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舌下含服卡托普利用于院前急救高血压急症的临床疗效及对患者血清sCD40L、sPECAM-1、PDGF-BB 水平的影响 *

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摘要 目的:探讨舌下含服卡托普利用于院前急救高血压急症的临床疗效及对患者血清可溶性 CD40L(sCD40L)、可溶性血小板内皮细胞黏附分子 1(sPECAM-1)、血小板衍生生长因子 -BB(PDGF-BB)水平的影响。方法:选择 2015 年 5 月到 2017 年 5 月我院院前急救高血压急症患者 65 例作为研究对象,按照随机数表法分为观察组(n=35)和对照组(n=30)。对照组给予硝苯地平舌下含化治疗,观察组采用舌下含服卡托普利治疗。比较两组治疗后的疗效,治疗前后血清 sCD40L、sPECAM-1、PDGF-BB 水平、收缩压(SBP)、舒张压(DBP)、心率(HR)的变化及不良反应的发生情况。结果:治疗后,观察组临床疗效总有效率为 94.29%,显著高于对照组(73.33%, $P<0.05$);两组血清 sCD40L、sPECAM-1、PDGF-BB、SBP、DBP 及 HR 水平均较治疗前明显下降,且观察组以上指标均显著低于对照组($P<0.05$);观察组患者不良反应发生率为 17.14%,明显低于对照组(56.67%, $P<0.05$)。结论:舌下含服卡托普利用于院前急救高血压急症患者的临床效果显著优于硝苯地平舌下含化治疗,其可更有效改善患者血清 sCD40L、sPECAM-1、PDGF-BB 水平。

关键词:卡托普利;院前急救高血压急症;可溶性 CD40L;可溶性血小板内皮细胞黏附分子 1;血小板衍生生长因子 -BB

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Curative Efficacy of Undertongue Contains Captopril in the Treatment of Pre-hospital Emergency Hypertension and Its Effects on the Serum sCD40L, sPECAM-1 and PDGF-BB Levels*

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ABSTRACT Objective: To study the curative efficacy of undertongue contains captopril in the treatment of Pre-hospital emergency hypertension and its effects on the serum Soluble CD40L (sCD40L), Soluble platelet endothelial cell adhesion molecule 1 (specam-1) and Platelet derived growth factor -BB (pdgf-bb) levels. **Methods:** 65 cases of emergency patients with hypertension in our hospital from May 2015 to May 2017 were selected as the study subjects, they were divided into the observation group (n=35) and the control group (n=30) by the random number table method. The control group was treated with nifedipine sublingual inclusion, and the observation group was treated with captopril. The clinical efficacy, changes of serum sCD40L, specam-1, pdgf-bb, SBP, DBP, HR levels before and after treatment and the incidence of adverse reactions were compared between two groups. **Results:** After treatment, the total effective rate of observation group was 94.29%, which was significantly higher than that of the control group (73.33%, $P<0.05$). The serum sCD40L, specam-1, pdgf-bb, SBP, DBP and HR levels of both groups after treatment were significantly lower than those before treatment, and the above indicators in the observation group were significantly lower than those in the control group ($P<0.05$). The incidence of adverse reactions in the observation group was 17.14%, which was significantly lower than that in the control group (56.67%, $P<0.05$). **Conclusion:** The clinical effect of sublingual administration of captopril in prehospital emergency hypertension patients is significantly better than that of nifedipine sublingual administration, which can more effectively improve the serum sCD40L, specam-1 and pdgf-bb levels of patients.

