅脑损伤患者血糖水平及预后的影响 [J]. *中华危重病急救医学*, 2013, 25(10): 627-630. DOI: 10.3760/cma.j.issn.2095-4352.2013.10.012.
- [7] Tan M, Lu XL, Duan JW, et al. Effect of probiotics on blood glucose levels and clinical outcomes in patients with severe cranio-cerebral trauma [J]. *Chin Crit Care Med*, 2013, 25(10): 627-630. DOI: 10.3760/cma.j.issn.2095-4352.2013.10.012.
- [8] Van den Berghe G, Wouters PJ, Bouillon R, et al. Outcome benefit of intensive insulin therapy in the critically ill; insulin dose versus glycemic control [J]. *Crit Care Med*, 2003, 31(2): 359-366. DOI: 10.1097/01.CCM.0000045568.12881.10.
- [9] Barth E, Albuszies G, Baumgart K, et al. Glucose metabolism and catecholamines [J]. *Crit Care Med*, 2007, 35(9 Suppl): S508-518. DOI: 10.1097/01.CCM.0000278047.06965.20.
- [10] Tayek CJ. Diabetes patients and non-diabetic patients intensive care unit and hospital mortality risks associated with sepsis [J]. *World J Diabetes*, 2012, 3(2): 29-34. DOI: 10.4239/wjd.v3.i2.29.
- [11] 柳学, 陈纯波, 叶珩, 等. 应激性高血糖对重症脑血管病患者预后的影响 [J]. *中华危重病急救医学*, 2016, 28(4): 359-363. DOI: 10.3760/cma.j.issn.2095-4352.2016.04.014.
- [12] Liu X, Chen CB, Ye Y, et al. Effect of stress hyperglycemia on the prognosis in patients with severe cerebral vascular diseases [J]. *Chin Crit Care Med*, 2016, 28(4): 359-363. DOI: 10.3760/cma.j.issn.2095-4352.2016.04.014.
- [13] Bosarge PL, Shultz TH, Griffin RL. Stress-induced hyperglycemia is associated with higher mortality in severe traumatic brain injury [J]. *J Trauma Acute Care Surg*, 2015, 79(2): 289-294. DOI: 10.1097/TA.0000000000000716.
- [14] Schaan M, Jaksche H, Boszczyk B. Predictors of outcome in head injury: proposal of a new scaling system [J]. *J Trauma*, 2002, 52(4): 667-674.
- [15] 刘小波, 林爱国, 何程, 等. 颅脑损伤伴颅内感染患者的临床特点和急性期预后的影响因素 [J]. *中国实用神经疾病杂志*, 2016, 19(7): 15-17. DOI: 10.3969/j.issn.1673-5110.2016.07.009.
- [16] Liu XB, Lin AG, He C, et al. Clinical features of traumatic brain injury with intracranial infection and the related factors for the prognosis in the acute phase [J]. *Chin J Pract Nerv Dis*, 2016, 19(7): 15-17. DOI: 10.3969/j.issn.1673-5110.2016.07.009.
- [17] 王忠安, 黎开谷, 刘金辉, 等. 重型颅脑损伤患者手术后颅内感染相关因素临床分析 [J]. *中华医院感染学杂志*, 2013, 23(16): 3903-3905.
- [18] Wang ZA, Li KG, Liu JH, et al. Related factors of intracranial infections after emergency surgery for severe craniocerebral injury [J]. *Chin J Nosocomiol*, 2013, 23(16): 3903-3905.