

doi: 10.13241/j.cnki.pmb.2018.15.033

血液透析联合血液灌流治疗急性肾损伤患者的疗效及对生化指标的影响

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摘要 目的:探讨血液透析(HD)联合血液灌流(HF)治疗对急性肾损伤(AKI)患者的疗效以及对生化指标的影响。**方法:**选取 2016 年 1 月-2017 年 2 月在我院进行治疗的 AKI 患者 56 例,按随机数字表法分为对照组和观察组,每组各 28 例。对照组进行 HD 治疗,观察组进行 HD 联合 HF 治疗。治疗 1 个月后,比较两组患者血肌酐(Scr)、血尿素氮(BUN)以及炎症因子水平,检验治疗疗效差异,并统计并发症发生情况。**结果:**治疗前,两组患者的 Scr、BUN、C 反应蛋白(CRP)、肿瘤坏死因子- α (TNF- α)和白细胞介素-2(IL-2)水平无明显差异($P>0.05$),治疗 1 个月后,两组患者的 Scr、BUN、CRP、TNF- α 和 IL-2 水平均较治疗前明显降低,且观察组的上述指标均较对照组降低($P<0.05$);观察组的总有效率明显高于对照组(89.29% vs 64.29%)($P<0.05$);观察组并发症发生率为 3.57%,明显低于对照组的 21.43%($P<0.05$)。**结论:**HD 联合 HF 治疗 AKI 患者具有较好的临床疗效,且能显著改善患者生化指标,控制炎症反应,较单用 HD 治疗优势明显,且安全性更高,值得临床推广应用。

关键词:急性肾损伤;血液透析;血液灌流;疗效;生化指标

中图分类号:R692;R459.5 **文献标识码:**A **文章编号:**1673-6273(2018)15-2950-04

Effect of Hemodialysis Combine with Hemoperfusion on the Treatment of Acute Kidney Injury and its Influence on the Biochemical Idexes of the Patients

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ABSTRACT Objective: To explore the effect of hemodialysis (HD) combine with hemoperfusion (HF) on the treatment of acute kidney injury (AKI) and its influence on the biochemical indexes of the patients. **Methods:** 56 patients with AKI who were treated in our hospital from January 2016 to February 2017 were selected, and they were randomly divided into control group and observation group according to the random number table method, 28 cases in each group. The control group was treated with HD, and the observation group was treated with HD combined with HF. At 1 month after treatment, the levels of serum creatinine (Scr), blood urea nitrogen (BUN) and inflammatory factors were compared between the two groups, the difference of treatment effect was observed, and the complications were observed. **Results:** Before treatment, there was no significant difference in Scr, BUN, C reactive protein (CRP), tumor necrosis factor- α (TNF- α) and interleukin-2 (IL-2) between the two groups ($P>0.05$). At 1 month after treatment, the levels of Scr, BUN, CRP, TNF- α and IL-2 in the two groups were significantly decreased, and the above indexes in the observation group were significantly lower than those in the control group ($P<0.05$). The total effective rate of the observation group was significantly higher than that of the control group (89.29% vs 64.29%) ($P<0.05$). The complication rate of the observation group was 3.57%, which was significantly lower than that of the control group (21.43%) ($P<0.05$). **Conclusion:** HD combined with HF has good clinical efficacy in the treatment of AKI, and it can significantly improve the patient's biochemical indicators, control inflammatory response. Compared with HD alone, the advantages of treatment are obvious, and the safety is higher, which is worthy of clinical application.

Key words: Acute kidney injury; Hemodialysis; Hemoperfusion; Clinical Effect; Biochemical indexes

Chinese Library Classification(CLC): R692; R459.5 **Document code:** A

Article ID: 1673-6273(2018)15-2950-04

前言

急性肾损伤(Acute kidney injury, AKI)是指由各种病因引起的突发的和持续的肾功能突然下降,其临床表现主要为水电解质和酸碱平衡紊乱、氮质血症以及全身多系统症状,部分患者可伴有少尿或无尿,严重时可引起患者全身多个系统的组织损伤,患者预后较差^[1,2]。相关研究调查发现^[3],全球范围内每年大

约有 200 万人死于 AKI,在需要实施肾脏替代治疗的 AKI 患者中的死亡率高达 50%-80%,在我国 AKI 的死亡率也较高,给我国居民的身体安康水平和生命安全造成了严重的威胁。目前血液透析(Hemodialysis, HD)是重症 AKI 最主要且有效的治疗方法,HD 是通过弥散/对流的方式将透析液与体内的代谢废物和过多的水分进行交换,以达到净化血液的目的,它的主要缺点在于不能清除脂溶性较高的、与蛋白质结合的大分子物质^[4,5]。而血液灌流(Hemoperfusion, HF)通过吸附作用能有效清除血液内肌酐、尿酸、酚类等物质,同时可清除甲状旁腺激素、

