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早期高压氧联合去骨瓣减压治疗重型颅脑损伤的疗效 及对患者神经功能、炎性因子的影响*

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摘要 目的:分析早期高压氧联合去骨瓣减压治疗重型颅脑损伤的疗效及对患者神经功能、炎性因子的影响。**方法:**选择我院自2018年1月至2021年10月接诊的106例重型颅脑损伤患者,随机分为对照组和观察组,各53例。两组均予以常规对症支持治疗,在此基础上,对照组采取去骨瓣减压治疗,观察组采取早期高压氧联合去骨瓣减压治疗。随访3个月,比较两组治疗前后的脑代谢指标、Fugl-Meyer运动功能评分、神经功能指标、炎性因子、严重并发症发生率及近期疗效。**结果:**观察组治疗后脑氧摄取率(CEO₂)、混合静脉血氧饱和度(SVO₂)均高于对照组($P<0.05$);观察组治疗后上肢、下肢及总体Fugl-Meyer运动功能评分均高于对照组($P<0.05$);观察组治疗后血清脑源性神经营养因子(BDNF)、神经元特异性烯醇化酶(NSE)、S100β蛋白、胶质纤维酸性蛋白(GFAP)水平均低于对照组,神经生长因子(NGF)水平高于对照组($P<0.05$);观察组治疗后血清C反应蛋白(CRP)、白介素-1β(IL-1β)、肿瘤坏死因子-α(TNF-α)均低于对照组($P<0.05$);观察组严重并发症发生率低于对照组,预后良好率高于对照组($P<0.05$)。**结论:**早期高压氧联合去骨瓣减压治疗重型颅脑损伤的疗效显著,能够有效优化患者神经功能,抑制炎症反应,促进肢体运动功能恢复,进而改善预后,值得临床予以重视。

关键词:重型;颅脑损伤;早期高压氧;去骨瓣减压;神经功能;炎性因子**中图分类号:**R651.1 **文献标识码:**A **文章编号:**1673-6273(2023)10-1889-05

Effect of Early Hyperbaric Oxygen combined with Decompressive Craniectomy on Severe Craniocerebral Injury and Its Effect on Neurological Function and Inflammatory Factors*

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ABSTRACT Objective: To analyze the effect of early hyperbaric oxygen combined with decompressive craniectomy on severe craniocerebral injury and its effect on neurological function and inflammatory factors. **Methods:** A total of 106 patients with severe craniocerebral injury admitted to our hospital from January 2018 to October 2021 were selected and randomly divided into matched group and observation group, 53 cases in each group. On this basis, the matched group was treated with decompressive craniectomy, and the observation group was treated with early hyperbaric oxygen combined with decompressive craniectomy. The brain metabolism index, Fugl-Meyer motor function score, neurological function index, inflammatory factors, incidence of serious complications and short-term efficacy were compared between the two groups before and after treatment for 3 months. **Results:** After treatment, the cerebral oxygen uptake rate (CEO₂) and mixed venous oxygen saturation (SVO₂) of the observation group were higher than those of the matched group ($P<0.05$). After treatment, the upper limb, lower limb and total Fugl-Meyer motor function scores of the observation group were higher than those of the matched group ($P<0.05$). After treatment, the levels of brain-derived neurotrophic factor (BDNF), neuronal specific enolase (NSE), S100β protein and glial fibrillary acidic protein (GFAP) in the observation group were lower than those in the matched group, and the levels of nerve growth factor (NGF) were higher than those in the matched group ($P<0.05$). The serum levels of C-reactive protein (CRP), interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) in the observation group after treatment were lower than those in the matched group ($P<0.05$). The incidence of serious complications in the observation group was lower than that in the matched group, and the good prognosis rate was higher than that in the matched group ($P<0.05$). **Conclusion:** Early hyperbaric oxygen combined with de-

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compressive craniectomy is effective in the treatment of severe craniocerebral injury, it can effectively optimize the neurological function of patients, inhibit inflammation, promote the recovery of limb motor function, and improve the prognosis, which is worthy of clinical attention.