Key words: Captopril; Pre-hospital emergency hypertension; Soluble CD40L; Soluble platelet endothelial cell adhesion molecule 1; Platelet derived growth factor-BB

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前言

高血压急症是内科危重症,是指在原发性或继发性高血压

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患者在一定诱因作用下, 血压突然升高, 同时伴有进行性心、脑、肾等临床综合征, 可在短时间内导致机体组织器官发生不可逆的损害, 处理不当将会给患者带来生命危险^[2]。院前急救是抢救高血压急症的重要环节, 能迅速、有效地降低血压^[3,4]。既往通常使用硝苯地平治疗该病, 硝苯地平是目前钙拮抗剂中最有效的降压药, 具有价廉、方便携带等优点, 但是其副作用较高, 且不能减少无症状性心肌缺血的发作次数^[5]。研究显示卡托普利对高血压有明显的疗效, 是一种血管紧张素转化酶抑制剂, 现已被临床广泛运用于治疗高血压和某些类型的充血性心力衰竭^[6,7]。本研究旨在探讨舌下含服卡托普利对院前急救高血压急症的临床疗效, 并观察其对患者血清 sCD40L、sPECAM-1、PDGF-BB 水平的影响, 现降结果报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 5 月到 2017 年 5 月在我院进行治疗的 65 例急救高血压急症患者进行研究。采用简单随机分组法分为两组。观察组 35 例, 年龄 31~67 岁, 平均(44.86±8.62)岁, 男 23 例, 女 12 例; 对照组男 20 例, 女 10 例; 年龄 34~70 岁, 平均(44.79±8.89)岁。两组患者一般资料比较差异无统计学意义(P>0.05), 具有可比性。

纳入标准: (1)符合中国高血压防治指南 2010 版^[8]诊断标准; (2)血压明显升高(>180/120 mmHg); (3)未服用任何药物者。排除标准: (1)甲状腺功能亢进、自身免疫病者; (2)合并失血性休克、多器官功能衰竭、凝血功能障碍者; (3)有脑肿瘤史、血栓史等。

1.2 治疗方法

对照组给予硝苯地平(规格 30 mg, 厂家: 拜耳医药保健股份公司德国, 国药准字 H20100651)10 mg 舌下含服。观察组采用卡托普利(规格 25 mg, 厂家: 中美上海施贵宝制药有限公司, 国药准字 H31022816)25 mg 舌下含服。

1.3 观察指标

于治疗前后, 采集清晨空腹血 8 mL, 将其常规分离后于 -80℃ 保存待检, 期间避免样本反复冻融, 采用双抗体夹心酶联免疫吸附法(ELISA)测定血清 sCD40L、sPECAM-1、PDGF-BB; 记录患者 SBP、DBP、HR; 记录术后不良反应发生情况。

疗效评定标准^[9]: 显效: 舒张压降低≥10 mmHg, 收缩压降低≥20 mmHg; 有效: 舒张压降低<10 mmHg, 收缩压降低 10~19 mmHg; 无效: 未达到上述任一标准。显效+有效=总有效率。

1.4 统计学分析

以 SPSS18.0 软件包处理数据, 计量资料均为正态分布, 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 两组临床疗效的比较

治疗后, 观察组和治疗组的总有效率分别为 94.29%、73.33%, 观察组显著高于对照组, 组间比较差异具有统计学意义(P<0.05), 见表 1。

表 1 两组临床疗效的比较[例(%)]

Table 1 Comparison of the clinical efficacy between the two groups[n(%)]

Groups	n	Effective	Valid	Invalid	Total effective rate
Observation group	35	30(85.71)	3(8.57)	2(5.71)	33(94.29)
Control group	30	17(56.67)	5(16.67)	8(26.67)	22(73.33)
χ^2 value					5.448
P value					0.020

2.2 两组患者治疗前后血清 sCD40L、sPECAM-1、PDGF-BB 水平的比较

两组患者治疗前血清 sCD40L、sPECAM-1、PDGF-BB 水平比较差异无统计学意义(P>0.05); 治疗后, 两组血清 sCD40L、

sPECAM-1、PDGF-BB 水平均较治疗前明显下降, 且观察组血清 sCD40L、sPECAM-1、PDGF-BB 水平均显著低于对照组, (P<0.05), 见表 2。

