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神经节苷脂钠联合高压氧治疗突发性耳聋患者的效果评估 *

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摘要 目的：探讨神经节苷脂钠联合高压氧治疗突发性耳聋患者的疗效，并分析其对患者血清高迁移率蛋白 -1(High mobility protein-1，HMGB1)、中性粒细胞激活肽 -78(Neutrophil activating peptide-78，ENA-78)的影响。**方法：**选择我院 2018 年 1 月至 2019 年 8 月接诊的 96 例突发性耳聋患者，通过随机数表法将其分为观察组和对照组，每组 48 例。对照组在常规治疗基础上给予高压氧治疗，观察组在对照组的基础上给予神经节苷脂钠注射液治疗，两组均连续治疗 2 个疗程。治疗后，比较两组的临床疗效、治疗前后纯音听阈测试结果、凝血功能、血清 HMGB1、ENA-78 水平的变化及不良反应的发生情况。**结果：**治疗 2 个疗程后，观察组临床疗效总有效率明显高于对照组(93.75%vs79.17%)，差异有统计学意义($P<0.05$)；观察组纯音听阈测试结果明显低于对照组[(32.14± 4.94)dB vs. (37.23± 5.12)dB]($P<0.05$)，凝血酶原时间(Prothrombin time，PT)、部分活化凝血酶原时间(Partial activated prothrombin time，APTT)、凝血酶时间(Thrombin time，TT)明显短于对照组，纤维蛋白原(Fibrinogen，FIB)明显低于对照组。**结论：**神经节苷脂钠联合高压氧治疗突发性耳聋患者的效果显著优于单用高压氧治疗，其可有效促进听力恢复，且不增加药物不良反应，其机制可能与降低血清 HMGB1、ENA-78 水平有关。

关键词：突发性耳聋；高压氧；神经节苷脂钠；高迁移率蛋白 -1；中性粒细胞激活肽 -78

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Effect of Ganglioside Sodium Combined with Hyperbaric Oxygen on the Patients with Sudden Deafness*

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ABSTRACT Objective: To study the effect of ganglioside sodium combined with hyperbaric oxygen on the patients with sudden deafness, and the mechanism of its action on serum high mobility protein-1(HMGB1) and neutrophil activating peptide-78(ENA-78) was analyzed. **Methods:** 96 patients of sudden deafness who received therapy fromJanuary 2018 to August 2019 in our hospital were selected as research objects, according to the random number table, they were divided into the observation group and the control group, each group had 48 cases. The control group was given hyperbaric oxygen treatment on the basis of routine treatment, and the observation group was combined with ganglioside sodium injection on the basis of the control group, the 2 groups were treated for 2 courses. After treatment, the clinical efficacy, the changes of the pure tone threshold test results, goagulation function, serum HMGB1, ENA-78 levels before and after treatment and adverse reactions were compared. **Results:** After 2 courses of treatment, the total effective rate in the observation group was significantly higher than those in the control group (93.75%vs79.17%), the difference was statistically significant ($P<0.05$); the pure tone threshold test results in the observation group was significantly lower than those in the control group [(32.14± 4.94) dB vs. (37.23± 5.12)dB], the prothrombin time (PT), partial activated prothrombin time (APTT) and thrombin time (TT) in the observation group were significantly shorter than those in the control group, and fibrinogen (FIB) was significantly lower than those in the control group. **Conclusion:** The effect of ganglioside sodium combined with hyperbaric oxygen in the treatment of sudden deafness is significantly better than that of hyperbaric oxygen alone, which can effectively promote hearing recovery, and not increase adverse drug reactions, the mechanism may be related to the reduction of serum HMGB1 and ENA-78 levels.

Key words: Sudden deafness; Hyperbaric oxygen; Ganglioside sodium; High mobility protein-1; Neutrophil activating peptide-78

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前言

突发性耳聋指突然发生、原因不详的一种感音神经性听力损伤疾病，以单侧听力降低为主要症状，部分患者可伴有耳鸣、

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耳闷、眩晕等反应，具有起病急、进展快等特点。相关数据显示在 10 万人中就约有 5~20 人罹患突发性耳聋，而美国每年发生突发性耳聋的患者有 4 千多人[1,2]。在突发性耳聋患者中由于存在着耳内缺氧缺血性损害，可出现红细胞聚集、血液粘稠度增加等表现，导致凝血功能障碍[3,4]。通过高压氧治疗，有助于缓解内耳水肿和缺血缺氧损害、调节内耳循环，达到改善听力的目的[5]。神经营养药物也是突发性耳聋的重要治疗环节，神经节苷脂是一种神经鞘糖酯，是神经细胞膜的天然组成成分，在修复神经元损害中具有较好的疗效[6]。