Key words: Heavy; Craniocerebral injury; Early hyperbaric oxygen; Decompressive craniectomy; Neurological function; Inflammatory cytokines

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前言

颅脑损伤往往是指外力作用于头部引起的脑组织损伤,对于重型颅脑损伤患者,病死率较高,及时有效治疗是挽救患者生命的关键所在^[1]。一直以来,去骨瓣减压是治疗重型颅脑损伤的主要疗法之一,目的是清除血肿、降低颅内压^[2]。由于去骨瓣减压治疗重型颅脑损伤的风险较大,术后神经功能恢复依赖于患者的自我调节能力,相当一部分患者遗留肢体功能障碍,严重影响后续生活质量^[3]。相关研究表明,去骨瓣减压治疗能在一定程度上提高重型颅脑损伤患者脑组织氧分压,但部分患者脑组织氧分压并无明显改善,是近期疗效不佳的主要原因^[4,5]。近年来,临床学者高度重视重型颅脑损伤患者去骨瓣减压治疗后的对症支持治疗,其中早期高压氧治疗尤为重要^[6]。当前研究发现早期高压氧治疗可能对重型颅脑损伤具有重要治疗作用,主要通过提高氧分压和血氧饱和度,增强机体携氧能力,改善血氧状态,使氧气弥散至常压下无法到达的病灶,进而纠正异常脑代谢,增加患者临床获益^[7,8]。与此同时,重型颅脑损伤患者的脑组织氧代谢不足,可诱导神经功能障碍,影响肢体运动功能,这为采取早期高压氧治疗提供理论依据^[9]。为进一步明确早期高压氧联合去骨瓣减压对重型颅脑损伤的治疗价值,本研究分析了早期高压氧联合去骨瓣减压治疗重型颅脑损伤的疗效及该治疗方法对患者神经功能、炎性因子的影响。

1 资料与方法

1.1 一般资料

选择联勤保障部队第 904 医院自 2018 年 1 月至 2021 年 10 月接诊的 106 例重型颅脑损伤患者作为研究对象,经医院伦理委员会批准。

纳入标准:年龄 18~70 岁;符合重型颅脑损伤的诊断标准^[10],格拉斯哥昏迷评分≤8 分;损伤至入院时间不超过 12 h;知悉研究内容,签署知情同意书,配合治疗、检查和随访。

排除标准:有脑出血、脑梗死及头颅手术史者;既往接受高压氧治疗者;合并严重的基础性疾病者;不耐受高压氧治疗者。

依据随机数字表法分为对照组和观察组,各 53 例。对照组男 29 例、女 24 例;年龄 21~67 岁,平均(49.15±6.06)岁;损伤至入院时间 1~12 h,平均(6.58±2.37)h;损伤原因:交通事故伤 19 例、高空坠落伤 18 例、砸伤 16 例;观察组男 30 例、女 23 例;年龄 21~68 岁,平均(49.15±6.06)岁;损伤至入院时间 1~12 h,平均(6.37±2.41)h;损伤原因:交通事故伤 20 例、高空坠落伤 19 例、砸伤 14 例;两组一般资料比较无差异($P>0.05$)。

1.2 检测方法

两组均予以常规对症支持治疗,如输液以恢复酸碱平衡、

抗体克、抗感染及脱水等治疗。在此基础上,对照组采取去骨瓣减压治疗,取仰卧位,手术切口始于颧弓上耳屏前 1 cm 部位,经耳廓上缘,由后上方延伸至顶结节,再经中线 2 cm 弧形向前,直至前额部发迹处。确定手术切口后,逐层切开,分离头皮和骨膜,显露颅骨,将颧骨开瓣并游离、去除,若检出硬膜下血肿,切开并减压,充分清除脑膜外血肿及坏死组织,采用人工补片减压缝合,在冲洗彻底后进行置管引流。观察组采取早期高压氧联合去骨瓣减压治疗,其中去骨瓣减压治疗与对照组相同,术后使用空气加压舱加压 20 min,确保舱内气压≥0.25 Mpa,患者每次戴上面罩吸纯氧 40 min,休息 10 min 后,吸舱内空气,待减压 30 min 后,出舱;每日治疗 1 次,治疗 10 日为 1 个疗程,连续治疗 3 个疗程。