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(收稿日期:2017-11-29 接受日期:2017-12-23)

β 2-微球蛋白等中大分子物质,理论上可弥补HD的不足^[6]。有研究指出^[7],对AKI患者联用HD和HF治疗效果更佳。本研究旨在探讨HD联合HF治疗对AKI患者的疗效以及对患者生化指标的影响,以期为AKI的治疗提供更多参考,现报道如下。

1 资料与方法

1.1 一般资料

选取2016年1月-2017年2月在我院治疗的AKI患者56例,纳入标准:(1)符合《肾脏病学》中关于AKI的诊断标准^[8];(2)临床资料完整;(3)患者及其家属对本研究知情同意。排除标准:(1)预计生存期<3个月的AKI患者;(2)合并高血压等慢性疾病或严重器质性损伤疾病者;(3)合并有恶性肿瘤者;(4)存在严重精神障碍者;(5)不配合治疗者。按随机数字表法将患者分为对照组和观察组,各28例。对照组男17例,女11例,年龄25~72岁,平均 (54.45 ± 8.31) 岁,体质质量指数为 $17 \sim 24 \text{ kg/m}^2$,平均 $(20.11 \pm 1.12) \text{ kg/m}^2$;观察组男15例,女13例,年龄22~68岁,平均 (55.63 ± 7.92) 岁,体质质量指数为 $18 \sim 24 \text{ kg/m}^2$,平均 $(20.26 \pm 1.17) \text{ kg/m}^2$ 。两组患者一般资料比较差异不显著($P>0.05$),可进行临床比较。本研究经医院伦理委员会批准可以进行。

1.2 治疗方法

所有患者均给予常规治疗,如抗感染、营养支持、调节电解质酸碱平衡紊乱等。经股静脉或者颈内静脉穿刺置管,建立血管通路。对照组采用费森尤斯4008B型血液透析机(厂商:Fresenius Medical Care, FMC)进行单纯HD治疗,碳酸盐透析液流量取500 mL/h,血流量为200~250 mL/min,根据患者的液体平衡调节超滤速度,1次/d,连续治疗3 d,随后改为3次/周,每次持续4 h,治疗2周为一个疗程。观察组进行HD联合HF治疗,将血液透析机和血液灌流器(珠海健帆生物科技有限公司)串联,并用肝素生理盐水冲洗管路,然后用双腔导管将两者另外端口进行连接,从而形成一个闭合的循环回路,血流量从50 mL/min开始,每5 min增加50~80 mL/min,15~20 min后可控制在180~200 mL/min,首次应用30~40 mg肝素抗凝剂,以5 mg/h的剂量追加2 h,肝素终剂量为50~60 mg,先进行HD联合HF治疗2 h,再继续进行HD治疗2~2.5 h,1次

/d,连续治疗3 d,随后改为3次/周,每次持续4 h,治疗2周为一个疗程。两组患者治疗期间均密切监测患者的基本体征变化,如心率、体温、血压、神志情况等,同时观察患者有无出现畏寒、寒战、低血压、胸闷、心悸、气促等副反应,发现异常立即进行相关处理。

1.3 观察指标

(1)两组患者入院前及治疗1个月后抽取空腹静脉血5 mL,以3500 r/min的速度离心10 min,离心半径为3 cm,分离血清。采用日立全自动生化分析仪检测血肌酐(Serum creatinine, Scr)、血尿素氮(Blood urea nitrogen, BUN)水平,并采用酶联免疫吸附法检测血清C反应蛋白(C reactive protein, CRP)、肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)和白细胞介素-2(Interleukin-2, IL-2)水平,严格按照试剂盒(购于北京北方生物技术研究所)指南操作步骤进行。(2)检验并比较两组治疗疗效;(3)统计治疗期间两组并发症发生情况。

1.4 疗效评价

治疗期间均密切监测两组患者的基本体征变化,在治疗1个月后评定疗效。显效:患者经治疗后,腹水、水肿等临床症状消失,血常规、尿常规及肝肾功能恢复正常。有效:患者经治疗后,腹水、水肿等临床症状明显减少,血常规、尿常规及肝肾功能大致恢复正常。无效:患者经治疗后,腹水、水肿等临床症状无好转或加重,血常规、尿常规及肝肾功能无明显变化或患者死亡。总有效率为显效与有效例数之和在总例数中的占比。