表 2 两组患者治疗前后血清 sCD40L、sPECAM-1、PDGF-BB 水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the serum sCD40L, sPECAM-1 and PDGF-BB levels between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	sCD40L(pg/mL)		sPECAM-1(ng/mL)		PDGF-BB(ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	35	5192.75±1145.62	2469.65±951.35	57.13±8.75	45.62±7.34	27.24±16.41	19.37±7.16
Control group	30	5201.34±1147.59	3624.28±1012.34	58.01±8.86	51.36±7.46	27.68±16.39	23.78±9.65
t value		0.030	4.736	0.402	3.120	0.108	2.111
P value		0.976	0.000	0.689	0.003	0.915	0.040

2.3 两组患者治疗前后 SBP、DBP 及 HR 水平的比较

治疗后, 两组 SBP、DBP 及 HR 水平均较治疗前明显下降, 且观察组 SBP、DBP 及 HR 水平显著低于对照组 (P<0.05), 见表 3。

2.4 两组患者并发症发生情况的比较

治疗后, 两组患者并发症发生率分别为 17.14%、56.67%, 观察组显著低于对照组。组间比较差异具有统计学意义(P<0.05), 见表 4。

表 3 两组患者治疗前后 SBP、DBP 及 HR 水平的比较($\bar{x} \pm s$)Table 3 Comparison of the SBP, DBP and HR between two groups before and after treatment($\bar{x} \pm s$)

Groups	n	SBP(mmHg)		DBP(mmHg)		HR(beat/min)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	35	213.45 $\pm$ 24.56	155.13 $\pm$ 12.24	124.56 $\pm$ 12.35	92.38 $\pm$ 9.68	94.24 $\pm$ 16.57	91.24 $\pm$ 14.13
Control group	30	212.79 $\pm$ 25.67	169.27 $\pm$ 15.24	123.97 $\pm$ 12.65	97.58 $\pm$ 9.59	93.86 $\pm$ 16.82	99.27 $\pm$ 13.97
t value		0.106	4.147	0.190	2.168	0.092	2.296
P value		0.716	0.000	0.850	0.034	0.927	0.025

表 4 两组患者不良反应发生情况的比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between the two groups[n(%)]

Groups	n	Flush on face	Tachycardia	Have a headache	Heart rate	The total incidence of
Observation group	35	2(5.71)	1(2.86)	2(5.71)	1(2.86)	6(17.14)
Control group	30	4(13.33)	2(6.67)	4(13.33)	7(23.33)	17(56.67)
χ^2 value		1.119	0.533	1.119	6.275	11.037
P value		0.290	0.466	0.290	0.012	0.001

3 讨论

高血压急症是指在高血压病程中因某些诱因使血压在短时间内升高,造成心脑肾等重要器官损害的临床综合征^[11-13]。院前急救是指患者从现场到医院之前就地抢救的救治,主要是抢救生命和减少伤残,为后续治疗创造条件,有效的院前急救能够缩短抢救时间,提高救治成功率,短时间内将血压控制在目标范围内^[14,15]。而院前急救受条件影响,限制了静脉用药。因此,医护人员需选择一种服用方便的平稳降压药,机体舌下下面有丰富的静脉丛,当药物在舌下发生作用时,可以快速的吸收,不受食物、胃酸及肝-肠循环影响,减少药物首过效应,提高生物利用率^[16-18]。

以往通常使用硝苯地平治疗此病,硝苯地平是一种二氢吡啶类钙拮抗剂,降压效果明显,但是其可引起反射性心动过速、且降压作用维持时间短,血压波动较大,需频繁监测,给院前特别是现场救治带来不便^[19-21]。卡托普利是一种人工合成的非肽类血管紧张素转化酶抑制剂,能抑制醛固酮系统的血管紧张素转换酶,并能抑制醛固酮分泌,减少水钠潴留,使心脏前后负荷减轻,对各种类型的高血压、心力衰竭等疾病有较好的疗效^[22-24]。