1.3 观察指标

以定期回院复查或电话联系的方式随访 3 个月;在治疗前及治疗结束后 1 d,检测脑代谢指标[脑氧摄取率(Cerebralextraction of oxygen, CEO₂)、混合静脉血氧饱和度(Mixed venous oxygen saturation, SVO₂)]、神经功能指标[脑源性神经营养因子(Brain-derived neuro-trophic factor, BDNF)、神经元特异性烯醇化酶(Neuron-specific enolase, NSE)、S100β 蛋白、胶质纤维酸性蛋白(Glial fibrillary acidic protein, GFAP)、神经生长因子(Nerve Growth Factor, NGF)]、炎性因子[C 反应蛋白(C-reactive protein, CRP)、白介素-1β(Interleukin-1β, IL-1β)、肿瘤坏死因子-α(Tumor necrosis factor-α, TNF-α)],进行 Fugl-Meyer 运动功能评分(上肢、下肢及总体 Fugl-Meyer 运动功能评分),其中上肢功能评分 66 分、下肢功能评分 34 分,总体 Fugl-Meyer 运动功能评分 100 分,评分与肢体运动功能成正比^[11]。

在院内及随访期间,记录肺部感染、颅内感染、脑积水、急性脑膨出等严重并发症发生情况,在末次随访时采用格拉斯哥预后评分量表评估近期疗效,评分越高,说明近期疗效越好,其中格拉斯哥预后评分量表评分为 5 分,说明预后良好^[12]。

1.4 统计学方法

使用 SPSS22.0 分析,计量资料以均数±标准差表达,使用 t 检验;计数资料以率表达,使用 χ^2 检验;以 $P<0.05$ 说明差异有统计学意义。

2 结果

2.1 治疗前后脑代谢指标比较

治疗后,观察组 CEO₂、SVO₂ 均高于对照组($P<0.05$);见表 1。

2.2 治疗前后 Fugl-Meyer 运动功能评分比较

观察组治疗后上肢、下肢及总体 Fugl-Meyer 运动功能评分均高于对照组($P<0.05$);见表 2。

表 1 脑代谢指标比较(%)
Table 1 Comparison of brain metabolic indicators (%)

Groups	n	CEO ₂		SVO ₂	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Matched group	53	26.43± 2.68	34.27± 3.61*	60.43± 4.29	66.53± 5.73*
Observation group	53	26.61± 2.75	40.86± 5.17**	60.61± 4.35	71.69± 7.08**

Note: compared with matched group, *P<0.05; compared with pretherapy, **P<0.05, the same below.

表 2 Fugl-Meyer 运动功能评分比较(分)
Table 2 Comparison of Fugl Meyer motor function score (score)

Groups	n	Upper limb		Lower limbs		Totality	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Matched group	53	36.53± 5.61	48.76± 6.45*	16.08± 3.06	22.29± 4.17*	51.26± 3.64	66.81± 5.07*
Observation group	53	37.10± 5.56	55.83± 8.12**	16.17± 3.32	28.75± 5.84**	50.99± 3.71	75.69± 7.89**

2.3 治疗前后神经功能指标比较

观察组治疗后血清 BDNF、NSE、S100β 蛋白、GFAP 水平

表 3 神经功能指标比较(ng/L)
Table 3 Comparison of neurological function indexes (ng/L)

