

doi: 10.13241/j.cnki.pmb.2019.23.038

银杏达莫注射液联合地塞米松治疗突发性耳聋的疗效及对血清 sVCAM-1、CGRP 水平的影响 *

谌祎玮¹ 周建波^{1Δ} 谢 昀¹ 李金徽¹ 胡丽立²

(1 湖南省人民医院耳鼻喉头颈外科 湖南 长沙 410006; 2 湖南师范大学医学院 湖南 长沙 410006)

摘要 目的:探讨银杏达莫注射液联合地塞米松治疗突发性耳聋的疗效及对血清可溶性血管细胞间黏附因子-1(sVCAM-1)、降钙素基因相关肽(CGRP)水平的影响。**方法:**选择2017年10月到2019年3月于我院进行治疗的突发性耳聋患者70例作为研究对象,根据随机数表法将其分为观察组(n=36)和对照组(n=34)。对照组使用地塞米松治疗,观察组在对照组的基础上加用银杏达莫进行治疗。比较两组的临床疗效、治疗前后血清sVCAM-1、CGRP水平、平均听阈比、耳鸣残疾量表(THI)评分的变化及并发症的发生情况。**结果:**治疗后,观察组总有效率为94.44%,显著高于对照组(73.53%, $P<0.05$)。两组患者治疗后血清sVCAM-1、CGRP水平、平均听阈比、THI评分均较治疗前显著改善,且观察组患者血清sVCAM-1水平、平均听阈比、THI评分均显著低于对照组,血清CGRP水平显著高于对照组($P<0.05$)。治疗期间,观察组患者并发症总发生率为11.11%,显著低于对照组(32.35%, $P<0.05$)。**结论:**银杏达莫联合地塞米松治疗突发性耳聋的效果显著优于单用地塞米松治疗,这可能与其显著改善患者血清sVCAM-1、CGRP水平有关。

关键词:银杏达莫;地塞米松;突发性耳聋;可溶性血管细胞间黏附因子-1;降钙素基因相关肽

中图分类号:R764.43 文献标识码:A 文章编号:1673-6273(2019)23-4565-04

Curative Efficacy of Ginkgo Dexamethasone Injection Combined with Dexamethasone in the Treatment of Sudden Deafness in Children and Its Effects on the Serum Svcam-1 and CGRP Levels*

SHEN Yi-wei¹, ZHOU Jian-bo^{1Δ}, XIE Yun¹, LI Jin-hui¹, HU Li-li²

(1 Department of Otorhinolaryngology Head and Neck Surgery, Hunan Provincial People's Hospital, Changsha, Hunan, 410006, China;

2 School of Medicine, Hunan Normal University, Changsha, Hunan, 410006, China)

ABSTRACT Objective: To study Curative efficacy of Ginkgo dexamethasone injection combined with dexamethasone in treatment of Sudden deafness in children and its effect on serum Soluble vascular intercellular adhesion factor-1 (svcam-1), calcitonin gene-related peptide (CGRP). **Methods:** 70 cases of patients with sudden deafness who were treated in our hospital from October 2017 to March 2019 were selected as the study objects, and they were divided into observation group (n=36) and control group (n=34) according to the random number table method. The control group was treated with dexamethasone and the observation group was treated with ginkgo biloba on the basis of the control group. The clinical efficacy, serum svcam-1, CGRP level, average hearing valve ratio, tinnitus disability scale (THI) score changes and complications were compared between the two groups. **Results:** After treatment, the total effective rate of the observation group was 94.44%, significantly higher than that of the control group (73.53%, $P<0.05$). After treatment, the serum levels of svcam-1, CGRP, average listening valve ratio and THI score in the two groups were significantly improved compared with that before treatment, and the serum levels of svcam-1, average listening valve ratio and THI score in the observation group were significantly lower than those in the control group, while the serum CGRP level was significantly higher than that in the control group ($P<0.05$). During treatment, the total incidence of complications in the observation group was 11.11%, significantly lower than that in the control group (32.35%, $P<0.05$). **Conclusion:** The effect of dexamethasone combined with ginkgo biloba in the treatment of sudden deafness is significantly better than that of dexamethasone alone, which may be related to the significant improvement of serum svcam-1 and CGRP levels in patients.