本研究结果显示卡托普利治疗的患者的临床总有效为 94.29%,明显高于使用硝苯地平治疗的患者。sCD40L 是目前最新发现的炎症因子,目前对它的研究还较少;sPECAM-1 是一种细胞黏附分子,具有调控血小板功能、血管再生以及介导白细胞在血管生物学,如血管内皮的迁移^[25-27];PDGF-BB 是血管平滑肌细胞增殖因子,可以诱导血管平滑肌细胞增殖,迁移趋化迁移到膜内血管平滑肌细胞从血管,聚集在脂质池,并可能促进成纤维细胞的生长,促进伤口修复相关的细胞化学联系加强和细胞增殖,促进肉芽组织的形成,促进伤口愈合,缩短愈合时间^[28-30]。本研究结果显示卡托普利治疗的患者的血清 sCD40L、sPECAM-1、PDGF-BB 明显低于使用硝苯地平治疗的患者,分析原因是因为卡托普利可以有效的阻止血管紧张素 I 转换或血管紧张素 II,并能抑制醛固酮分泌。研究结果还显示卡托普利治疗的患者的 SBP、DBP 及 HR 水平明显低于使用硝苯地平治疗的患者,提示卡托普利应用于院前急救高血压急症可有效控制血压,且卡托普利起效迅速,对患者的心率影响小。此外,卡托普利治疗的患者不良反应发生率为 17.14%,明显低于

使用硝苯地平治疗的患者,进一步证实了卡托普利具有较高的安全性。

综上所述舌下含服卡托普利用于院前急救高血压急症患者的临床效果显著优于硝苯地平舌下含化治疗,其可更有效改善患者血清 sCD40L、sPECAM-1、PDGF-BB 水平。

参考文献(References)

- [1] Pura G P, Leucuta D C, Marc G, et al. The impact of urapidil use in hypertension prehospital emergency intervention [J]. Farmacia, 2017, 65(6): 896-899
- [2] Dhungel S, Malla R, Adhikari C, et al. Prehospital Events in ST- Elevation Myocardial Infarction Undergoing Primary Angioplasty[J]. J Nepal Med Assoc, 2017, 56(208): 421-425
- [3] Ariès P, Montelecaut E, Pessey F, et al. Pre-hospital emergency medicine: pain control[J]. Lancet, 2016, 387(10020): 747
- [4] Park H A, Ahn K O, Shin S D, et al. The Effect of Emergency Medical Service Use and Inter-hospital Transfer on Prehospital Delay among Ischemic Stroke Patients: A Multicenter Observational Study[J]. Journal of Korean Medical Science, 2016, 31(1): 139-146
- [5] Safdari R, Shoshtarian M J, Mohammadzadeh N, et al. A Multi Agent Based Approach for Prehospital Emergency Management[J]. Bull Emerg Trauma, 2017, 5(3): 171-178
- [6] Dhadke S V, Dhadke V N, Batra D S. Clinical Profile of Hypertensive Emergencies in an Intensive Care Unit [J]. J Assoc Physicians India, 2017, 65(5): 18-22
- [7] Chamberlain M A, Neumann V, Tennant A. Traumatic Brain Injury Rehabilitation [J]. Physical Medicine & Rehabilitation Clinics of North America, 2017, 7(3): 77-81
- [8] Kerner T, Schmidbauer W, Tietz M, et al. Use of checklists improves the quality and safety of prehospital emergency care [J]. European Journal of Emergency Medicine, 2017, 24(2): 114-119
- [9] Murphy A, Wakai A, Walsh C, et al. Development of key performance indicators for prehospital emergency care [J]. Emergency Medicine Journal, 2016, 33(4): 286-292
- [10] Abellson A, Rystedt I, Suserud B O, et al. Learning by simulation in prehospital emergency care - an integrative literature review[J]. Scandinavian Journal of Caring Sciences, 2016, 30(2): 234-240
- [11] Lee S U, Suh D, Kim H B, et al. Epidemiology of prehospital emergency medical service use in Korean children [J]. Clinical & Experimental Emergency Medicine, 2017, 4(2): 102-108 (下转第 1305 页)

