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血必净注射液联合静脉胰岛素泵入治疗糖尿病酮症酸中毒的效果 及对氧化应激反应的影响*

刘佳¹ 朱爱华¹ 吴艳杰¹ 盛佳曦² 邢兰访¹

(1 唐山市人民医院急诊科 河北 唐山 063000; 2 华北理工大学附属医院内分泌科 河北 唐山 063000)

摘要 目的:探讨血必净注射液联合静脉胰岛素泵入治疗糖尿病酮症酸中毒的效果及对氧化应激反应的影响。**方法:**选择 2016 年 8 月至 2018 年 8 月我院收治的糖尿病酮症酸中毒患者 80 例,根据随机数表法分为观察组(n=41)和对照组(n=39)。对照组给予胰岛素泵治疗,观察组在对照组的基础上采用血必净注射液治疗。比较两组患者的临床疗效、治疗前后单核细胞趋化蛋白(MCP)、空腹血糖(FBG)、餐后血糖(PBG)、丙二醛(MDA)、超氧化物歧化酶(SOD)、总抗氧化能力(TAC)水平的变化及临床症状改善时间。**结果:**治疗后,两组单核细胞趋化蛋白水平均较治疗前显著下降,且观察组明显低于对照组($P<0.05$)。治疗后,观察组 MDA 低于对照组, SOD、TAC 水平均显著高于对照组($P<0.05$);观察组血糖达标、尿酮体转阴、PH 恢复时间及胰岛素用量均显著低于对照组($P<0.05$)。**结论:**血必净注射液联合胰岛素泵治疗糖尿病酮症酸中毒患者的效果显著明显优于单用血必净治疗,可能与其有效提高机体的抗氧化能力有关。

关键词:血必净注射液;胰岛素泵;糖尿病酮症酸中毒;单核细胞趋化蛋白

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Curative Efficacy of Xuebijing Injection Combined with Intravenous Insulin Pump in the Treatment of Diabetic Ketoacidosis and Its Effects on the Oxidative Stress Response*

LIU Jia¹, ZHU Ai-hua¹, WU Yan-jie¹, SHENG Jia-xi², XING Lan-fang¹

(1 Emergency department of Tangshan people's Hospital, Tangshan, Hebei, 063000, China;

2 Department of Endocrinology, Affiliated Hospital of North China University of technology, Tangshan, Hebei, 063000, China)

ABSTRACT Objective: To study the curative efficacy of Xuebijing injection combined with intravenous insulin pump in the treatment of Diabetic ketoacidosis and its effects on the oxidative stress response. **Methods:** 80 patients with diabetic ketoacidosis admitted to our hospital from August 2016 to August 2018 were selected and divided into the observation group (n=41) and the control group (n=39) according to the random number table method. The control group was treated with insulin pump and the observation group was treated with Xuebijing injection on the basis of control group. The changes of monocyte chemoattractant protein (MCP), fasting blood glucose (FBG), postprandial blood glucose (PBG), malondialdehyde (MDA), superoxide dismutase (SOD) and total antioxidant capacity (TAC) levels before and after treatment and the improvement time of clinical symptoms were compared between the two groups. **Results:** After treatment, the MCP levels in both groups were significantly decreased compared with those before treatment, which was significantly lower in the observation group than that of the control group ($P<0.05$). After treatment, the MDA in the observation group was lower than that in the control group, and SOD and TAC levels were significantly higher than those in the control group ($P<0.05$). In the observation group, the blood glucose standard, urine ketone body negative, PH recovery time and insulin dosage were significantly lower than those in the control group ($P<0.05$). **Conclusion:** The therapeutic effect of Xuebijing injection combined with insulin pump on the patients with diabetic ketoacidosis was significantly better than that of xuebijing injection alone, which may be related to the effective improvement of the antioxidant capacity.

Key words: Xuebijing injection; Insulin pump; Diabetic ketoacidosis; Monocyte chemotactic proteins

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前言

酮症酸中毒是糖尿病患者的严重并发症,病情发展迅速,

临床主要表现为高血糖、代谢性酸中毒、电解质紊乱等症状,严重者可并发急性肾衰竭、休克,若得不到及时治疗可能威胁患者生命^[1-3]。外周血单核细胞趋化蛋白由内皮细胞及血管平滑肌

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作者简介:刘佳(1984-),女,硕士,主治医师,研究方向:内科急危重症,电话:13633302523, E-mail: qianxuefeng065@163.com