Groups	n	BDNF		NSE		S100 protein		GFAP		NGF	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Matched group	53	3.65± 0.38	21.47± 4.09	1.83± 0.28	5.56± 0.82	0.76± 0.13					
		2.66± 0.32*	18.64± 3.56*	1.45± 0.19*	1.37± 0.35*	1.57± 0.34*					
Observation group	53	3.38± 0.39	21.53± 4.12	1.82± 0.31	5.61± 0.79	0.79± 0.11					
		1.71± 0.26**	12.79± 2.08**	0.95± 0.20**	0.65± 0.13**	2.28± 0.56**					

2.4 治疗前后炎性因子水平比较

观察组治疗后血清 CRP、IL-1β、TNF-α 均较对照组低(P<

表 4 炎性因子水平比较(ng/L)
Table 4 Comparison of inflammatory factors in levels (ng/L)

Groups	n	CRP(mg/L)		IL-1β(ng/L)		TNF-α(ng/L)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Matched group	53	39.16± 4.08	27.56± 3.57*	162.35± 15.82	131.24± 9.98*	26.53± 5.17	14.79± 3.46*
Observation group	53	39.45± 4.13	17.34± 2.16**	163.07± 16.13	114.08± 7.86**	26.49± 5.24	8.51± 2.05**

2.5 严重并发症发生率和预后良好率比较

与对照组相比, 观察组严重并发症发生率较低, 预后良好

表 5 严重并发症发生率和预后良好率比较[n(%)]

Table 5 Comparison of serious complication rates and good prognosis rates between the two groups [n (%)]

Groups	n	Serious complications	Eusemia
Matched group	53	15(28.30)	9(16.98)
Observation group	53	7(13.21)†	21(39.62)†

3 讨论

神经中枢结构受损而导致一系列功能障碍, 常伴有颅内出血而引起颅内压升高, 血液无法流到颅内, 脑低氧使二氧化碳潴留, 导致大量脑细胞死亡; 而缺血使脑血管扩张, 造成血管痉挛或

重型颅脑损伤的病情严重、复杂且进展迅急, 患者往往因

麻痹,使脑代谢紊乱、自由基聚集,最终造成脑水肿和脑低氧的恶性循环,严重影响后续生活质量^[13]。对于重型颅脑损伤患者,神经功能受损和炎性应激均较为突出。因此,不管采用何种治疗方案,其治疗目的为改善神经功能,抑制炎症反应,对于改善预后尤为重要^[14,15]。一直以来,去骨瓣减压治疗被公认为重型颅脑损伤的最有效疗法之一,整体疗效得到认可^[16]。与此同时,发现氧需/氧供的矛盾是导致重型颅脑损伤病情恶化的重要原因,而早期高压氧治疗重型颅脑损伤,能在一定程度上提高患者认知功能,改善颅脑血流动力学,具体作用机制尚未明确^[17,18]。

在本研究中,观察组予以早期高压氧联合去骨瓣减压治疗,期望在降低颅内压的基础上,进而改善脑氧供给,以促进脑组织血流,为恢复神经功能、抑制炎症反应创造有利条件。从本研究表1结果可知,观察组治疗后CEO₂、SVO₂均高于对照组,与魏琳^[19]等的研究结果相符,提示早期高压氧联合去骨瓣减压治疗能有效改善重型颅脑损伤的脑代谢,出现上述结果的原因,考虑如下:去骨瓣减压治疗可有效清除颅内额颞底部挫伤,彻底减压,使脑动脉供血;早期高压氧治疗可改善脑细胞供氧情况,降低脑组织的氧耗,促进脑血管收缩和侧支循环形成,有利于脑血管收缩,减少脑血流量、减轻脑水肿,提高上行性网状系统的兴奋性,保护正常脑组织。