- [18] Jang DH, Da Silva E, Tavakkoli J, et al. Assessment of the effect of strontium, lead, and aluminum in bone on dual-energy x-ray absorptiometry and quantitative ultrasound measurements: A phantom study [J]. *Med Phys*, 2018, 45(1): 81-91
- [19] 刘金山,李迪,武首先,等.脂联素对老化骨髓间充质干细胞自发性骨化的影响[J].*山东医药*, 2017, 57(16): 41-43
- [20] Lekva T, Michelsen AE, Aukrust P, et al. Leptin and adiponectin as predictors of cardiovascular risk after gestational diabetes mellitus[J]. *Cardiovasc Diabetol*, 2017, 16(1): 5
- [21] Nicolas S, Debayle D, B  chade C, et al. Adiporon, an adiponectin receptor agonist acts as an antidepressant and metabolic regulator in a mouse model of depression[J]. *Transl Psychiatry*, 2018, 8(1): 159
- [22] 晋芙莉,宋红霞,宋文萍,等.脂联素、胰岛素生长因子 - I 、前清蛋白与早产儿宫外发育缓慢的相关性[J].*现代生物医学进展*, 2017, 17(26): 5128-5130, 5180
- [23] Cruz-Mej  a S, Dur  n L  pez HH, Navarro Meza M, et al. Body mass index is associated with interleukin-1, adiponectin, oxidative stress and ioduria levels in healthy adults[J]. *Nutr Hosp*, 2018, 35(4): 841-846
- [24] Krikke M, Yumani D, Rustenburg C, et al. Assessing bone development in preterm infants using quantitative ultrasonography showed a decline in the early postnatal period [J]. *Acta Paediatr*, 2018, 107(2): 227-233
- [25] Nakano Y, Itabashi K, Sakurai M, et al. Accumulation of subcutaneous fat, but not visceral fat, is a predictor of adiponectin levels in preterm infants at term-equivalent age [J]. *Early Hum Dev*, 2014, 90(5): 213-217
- [26] Stern JH, Rutkowski JM, Scherer PE. Adiponectin, Leptin, and Fatty Acids in the Maintenance of Metabolic Homeostasis Through Adipose Tissue Crosstalk[J]. *Cell Metab*, 2016, 23(5): 770-784
- [27] 尚利宏,杨真录,王颖源,等.早产儿宫外生长发育迟缓与血清脂联素的关系[J].*中国妇幼保健*, 2015, 30(34): 6011-6014
- [28] Scheller EL, Burr AA, MacDougald OA, et al. Inside out: Bone marrow adipose tissue as a source of circulating adiponectin [J]. *Adipocyte*, 2016, 5(3): 251-269
- [29] Vaitkeviciute D, L  tt E, M  estu J, et al. Adipocytokines and bone metabolism markers in relation to bone mineral values in early pubertal boys with different physical activity [J]. *J Pediatr Endocrinol Metab*, 2016, 29(6): 723-729
- [30] 庞隐,张汝娟,杜晓姬.血清脂联素对极低出生体重早产儿胃肠外营养相关性胆汁淤积的相关性分析[J].*中国儿童保健杂志*, 2016, 24(9): 951-954