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细胞分泌,可趋化血液循环中的单核细胞进入肾组织,在肾小球基底膜下活化成巨噬细胞,与糖尿病酮症酸中毒的发生关系密切^[4]。糖尿病酮症酸中毒患者体内持续存在的高糖环境生成大量氧自由基,进而通过氧化应激反应来造成组织损伤。MDA、SOD、TAC 是临床常用的氧化应激指标,在氧化应激反应激活过程中 MDA、SOD、TAC 等抗氧化酶能够在一定程度上清除氧自由基,造成抗氧化酶过度消耗并导致抗氧化力减弱^[5]。因此治疗应以改善患者氧化应激反应水平促进患者恢复。胰岛素泵是临床治疗糖尿病酮症酸中毒的常用方法,可通过微管将胰岛素持续输,在短时间内控制患者血糖水平,已被广泛运用于临床^[6,7]。

血必净注射液可有效拮抗内毒素诱导单核细胞产生的内源性炎症介质失控性释放,下调促炎介质水平,但其对外周血单核细胞趋化蛋白的影响尚无相关报道^[8,9]。因此,本研究主要探讨了联合治疗的临床疗效,并观察其对外周血单核细胞趋化蛋白及氧化应激反应的影响。

1 资料与方法

1.1 一般资料

选择 2016 年 8 月至 2018 年 8 月于我院进行治疗的 80 例糖尿病酮症酸中毒患者。采用随机分组法分为 2 组,观察组 41 例,其中男 28 例,女 13 例;年龄 26~77 岁,平均(58.37±5.36)岁,病程 2~10 年,平均(6.59±2.08)年。对照组男 25 例,女 14 例;年龄 28~78 岁,平均(58.42±5.42)岁,病程 2~11 年,平均(6.63±2.15)年。两组基线资料无明显差异,具有可比性。

纳入标准:(1)符合《糖尿病酮症酸中毒的诊断和防治》^[10]的诊断标准;(2)患者知情同意。排除标准:(1)心功能异常者;(2)伴

有恶性肿瘤者;(3)血液系统异常者。(4)合并重症感染疾病;(5)有严重过敏史者;(6)严重肝肾异常者。

1.2 治疗方法

入院后,两组患者均给予常规补液、纠正水电解质紊乱等对症支持治疗。对照组给予静脉胰岛素输液泵:持续静脉滴注输入胰岛素,全天总量为 0.05~0.1 U/kg。当血糖低于 13.9 mmol/L 时,停用静脉微泵并按照 1U 胰岛素:4~6 g 葡萄糖的比例将胰岛素加入 5% 葡萄糖注射液,静脉滴注。观察组在对照组的基础上给予血必净注射液:血必净注射液(规格 10 mL,厂家:天津红日药业股份有限公司,国药准字 Z20040033)50 mL 静脉滴注,1d 1 次。

1.3 观察指标

采集治疗前、后肘静脉血 4 mL,3500 r·min⁻¹ 离心 10 min,提取血清,采用酶联免疫吸附试验(ELISA)测定单核细胞趋化蛋白、MDA、SOD、TAC 水平,试剂盒均由海源叶生物科技有限公司提供;记录患者临床症状的改善情况。

1.4 统计学分析

采用 spss18.0 软件包处理数据,符合正态分布计量资料用均数±标准差($\bar{x} \pm s$)表示,组间比较使用独立样本 t 检验,计数资料以率表示,组间比较采用 χ^2 检验,以 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组治疗前后血清单核细胞趋化蛋白水平的比较

治疗后,两组单核细胞趋化蛋白水平均较治疗前显著下降,且观察组明显低于对照组($P < 0.05$),见表 1。

表 1 两组治疗前后血清单核细胞趋化蛋白水平的比较($\bar{x} \pm s$, pg/mL)

Table 1 Comparison of the serum chemotactic protein levels between the two groups before and after treatment ($\bar{x} \pm s$, pg/mL)

Groups	n	Monocyte chemotactic proteins	
		Before the treatment	After treatment
Observation group	41	6.86±2.61	4.31±1.19
Control group	39	6.83±2.59	5.32±1.93
t value		0.052	2.833
P value		0.959	0.006

2.2 两组抗氧化能力指标水平比较

治疗后,两组 MDA、SOD、TAC 水平均显著改善,且观察

组优于对照组($P < 0.05$),见表 2。

表 2 两组治疗前后抗氧化能力指标的水平比较($\bar{x} \pm s$)

Table 2 Comparison of Antioxidant capacity indicators between the two groups($\bar{x} \pm s$)