有研究显示炎症反应、血管内皮紊乱是导致突发性耳聋的发病的重要原因之一。血清高迁移率蛋白 -1 (High mobility protein-1，HMGB1) 是一种重要的炎症介质，参与组织后的修复、炎症反应等过程。中性粒细胞激活肽 -78(Neutrophil activating peptide-78，ENA-78)具有趋化、激活中性粒细胞作用，在参与机体炎症反应的同时也具有调节血管生成因子活性的作用，二者在突发性耳聋的发生发展过程中均发挥着作用[7,8]。本研究将神经节苷脂钠联合高压氧用于治疗突发性耳聋，旨在探讨其疗效和对血清 HMGB1、ENA-78 水平的影响。

1 资料与方法

1.1 一般资料

选择我院 2018 年 1 月至 2019 年 8 月接诊的 96 例突发性耳聋患者。纳入标准，(1)诊断标准参照文献[9]，出现突然的单侧听力降低，伴或不伴耳鸣、耳闷、眩晕等症状，并通过常规耳科检查、音叉检查、纯音测听、声导抗检查、听力学检查、影像学检查等确诊；(2) 听道及颅脑内无器质性病变；(3) 发病至入院时间＜2 周；(4)入院前未接受过其余治疗；(5)签署研究知情书。排除标准[10]，(1)合并蜗窗破裂；(2)合并其余中耳病变；(3)合并脑卒中、鼻咽癌、听神经瘤、梅尼埃病等疾病；(4)合并其余重要器质功能障碍；(5) 合并出血性疾病；(6) 合并神经功能障碍性疾病；(7)对研究方案不耐受或过敏。通过随机数表法分为观察组和对照组，每组 48 例，两组一般资料见表 1，差异无统计学意义(P＞0.05)。

表 1 两组一般资料的比较[$\bar{x}\pm s$，n(%)]

Table 1 Comparison of the general information between two groups[$\bar{x}\pm s$, n(%)]

Item		Observation group(n=48)	Control group(n=48)
Sex(M/F)		28/20	25/23
Age(years)		40.76± 8.59	41.21± 7.67
Course of disease(d)		7.05± 2.11	6.97± 2.45
Position	Left ear	22(45.83)	25(52.08)
	Right ear	26(54.17)	23(47.92)
Degree of hearing impairment	Light(20~40)dB	10(20.83)	12(25.00)
	Moderate(41~60)dB	29(60.42)	25(52.08)
	Severe(61~90)dB	9(18.75)	11(22.92)
Type	Low-if frequency descent type	18(37.50)	17(35.42)
	High frequency descent type	15(31.25)	17(35.42)
	Flat descent type	11(22.92)	9(18.75)
	Total deafness type	4(8.33)	5(10.42)
Combined symptoms	Tinnitus	33(68.75)	34(70.83)
	Vertigo	18(37.50)	15(31.25)

1.2 治疗方法

两组均进行常规处理，地塞米松注射液(规格：1 mL:5 mg，厂家：天津金耀集团湖北天药药业股份有限公司，国药准字 H42020019)，剂量 10 mg 加入 5%葡萄糖注射 500 mL 中静脉滴注，1 次 /d，连续给药 3d 后，调整剂量为 5 mg，连续给药 5d 后停药；银杏叶提取物注射液(规格：5 mL:17.5 mg，厂家：台湾济生化学制药厂股份有限公司，批准文号：HC20090014)，剂量 35 mg 加入生理盐水 250 mL 中静脉滴注，1 次 /d；胞二磷胆碱注射液(规格：2 mL:0.1 g，厂家：吉林百年汉克制药有限公司，国药准字 H22026207)，剂量 0.5 g 加入 5%葡萄糖注射液 500 mL 中静脉滴注，1 次 /d。

对照组在此基础上给予高压氧(烟台宏远氧业有限公司)治疗，进舱后加压 20 min，直至压力到 0.25MPa，面罩吸氧 60 min，减压 20 min 后即可出舱，1 次 /d；观察组在对照组基础上，联合神经节苷脂钠注射液(规格：2 mL:20 mg，厂家：齐鲁制药有限公司，国药准字 H20056783) 治疗，20 mg 加入 250 mL 生理盐水，静脉滴注，1 次 /d。2 组均以 7d 为 1 个疗程，持续治疗 2 个疗程。

1.3 观察指标

1.3.1 **疗效评价标准** 完成 2 个疗程后，参照文献[11]评价疗效。治愈：受损频率听阈得到正常恢复，和健耳水平相似；显效：受损频率听阈改善程度＞30 dB；有效：受损频率听改善程度 15~30 dB；无效：未满足上述标准。总有效率 = 痊愈率 + 显效率 + 有效率。

1.3.2 **纯音听阈测试** 对两组治疗前、治疗 2 个疗程后进行纯音听阈测试，记录听力情况。

1.3.3 **凝血功能** 收集治疗前、治疗 2 个疗程后的空腹静脉血 5 mL，使用日本 Sysmex Ca-1500 型全自动血凝仪检测凝血功能的变化，指标包括凝血酶原时间(Prothrombin time，PT)、部分活化凝血酶原时间 (Partial activated prothrombin time，APTT)、凝血酶时间(Thrombin time，TT)、纤维蛋白原(Fibrinogen，FIB)。