关于早期高压氧治疗重型颅脑损伤的作用机制尚未十分清楚,既往大多数研究认为,其通过提高血液中氧的溶解度,增加脑组织的供氧,改善全身组织有氧代谢^[20]。黄琼^[21]等研究表明,早期高压氧辅助治疗行去骨瓣减压的重型颅脑损伤患者,能够增大动脉血流速度,提高脑动脉血运能力,有利于神经功能的恢复。从本研究结果可知,观察组治疗后血清BDNF、NSE、S100β蛋白、GFAP水平均低于对照组,NGF水平高于对照组,与Lippert^[22]等的研究结果相符,表明早期高压氧联合去骨瓣减压治疗重型颅脑损伤,能够有效优化患者神经功能,分析原因在于去骨瓣减压治疗能有效清除颅内血肿,恢复颅内压,改善血运;与此同时,早期高压氧治疗可最大限度改善血氧供给,减少自由基的产生,促进心血管的形成有关,在脑细胞中维持稳定,从而使颅内压降低,减轻脑水肿,并明显减少氧自由基的产生,促使受损的神经功能恢复^[23]。另外,有研究表明,重型颅脑损伤患者的神经功能障碍与机体炎症反应有关,炎性因子水平的变化有助于反映病情的演变^[24]。基于本研究结果,早期高压氧联合去骨瓣减压治疗有助于重型颅脑损伤患者神经功能的恢复,由此认为,该治疗方案亦能缓解患者机体炎症反应。从本研究表4结果可知,观察组治疗后血清CRP、IL-1β、TNF-α均低于对照组,进一步佐证了上述观点,这可能与该治疗方案能缓解局部缺血缺氧状态,拮抗炎性应激反应有关。

在重型颅脑损伤的治疗过程中,改善患者肢体运动功能,减少严重并发症发生,是改善患者预后的关键所在^[25]。Zeiler^[26]等研究证实,去骨瓣减压治疗不仅能够有效降低颅内压,还有利于术后肢体运动功能的恢复。我们认同上述观点,并认为去骨瓣减压治疗可迅速清除局部血肿,降低颅内压,减轻脑干的压迫性损伤,为后续各项治疗能够顺利开展创造机会。也有研究认为,早期高压氧治疗可提高重型颅脑损伤患者的动脉血氧分压,减轻氧自由基对脑组织的损伤,亦有助于改善神经功能,减少并发症^[27,28]。在本研究中,观察组治疗后上肢、下肢及总体

Fugl-Meyer运动功能评分均高于对照组,提示早期高压氧联合去骨瓣减压治疗可协同改善患者的肢体运动功能。其主要机制为重型颅脑损伤患者在去骨瓣减压治疗后颅内压得到缓解,联合早期高压氧治疗,通过改善细胞内环境,提高脑组织对葡萄糖的利用率,使能量供给得以保障,使受损的脑细胞得到修复,进而改善预后^[29,30]。此外,本研究比较了两组严重并发症发生率和近期疗效,结果显示:观察组严重并发症发生率低于对照组,预后良好率高于对照组,提示早期高压氧联合去骨瓣减压治疗重型颅脑损伤,可促进肢体运动功能恢复,减少严重并发症发生,改善预后。其主要机制为早期高压氧联合去骨瓣减压治疗可预防继发性脑损害,阻断缺氧-脑水肿这一恶性循环,有助于减轻脑水肿,改善脑缺氧状态。

综上所述,早期高压氧联合去骨瓣减压治疗重型颅脑损伤的疗效显著,可改善神经功能,并对炎症反应产生抑制作用,有利于肢体运动功能恢复,进而改善预后,值得临床予以重视。本研究存在一定不足之处,研究规模较小,样本量不多,未分析早期高压氧联合去骨瓣减压治疗对患者远期预后的影响,有待日后扩大研究规模,深入分析上述治疗方案对重型颅脑损伤的疗效及其疗效影响因素,为进一步优化治疗方案,提高患者的治疗水平提供依据。

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