1.5 统计学处理

应用SPSS 19.0进行数据分析,治疗疗效、并发症发生率等计数资料以率(%)表示,采用 χ^2 检验,Scr、BUN及炎症因子水平等计量资料以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用t检验,检验水准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者治疗前、治疗1个月后生化指标的比较

治疗前,两组患者的Scr、BUN水平无明显差异($P>0.05$),治疗1个月后,两组患者的Scr、BUN水平均明显降低,且观察组的Scr、BUN水平明显低于对照组($P<0.05$),见表1。

表1 两组患者生化指标对比($\bar{x} \pm s$)

Table 1 Comparison of biochemical indexes between two groups ($\bar{x} \pm s$)

Groups	n	Scr($\mu\text{mol} \cdot \text{L}^{-1}$)		BUN($\text{mmol} \cdot \text{L}^{-1}$)	
		Before treatment	1 months after treatment	Before treatment	1 months after treatment
Control group	28	63.41 $\pm$ 1.86	45.72 $\pm$ 5.31*	18.31 $\pm$ 3.05	14.01 $\pm$ 1.75*
Observation group	28	64.32 $\pm$ 2.06	21.36 $\pm$ 5.15*	18.26 $\pm$ 2.21	10.35 $\pm$ 1.12*
t	-	1.391	13.972	0.056	7.474
P	-	0.173	0.000	0.956	0.000

Note: compared with before treatment, * $P<0.05$.

2.2 两组患者治疗前、治疗1个月后CRP、TNF- α 、IL-2水平比较

治疗前,两组患者的CRP、TNF- α 、IL-2水平无明显差异($P>0.05$),治疗1个月后,两组患者的CRP、TNF- α 、IL-2水平均较治疗前明显降低,且相较对照组而言,观察组以上各指标

均降低($P<0.05$),见表2。

2.3 两组患者治疗效果的比较

观察组的总有效率明显较对照组升高(89.29%vs64.29%)($P<0.05$)。见表3。

表 2 两组患者 CRP、TNF- α 、IL-2 水平比较($\bar{x} \pm s$)

Table 2 Comparison of CRP, TNF- α and IL-2 levels between the two groups ($\bar{x} \pm s$)

Groups	n	CRP(mg·L ⁻¹)		TNF- α (pg·mL ⁻¹)		IL-2(pg·mL ⁻¹)	
		Before treatment	1 months after treatment	Before treatment	1 months after treatment	Before treatment	1 months after treatment
Control group	28	18.31 $\pm$ 2.40	12.62 $\pm$ 2.12*	3.42 $\pm$ 1.02	2.93 $\pm$ 0.61*	17.64 $\pm$ 2.52	12.36 $\pm$ 2.30*
Observation group	28	18.12 $\pm$ 2.51	9.21 $\pm$ 1.53*	3.34 $\pm$ 1.12	2.13 $\pm$ 0.52*	17.23 $\pm$ 2.61	8.42 $\pm$ 2.03*
t	-	0.305	6.971	0.356	5.420	0.587	6.771
P	-	0.761	0.000	0.723	0.000	0.560	0.000

Note: compared with before treatment, *P<0.05.

表 3 两组治疗效果的比较[n(%)]

Table 3 Comparison of therapeutic effects between the two groups [n (%)]

Groups	n	Excellent	Effective	Invalid	Total effective rate
Control group	28	10(35.71)	8(28.57)	10(35.71)	18(64.29)
Observation group	28	14(50.00)	11(39.29)	3(10.71)	25(89.29)
χ^2					4.909
P					0.027

2.4 两组患者并发症的比较

观察组治疗期间有 1 例患者并发腹膜炎,并发症发生率为 3.57%;对照组治疗期间有 3 例并发腹膜炎、1 例并发水电解质紊乱、2 例并发容量依赖性低血压,并发症发生率为 21.43%。两组并发症发生率比较差异有统计学意义($\chi^2=4.082$, $P=0.043$)。