Key words: Ginkgo biloba; Dexamethasone; Sudden deafness; Soluble vascular intercellular adhesion factor-1; Calcitonin gene-related peptide

Chinese Library Classification(CLC): R764.43 **Document code:** A

Article ID: 1673-6273(2019)23-4565-04

* 基金项目:湖南省科技厅基金资助项目(707273922010)

作者简介:谌祎玮(1994-),女,硕士研究生,住院医师,研究方向:中耳炎,突聋,鼻窦炎

Δ 通讯作者:周建波(1975-),男,硕士生导师,主任医师,电话:18570382886, E-mail: wanmyx2018@163.com

(收稿日期:2019-06-02 接受日期:2019-06-28)

前言

突发性耳聋简称“突发性聋”，是耳鼻喉头颈外科常见疾病，是指突然发生的感音神经性听力损失，多数患者在短时间内听力明显降低，临床表现为单侧听力下降，且伴有耳鸣、耳堵塞感、眩晕、呕吐等症状，严重影响患者的生活质量^[1-3]。该病的发病机制尚不明确，但有研究表明其与微循环障碍、病毒感染、自身免疫性疾病、圆窗膜破裂等因素有关^[6]。sVCAM-1 表达异常可介导炎性细胞以及血小板趋化，从而导致患者发生内皮损伤，进而出现微栓塞症状，有研究显示，突发性耳聋患者 sVCAM-1 升高^[7]。CGRP 主要由神经细胞合成，可通过抗内皮素的生物活性，保护内耳功能。

目前，临床上治疗该病通常使用类固醇激素、抗炎剂、抗病毒类药物。地塞米松是常用的糖皮质激素，具有抗炎、免疫抑制功能，对突发性耳聋有较好的疗效，但是副作用较大^[8]。银杏达莫注射液是一种复方制剂，是由双嘧达莫和银杏叶提取的，能够抑制血小板和红细胞对腺苷的摄取，提高血小板内环磷酸腺苷的含量，促进内耳血流灌注，解除内耳缺血状况，改善内耳微循环^[9,10]。目前，临床上关于两种药物治疗突发性耳聋的相关报道较多，但是关于其对儿童突发性耳聋疗效的报道较少。因此，本研究主要探讨了银杏达莫注射液联合地塞米松治疗突发性耳聋的疗效，并观察其对血清 sVCAM-1、CGRP 水平的影响，现报道如下。

1 资料与方法

1.1 一般资料

选择 2017 年 10 月到 2019 年 3 月于我院进行治疗的突发性耳聋患者 70 例进行研究。将患者通过随机数表法分为 2 组，观察组 36 例，其中男 19 例，女 17 例，年龄 19~68 岁，平均(44.72±5.41)岁，单耳 11 例，双耳 25 例。对照组 34 例，包括男 17 例，女 17 例，年龄 20~73 岁，平均(48.81±5.43)岁，单耳 10 例，双耳 24 例。两组患儿性别、年龄等一般资料无显著差异

($P>0.05$)，具有可比性。

纳入标准^[11]：(1)符合《突发性耳聋》诊断标准；(2)就诊前未接受过相关治疗；(3)无中耳炎病史；(4)监护人知情同意并签署知情同意书。排除标准：(1)近期采用耳毒性药物者；(2)沟通障碍者；(3)听神经瘤。