Groups	n	MDA(nmol/mL)		SOD(U/L)		TAC(U/ mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	41	8.93±2.17	4.01±1.79	22.73±7.13	31.05±8.41	17.85±5.21	26.89±4.27
Control group	39	8.87±2.21	4.98±2.04	22.81±7.23	27.21±7.35	17.79±5.36	22.19±5.07
t value		0.123	2.264	0.049	2.170	0.051	4.493
P value		0.903	0.026	0.960	0.033	0.959	0.000

2.3 两组临床症状改善时间比较

均显著低于对照组($P<0.05$),见表3。

观察组血糖达标、尿酮体转阴、PH 恢复时间及胰岛素用量

表3 两组临床症状改善时间比较($\bar{x}\pm s$)

Table 3 Comparison of the clinical symptom improvement time between the two groups($\bar{x}\pm s$)

Groups	n	Blood glucose control is at target(h)	Urine ketone body turns negative(h)	PH restore(h)	Insulin dosage(U)
Observation group	41	5.29±1.71	21.28±6.07	9.21±2.61	54.58±7.31
Control group	39	6.98±2.29	33.84±10.41	15.17±3.29	76.28±9.25
t value		3.752	6.632	8.999	11.672
P value		0.000	0.000	0.000	0.000

3 讨论

近年来,受环境污染及生活方式等多种因素的影响,糖尿病发生率逐年上升,其并发症导致的死亡率也随之升高^[11-13]。糖尿病酮症酸中毒由急性感染、暴饮暴食及应激反应等因素引起,起病急,病情进展快,是造成糖尿病患者死亡的重要原因^[14,15]。大量研究显示糖尿病酮症酸中毒患者机体血糖水平显著升高,且伴有胰岛素分泌不足,使脂肪大量分解产能,血液中酮体聚集,导致机体中毒^[16-18]。因此,治疗应以控制血糖及纠正机体中毒状态为主。

胰岛素是治疗糖尿病酮症酸中毒的常用药物,可促进胰岛β细胞功能恢复,抑制脂肪分解产生酮体及视网膜、神经等,改善患者机体症状,但是其单一治疗效果并不明显,故较多学者提出在此基础上联合用药^[19,20]。血必净注射液可减少炎性渗出、改善微循环,保护血管内皮细胞,并减轻血液高凝状态,治疗糖尿病酮症酸中毒的效果良好^[21,22]。有研究显示血必净注射液可改善糖尿病酮症酸中毒患者的肾功能,提高糖尿病酮症酸中毒的治疗效果^[23]。

外周血单核细胞趋化蛋白在单核细胞成纤维细胞、血管及平滑肌细胞上均可表达^[24]。有研究显示单核细胞趋化蛋白可引起肾小管周围大量巨噬细胞的募集,造成小管受损,加重肾损伤,从而导致糖尿病酮症酸中毒的发生^[25,26]。Jayalakshmi K^[27]等研究显示在糖尿病酮症酸中毒早期,单核细胞趋化蛋白可通过引起肾小球巨噬细胞的浸润,诱导肾纤维化的发生,其通过直接与肾小球基底膜细胞上的趋化因子受体2结合,引起纤维化反应,加快糖尿病酮症酸中毒患者的肾脏纤维化进程。本研究中,糖尿病酮症酸中毒患者单核细胞趋化蛋白升高,经治疗后其水平降低,且血必净注射液联合胰岛素泵治疗的患者单核细胞趋化蛋白水平低于单独使用胰岛素泵治疗的患者。分析其原因可能是因为胰岛素泵可迅速控制机体血糖,抑制脂肪分解产生酮体,酮体代谢恢复;血必净注射可抑制肝脏葡萄糖异生,增加外周组织对葡萄糖的利用,抑制脂肪分解,同时降低患者血中过高的胰岛素拮抗激素水平,提高对胰岛素的敏感性,调节体内物质代谢,从而降低患者的单核细胞趋化蛋白水平。

有研究显示血必净注射液可改善糖尿病酮症酸中毒患者的炎症反应,降低体内氧化应激反应水平^[28,29]。本研究结果显示联合治疗的患者抗氧化能力改善情况由于单独使用胰岛素泵的患者,与 You JH^[30]等研究结果相似,提示联合治疗可改善患

者血糖水平及氧化应激反应指标水平。分析其原因是因为血必净注射液可改善血液高凝状态,可激活脂蛋白酶,促进三酰甘油水解,降低血液黏稠度及血脂水平,从而改善患者血糖水平。此外,联合治疗患者临床症状改善时间均显著低于单独使用胰岛素泵的患者,提示血必净注射液联合胰岛素泵可改善患者的临床症状。

综上所述,血必净注射液联合胰岛素泵治疗糖尿病酮症酸中毒患者的效果显著明显优于单用血必净治疗,可能与其有效提高机体的抗氧化能力有关。

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