3 讨论

AKI 患者起病迅速、病情进展快,在内科系统疾病中其病死率一直居高不下^[9]。该病的发生机制较为复杂,总结目前的学术观点,可分为微循环障碍、胰酶激活、自身消化学说、细胞因子级联反应学说等,而在 AKI 的发生、发展和转归过程中炎症递质均发挥着至关重要的作用^[10,11]。在发病初期,由于肾损伤导致机体产生严重的急性炎症反应,机体 CRP、TNF- α 和 IL-2 等促炎症因子水平被大量合成并释放入血液中,并相互产生协同作用诱发甚至加重器官功能损伤^[12]。Scr 是人体肌肉的代谢产物,其主要由肌酸通过不可逆的非酶脱水反应逐渐形成,经血管再释放到血液中,由于 Scr 是小分子物质,其在肾小管内很少被吸收,通常可通过肾小球的滤过随尿液排出体外,是衡量肾功能的重要指标,当肾功能受损严重时,肾小球的滤过能力下降明显,造成 Scr 浓度升高^[13,14]。BUN 主要产生于肾代谢系统,是蛋白质代谢的主要终末产物,也是血清中除蛋白质以外的一种含氮化合物,其一般以废物的形式通过肾小球滤过排出体外,当肾小球滤过率下降到正常的 50%以下时,BUN 的浓度会迅速升高,因此临床上常用 BUN 来评估肾功能的受损程度^[15,16]。因此,对于 AKI 患者,在选择临床治疗方案的同时需要考虑到积极改善血清学指标,才能达到理想的预期效果,改善预后,应当将清除炎症递质、维持内环境平衡作为 AKI 治疗的根本原则。

本研究发现,治疗 1 个月后,观察组的 Scr、BUN、CRP、TNF- α 、IL-2 水平明显低于对照组,观察组的有效率明显高于对照组($P<0.05$)。说明 HD 和 HF 两种疗法联合使用能取长补短,发挥各自的优势,能更有效的降低 AKI 患者体内的 Scr、

BUN、CRP、TNF- α 、IL-2 水平,改善肾功能,控制炎症反应。HD 作为治疗 AKI 的主要方法之一,它利用半透膜的原理,将患者血液和透析液同时引入透析器,借助于透析膜两侧的浓度梯度、压力梯度,将新鲜血液和透析液与体内的代谢废物进行交换,以达到清除患者体内毒素、滞留的过多水分、补充机体所需物质的目的,进而纠正机体内电解质和酸碱平衡紊乱,具有操作简便、安全性好等优点^[17,18]。但是 HD 只能清除 Scr、BUN 等小分子物质,而难以清除易结合蛋白质脂溶性高的大分子毒物^[19]。HF 是以吸附剂为媒介,通过其强力的吸附作用,清除机体血液中的外源性或内源性毒素,并将净化好的血液通过吸附剂装置回输体内的一种血液净化方法,HF 对清除脂溶性高与蛋白质结合率高的大分子物质的效果明显优于 HD,能够弥补单纯 HD 治疗的不足^[20,21]。但是它也存在缺点,单纯的 HF 治疗所用的吸附剂具有生物不相容性,易发生吸附颗粒栓塞,造成凝血功能紊乱,因此单纯 HF 治疗必需严格控制抗凝剂肝素的使用量和使用方法^[22]。除此之外,HF 也不能去除尿素,对酸中毒、电解质紊乱无纠正作用^[23]。HD 联合 HF 治疗效果更佳的原因分析如下:HD 只能将 AKI 患者机体的内源性和外源性有毒物质清除,但是对炎症细胞因子的清除作用并不理想,虽然有一定的效果,但是作用不佳^[24,25]。将二者串联用于 AKI 患者肾脏替代治疗中能够借助吸附和弥散之间的对流作用,同时清除血液中的炎症递质与有毒物质,并且对于维持内环境稳定、保护脏器功能、提高临床效果和改善预后成效均具有积极的作用^[26,27]。此外,联合应用 HF 和 HD 治疗 AKI 还能够调节电解质和酸碱平衡,更好的恢复肾功能,具有较好的临床效果,能明显改善患者的生化指标^[28]。值得注意的是,HD 和 HF 联合应用于 AKI 的患者时,血液灌流器应置于血液透析机前面,这样有助于回血保温,能避免透析脱水后血液浓缩发生凝血,同时有利于血液透析机对电解质和酸碱平衡的调节^[29,30]。此外,本研究结果发现,观察组并发症发生率为 3.57%,明显低于后者的 21.43% ($P<0.05$),可知在 AKI 患者临床治疗中,相较于单纯的 HD 治

疗方案, HF 联合 HD 方案具有更高的安全性。

综上所述, 与单纯使用 HD 治疗相比, HD 联合 HF 对 AKI 患者的治疗效果更佳、对生化指标、炎症因子指标的改善程度更明显, 且并发症更少, 值得在临床上推广应用。

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检测,也为未来多肿瘤标志物同时检测提供了可参考的新途径。

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