1.2 治疗方法

对照组采用地塞米松治疗：地塞米松(规格 1 mL:2 mg, 厂家：广州白云山天心制药股份有限公司，国药准字 H44022090) 5 mg/次，鼓室内注射，1 周 3 次。观察组在对照组的基础上加用巴曲酶治疗：银杏达莫(规格 5 mL, 厂家：湖北民康制药有限公司，国药准字 H42022870)450 mL 加入 10%葡萄糖注射液静脉滴注。1 次 1 d。两组患者均连续治疗 10d。

1.3 观察指标

采集空腹静脉血 5 mL，以 3000 r·min⁻¹ 的速度进行离心，时间 10 min，提取上层血清后，置于零下 20℃ 的冷冻箱内存储以备检测，血清 sVCAM-1、CGRP 的测定采用双抗体夹心酶联免疫吸附法(ELISA)；采用纯音听阈测试平均听阈比；THI：分值越高，耳鸣越严重；记录不良反应的发生情况。

疗效评定标准：显效：听力完全恢复，眩晕、耳鸣等症状消失；有效：眩晕、耳鸣等症状少有发生，听力提升>30 dB；无效：临床症状无明显改善甚至加重，显效+有效为总有效率。

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，以均数±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 两组患儿疗效的比较

治疗后，观察组总有效率为 94.44%，显著高于对照组(73.53%， $P<0.05$)，见表 1。

表 1 两组患者疗效比较[例(%)]

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

Groups	n	Excellent	Effective	Invalid	Total effective rate
Observation group	36	23(63.89)	11(30.56)	2(5.56)	34(94.44)
Control group	34	13(38.24)	12(35.29)	9(26.47)	25(73.53)
χ^2 value					5.775
P value					0.016

2.2 两组患儿治疗前后血清 sVCAM-1、CGRP 水平的比较

治疗后，两组患者血清 sVCAM-1、CGRP 水平均较治疗前显著改善，且观察组患者 sVCAM-1 水平显著低于对照组，而血清 CGRP 水平明显高于对照组($P<0.05$)，见表 2。

2.3 两组患儿治疗前后平均听阈、THI 量表的比较

治疗前，两组患者平均听阈比、THI 评分比较无显著性差异($P>0.05$)；治疗后，两组患者平均听阈比、THI 评分均较治疗前显著降低，且观察组患者以上指标均显著低于对照组($P<0.05$)，见表 3。

2.4 两组患者并发症发生情况的比较

治疗期间，两组患者并发症总发生率分别为 11.11%、32.35%，观察组显著低于对照组($P<0.05$)，见表 4。

3 讨论

突发性耳聋是临床常见的急性病症，研究显示我国突发性耳聋发生率呈逐年上升趋势，若得不到及时治疗，会导致终身耳鸣、耳聋，严重影响患者的生活质量^[12-14]。突发性耳聋的诊断一般不难，但有时和梅尼埃病相鉴别，发病机制尚不明确，有学

表 2 两组患者治疗前后血清 sVCAM-1、CGRP 水平的比较($\bar{x} \pm s$, ng/mL)Table 2 Comparison of the serum svcam-1 and CGRP levels before and after treatment between two groups ($\bar{x} \pm s$, ng/mL)

Groups	n	sVCAM-1		CGRP	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	36	326.47 $\pm$ 15.51	211.24 $\pm$ 10.49	236.51 $\pm$ 20.49	425.63 $\pm$ 29.21
Control group	34	327.03 $\pm$ 16.78	279.69 $\pm$ 13.24	235.98 $\pm$ 21.29	386.24 $\pm$ 26.73
t value		0.145	24.045	0.106	5.875
P value		0.885	0.000	0.916	0.000

表 3 两组患儿治疗前后平均听阈比、THI 评分的比较($\bar{x} \pm s$)Table 3 Comparison of the mean auditory valve ratio and THI score before and after treatment between two groups ($\bar{x} \pm s$)