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- [12] Hohenstein C, Fleischmann T, Rupp P, et al. German critical incident reporting system database of prehospital emergency medicine: Analysis of reported communication and medication errors between 2005-2015 [J]. *World Journal of Emergency Medicine*, 2016, 7(2): 90-96
- [13] O'Dwyer G, Machado C V, Alves R P, et al. Mobile prehospital emergency care: an analysis of implementation in the State of Rio de Janeiro, Brazil[J]. *Cien Saude Colet*, 2016, 21(7): 2189-2200
- [14] Enumah S, Scott J W, Maine R, et al. Rwanda's Model Prehospital Emergency Care Service: A Two-year Review of Patient Demographics and Injury Patterns in Kigali [J]. *Prehospital & Disaster Medicine*, 2016, 31(6): 614-620
- [15] Schwartz J, Dreyer R P, Murugiah K, et al. Contemporary Prehospital Emergency Medical Services Response Times for Suspected Stroke in the United States [J]. *Prehospital Emergency Care*, 2016, 20(5): 560-565
- [16] Demaret P, Lebrun F, Devos P, et al. Pediatric pre-hospital emergencies in Belgium: a 2-year national descriptive study [J]. *European Journal of Pediatrics*, 2016, 175(7): 921-930
- [17] Haider D G, Lindner G, Wolzt M, et al. Use of Diuretics is not associated with mortality in patients admitted to the emergency department: results from a cross-sectional study[J]. *Journal of Negative Results in Biomedicine*, 2016, 15(1): 1-4
- [18] Nakprasert P, Musikataworn K, Rojanasartikul D, et al. Effect of pre-discharge blood pressure on follow-up outcomes in patients with severe hypertension in the ED [J]. *American Journal of Emergency Medicine*, 2016, 34(5): 834-839
- [19] Nakprasert P, Musikataworn K, Rojanasartikul D, et al. Effect of Pre-discharge Blood Pressure on Follow-up Outcomes in Patients with Severe Hypertension in the Emergency Department[J]. *American Journal of Emergency Medicine*, 2016, 34(5): 834-839
- [20] Newton E, Lasso A, Petreich W, et al. An outcomes analysis of anterior epistaxis management in the emergency department[J]. *Journal of Otolaryngology - Head & Neck Surgery*, 2016, 45(1): 1-5
- [21] Prasanna N, Dissanayake H A, Constantine G R. Sublingual nitroglycerin for early blood pressure control in hypertensive emergencies: observations from an emergency department clinical audit in Sri Lanka [J]. *Bmc Research Notes*, 2018, 11(1): 355
- [22] Froehlich R J, Maggio L, Has P, et al. Improving Obstetric Hypertensive Emergency Treatment in a Tertiary Care Women's Emergency Department[J]. *Obstetrics & Gynecology*, 2018, 132(4): 850-858
- [23] Dimitriadis K, Tsioufis C, Tousoulis D. Modern management of hypertensive emergencies and urgencies: Do we need more technology, paramedics, or physicians?[J]. *Journal of Clinical Hypertension*, 2017, 19(7): 702
- [24] Watson K, Brosnahan R, Devabhakthuni S, et al. Focused Update on Pharmacologic Management of Hypertensive Emergencies[J]. *Current Hypertension Reports*, 2017, 20(7): 56
- [25] Swergold N, Kozusko S, Rivera C, et al. Hypertensive emergency presenting with an isolated celiac artery dissection: A rare case study [J]. *International Journal of Surgery Case Reports*, 2016, 27(C): 147-151
- [26] Ito T, Okamoto R, Taniguchi M, et al. Hypertensive emergency preceding the progression of periaortitis and retroperitoneal fibrosis: case report and review of the literature[J]. *Blood Pressure*, 2016, 25(5): 1-4
- [27] Piqueras-Flores J, Jurado-Rom  n A, L  pez-Lluisa M, et al. Acute pulmonary edema secondary to a hidden hypertensive emergency [J]. *Journal of Cardiology Cases*, 2016, 14(2): 56-58
- [28] Kaya A, Tatlisu M A, Kaplan K T, et al. Sublingual vs. Oral Captopril in Hypertensive Crisis.[J]. *Journal of Emergency Medicine*, 2016, 50(1): 108-115
- [29] Mukherjee D, Sinha R, Akhtar M S, et al. Hyponatremic hypertensive syndrome - a retrospective cohort study: [J]. *World Journal of Nephrology*, 2017, 6(1): 41-44
- [30] Cranmer J N, Dettinger J, Calkins K, et al. Beyond signal functions in global obstetric care: Using a clinical cascade to measure emergency obstetric readiness[J]. *Plos One*, 2018, 13(2): e0184252