Groups	n	Average listening valve ratio(dB)		THI score(points)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	36	70.12 $\pm$ 6.86	50.45 $\pm$ 4.03	35.24 $\pm$ 5.97	15.67 $\pm$ 3.35
Control group	34	70.16 $\pm$ 6.49	61.59 $\pm$ 5.52	35.67 $\pm$ 6.32	20.19 $\pm$ 4.16
t value		0.025	9.682	0.293	5.020
P value		0.980	0.000	0.771	0.000

表 4 两组患者并发症发生情况比较[例(%)]

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

Groups	n	Dizziness, headache	Nausea and vomiting	Alanine aminotransferase increased	The total incidence of
Observation group	36	1	2	1	4(11.11)
Control group	34	4	5	2	11(32.35)
χ^2 value					4.686
P value					0.030

者提出可能与内耳循环障碍、病毒感染等因素有关^[15,16]。国外有研究显示突发性耳聋患者内耳损伤后缺血或感染引起纤维蛋白原、红细胞和白细胞沉积率增高^[17-19]。地塞米松是治疗突发性耳聋的常用药物,但是靶向定位差,传统静脉给药效果不佳,而鼓室内注射地塞米松能在短时间内增加耳局部药物浓度,见效快,可巩固耳局部治疗效果^[20,21]。银杏达莫注射液属于中药制剂,主要成分为银杏苦内酯、银杏黄酮甙、白果内酯,能够抑制血小板聚集和抑制环磷酸鸟苷磷酸二酯酶,强化内皮舒张因子^[22,23]。有研究显示银杏达莫联合基础用药在治疗突发性耳聋的临床效果上优于单纯应用基础用药^[24]。

本研究中,联合治疗的患者总有效率为 94.44%,明显高于单独治疗的患者,且头晕头痛、恶心呕吐等发生率显著降低,提示联合治疗可明显提高临床疗效和安全性。Qian Z^[25]等结果表明银杏达莫注射液对耳蜗毛细胞和神经细胞具有保护作用,地塞米松注射液具有协同作用,互补作用。本研究结果也显示联合治疗的患者的平均听阈比、THI 评分水平均显著低于单独使用地塞米松治疗的患者。分析是因为地塞米松具有抗炎功能,对血液循环具有促进作用;银杏达莫注射液成分中的银杏苦内酯和白果内酯能够抑制血小板的活化因子和血小板聚集,同时银杏黄酮甙能有效清除血管内脂质堆积,从而降低血液粘稠度,促进内耳血流灌注,最终改善患者平均听阈比,提高临床疗效。

sVCAM-1 在炎症反应中有着重要的作用,与耳内的微循

环息息相关^[26,27]。CGRP 由 37 个氨基酸组成,是人类用分子生物学方法发现的第一个活性多肽,具有强大生理活性,参与耳蜗神经刺激引发的内皮血管扩张作用,能保护内耳功能^[28,29]。本研究结果显示联合治疗患者的血清 sVCAM-1、CGRP 水平均优于单独治疗的患者,与 Merkel S F^[30]等研究结果相似。分析是因为突发性耳聋患者常会有毛细胞损伤、血管纹功能障碍等,而地塞米松可减轻和防止组织对炎症的反应,抑制溶酶体酶的释放以及炎症化学中介物的合成;银杏达莫注射液则为复方制剂,其中银杏总黄酮提取自中药材银杏叶,具有破血逐瘀、通脉止痛之功效,同时有强大的抗脂质过氧化,调节患者神经递质的释放,改善了内耳的微循环,保护患者血管内皮细胞,降低其血清 sVCAM-1 水平,从而改善患者的听力情况。

综上所述,银杏达莫联合地塞米松治疗突发性耳聋的效果显著优于单用地塞米松治疗,这可能与显著改善患者血清 sVCAM-1、CGRP 水平有关。

参考文献(References)

- [1] Lee J S, Hong S K, Dong H K, et al. The neutrophil-to-lymphocyte ratio in children with sudden sensorineural hearing loss: a retrospective study[J]. Acta Oto-Laryngologica, 2017, 137(1): 35-38
- [2] Mierzwiński J, Kosowska J, Tyra J, et al. Different clinical presentation and management of temporal bone fibrous dysplasia in children [J]. World Journal of Surgical Oncology, 2018, 16(1): 5
- [3] Sladen D P, Carlson M L, Dowling B P, et al. Early outcomes after

- cochlear implantation for adults and children with unilateral hearing loss[J]. *Laryngoscope*, 2017, 127(7): 1683
- [4] Cho, Tsung-Yi, Cheng, Po-Wen, Young, Yi-Ho. Evolution of postirradiated sudden deafness in nasopharyngeal carcinoma survivors during the past two decades[J]. *Laryngoscope*, 2016, 126(9): 2016-2021
- [5] Chen K, Sun L, Zong L, et al. GJB2 and mitochondrial 12S rRNA susceptibility mutations in sudden deafness [J]. *European Archives of Oto-Rhino-Laryngology*, 2016, 273(6): 1393-1398
- [6] Fang X, Yu L S, Ma X, et al. Correlation between the changes of fibrinogen and the treatment effect of all-frequency sudden deafness[J]. *Chinese journal of otorhinolaryngology head and neck surgery*, 2018, 53(1): 3-8
- [7] Ranyang M A, Hong Y U, Wang X. Evaluation on clinical efficacy of hyperbaric oxygenation in treatment of sudden deafness:A Meta-analysis[J]. *Journal of Jilin University*, 2017, 43(2): 298-305
- [8] Wang X, Ma R Y, Yu Z, et al. Neurosyphilis and HIV co-infection with the initial symptom of sudden deafness and optic atrophy: a case report [J]. *Journal of clinical otorhinolaryngology, head, and neck surgery*, 2017, 31(19): 1524
- [9] Chen C H, Young Y H. N-acetylcysteine as a single therapy for sudden deafness[J]. *Acta Oto-Laryngologica*, 2016, 137(1): 5
- [10] Xing Y Z, Pei J J, Sun Y T, et al. Clinical research of anxiety and depression state among patients suffered from sudden deafness with vertigo [J]. *Journal of Clinical Otorhinolaryngology Head & Neck Surgery*, 2017, 31(24): 1919
- [11] Sang H K, Jung A R, Su I K, et al. Refractory Granulomatosis with Polyangiitis Presenting as Facial Paralysis and Bilateral Sudden Deafness[J]. *Journal of Audiology & Otology*, 2016, 20(1): 55-58
- [12] Liu J, Bie X, Zhang J N. Sudden deafness and vertigo as starting symptoms of relapsing polychondritis: one case report [J]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*, 2017, 52(4): 296-297
- [13] Ryu I Y, Park S H, Park E B, et al. Factors Prognostic of Season-Associated Sudden Sensorineural Hearing Loss: A Retrospective Observational Study [J]. *Journal of Audiology & Otology*, 2017, 21(1): 44-48
- [14] Zhang Y L, Cheng Y, Wang G P, et al. Hypokalemic paralysis induced by methylprednisolone in patient with sudden deafness: one case report [J]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*, 2016, 51(10): 783-784
- [15] Swachia K, Sharma D, Singh J. Efficacy of oral vs. intratympanic corticosteroids in sudden sensorineural hearing loss[J]. *Journal of Basic & Clinical Physiology & Pharmacology*, 2016, 27(4): 371-377
- [16] Li D B, Zhou S, Xu W J. Intratympanic dexamethasone versus post-auricular subperiosteal injection of methylprednisolone treatment for sudden hearing loss[J]. *Journal of clinical otorhinolaryngology, head, and neck surgery*, 2017, 31(16): 1265
- [17] Attal M, Lauwers-Cances V, Hulin C, et al. Lenalidomide, Bortezomib, and Dexamethasone with Transplantation for Myeloma [J]. *N Engl J Med*, 2017, 376(14): 1311-1320
- [18] Róka R, Aitbelgnaoui A, Salvadorcartier C, et al. Dexamethasone prevents visceral hyperalgesia but not colonic permeability increase induced by luminal protease-activated receptor-2 agonist in rats[J]. *Gut*, 2017, 56(8): 1072-1078
- [19] Li X, Wang N, Liang X, et al. Safety and efficacy of dexamethasone intravitreal implant for treatment of macular edema secondary to retinal vein occlusion in Chinese patients: randomized, sham-controlled, multicenter study [J]. *Graefes Archive for Clinical & Experimental Ophthalmology*, 2018, 256(1): 59-69
- [20] Mccorley S T, Roxburgh C S D, Horgan P G, et al. The Impact of Preoperative Dexamethasone on the Magnitude of the Postoperative Systemic Inflammatory Response and Complications Following Surgery for Colorectal Cancer[J]. *Annals of Surgical Oncology*, 2017, 24(8): 2104-2112
- [21] Shah J J, Kaufman J L, Zonder J A, et al. A Phase 1 and 2 study of Filanesib alone and in combination with low-dose dexamethasone in relapsed/refractory multiple myeloma[J]. *Cancer*, 2017, 123(23): 4617
- [22] Chalifoux F, Colin F, StPierre P, et al. Low dose intravenous dexamethasone (4 mg and 10 mg) significantly prolongs the analgesic duration of single-shot interscalene block after arthroscopic shoulder surgery: a prospective randomized placebo-controlled study[J]. *Canadian journal of anaesthesia*, 2017, 64(3): 280
- [23] Durie B G, Hoering A, Abidi M H, et al. Bortezomib with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in patients with newly diagnosed myeloma without intent for immediate autologous stem-cell transplant (SWOG S0777): a randomised, open-label, phase 3 trial [J]. *Lancet*, 2017, 389(10068): 519-527
- [24] Chong M A, Berbenetz N M, Lin C, et al. Perineural Versus Intravenous Dexamethasone as an Adjuvant for Peripheral Nerve Blocks: A Systematic Review and Meta-Analysis [J]. *Regional Anesthesia & Pain Medicine*, 2017, 42(3): 319
- [25] Qian Z, Yang D, Sun F, et al. Risk factors for recurrence of chronic subdural hematoma after burr hole surgery: potential protective role of dexamethasone[J]. *British Journal of Neurosurgery*, 2017, 31(1): 5
- [26] Moreau P, Joshua D, Chng W J, et al. Impact of prior treatment on patients with relapsed multiple myeloma treated with carfilzomib and dexamethasone vs bortezomib and dexamethasone in the phase 3 ENDEAVOR study[J]. *Leukemia*, 2017, 103(103): 1183-1200
- [27] Vogl D T, Raje N S, Jagannath S, et al. Ricolinostat, the first selective histone deacetylase 6 inhibitor, in combination with bortezomib and dexamethasone for relapsed or refractory multiple myeloma[J]. *Clinical Cancer Research*, 2017, 23(13): 3307-3315
- [28] Xu D, Gao Y, Hu N, et al. miR-365 Ameliorates Dexamethasone-Induced Suppression of Osteogenesis in MC3T3-E1 Cells by Targeting HDAC4[J]. *International Journal of Molecular Sciences*, 2017, 18(5): 977
- [29] Büyükkaramikli N C, Groot S D, Fayter D, et al. Pomalidomide with Dexamethasone for Treating Relapsed and Refractory Multiple Myeloma Previously Treated with Lenalidomide and Bortezomib: An Evidence Review Group Perspective of an NICE Single Technology Appraisal[J]. *Pharmacoeconomics*, 2018, 36(2): 145-159
- [30] Merkel S F, Andrews A M, Lutton E M, et al. Dexamethasone Attenuates the Enhanced Rewarding Effects of Cocaine Following Experimental Traumatic Brain Injury [J]. *Cell Transplantation*, 2017, 26(7): 1178-1192