1.3.4 **血清** HMGB1、ENA-78 留取上述血液样本 2 mL，置于 3500 r/min 的条件，进行 10 min 的离心，提取血清液，选用酶联免疫吸附法(Enzyme linked immunosorbent assay，ELISA)试剂盒(美国 R&D 公司)予以检测，仪器为意大利 ALISEI 全自动酶标仪。

1.3.5 **安全性评价** 记录治疗期间两组相关药物不良反应。

1.4 **统计学方法**

以 SPSS18.0 软件包处理数据，正态计量资料用 ($\bar{x}\pm s$)表示，组间比较使用独立样本 t 检验，组内比较使用配对样本 t 检验，计数资料以率表示，组间比较采用 x^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，观察组治愈 11 例、显效 24 例、有效 10 例、无效 3 例；对照组治愈 5 例、显效 20 例、有效 13 例、无效 10 例。观察组临床疗效总有效率显著高于对照组($P<0.05$)，见表 2。

表 2 两组临床疗效的比较[n(%)]

Table 2 Comparison of the clinical efficacy between two groups [n(%)]

Groups	Invalid	Total effective rate
Observation group(n=48)	3(6.25)	45(93.75)*
Control group(n=48)	10(20.83)	38(79.17)

Note: Compared with the control group, *$P<0.05$.

2.2 **两组治疗前后纯音听阈测试结果的比较**

治疗后，2 组纯音听阈测试结果均显著低于治疗前($P<0.05$)，且观察组明显低于对照组($P<0.05$)，见表 3。

表 3 两组治疗前后纯音听阈测试结果比较($\bar{x}\pm s$，dB)

Table 3 Comparison of the pure tone threshold test results between two groups before and after treatment ($\bar{x}\pm s$, dB)

Groups	Time	Pure tone threshold test results
Observation group(n=48)	Before treatment	58.52± 10.86
	After treatment	32.14± 4.94*#
Control group(n=48)	Before treatment	58.91± 9.07
	After treatment	37.23± 5.12*

Note: Compared with the before treatment, *$P<0.05$; compared with the control group, #$P<0.05$.

2.3 **两组治疗前后凝血功能比较**

治疗后，2 组 PT、APTT、TT 较治疗前均缩短，FIB 降低($P<0.05$)，且观察组 PT、APTT、TT 短于对照组，FIB 低于对照组 ($P<0.05$)，见表 4。

表 4 两组治疗前后凝血功能的比较($\bar{x}\pm s$)

Table 4 Comparison of the coagulation function between two groups($\bar{x}\pm s$)

Groups	Time	PT(s)	APTT(s)	TT(s)	FIB(g/L)
Observation group (n=48)	Before treatment	9.03± 1.47	24.86± 2.79	15.03± 1.76	5.47± 0.95
	After treatment	12.04± 0.64*#	32.45± 2.60*#	17.12± 0.59*#	2.89± 0.46*#
Control group(n=48)	Before treatment	9.08± 1.41	24.70± 2.85	14.97± 1.88	5.55± 0.84
	After treatment	10.92± 0.82*	28.11± 2.10*	16.08± 0.63*	3.62± 0.71*

Note: Compared with the before treatment, *$P<0.05$; compared with the control group, #$P<0.05$.

3 讨论

突发性耳聋是耳鼻喉科较为常见的一种急症，对患者的听力有着严重不良影响，我国近年突发性耳聋的发病率有明显上升趋势[12,13]。目前，突发性耳聋的确切发病机制仍不明确，局部因素和全身因素均可诱发该病，在临床上仅有 10%~15%的患者在发病期间可以明确病因，另外约有 1/3 的患者的发病原因需通过长期随访评估推测才可确认，一般认为情绪波动、精神压力、作息不规律、睡眠障碍等可能是该病的主要诱因[14,15]。

临床上针对突发性耳聋患者仍以综合治疗为主，糖皮质激素可发挥抗炎、抗感染的作用，有助于增加缺血部位血流，而银杏叶提取物、胞二磷胆碱注射液等的主要作用则是改善局部微

循环，但常规的治疗疗效约在 70%的左右[21,22]。突发性耳聋患者普遍存在着毛细血管水肿表现，可导致耳蜗血流减少，加重耳蜗缺氧程度，影响耳部微循环，这一系列症状均会影响到机体正常的凝血功能，加重病情严重程度。高压氧是突发性耳聋的患者较为常用的治疗方案，可迅速提高血液、组织的氧分压及含氧量，达到增加内耳血氧供应，改善内耳循环的目的[23]。目前已有研究证实，许多神经营养因子对听觉具有保护作用，并指出应重视神经营养药物在突发性耳聋患者中的应用，但既往较多试验仍停留在维生素 B12、辅酶 A 等药物上[24]。神经节苷脂作为一种神经鞘糖酯，主要表达于神经元细胞的胞膜中，在正常情况下可发挥修复神经系统的作用。有研究显示通过给予外源性的神经节苷脂可促进神经轴索的生长，有助于损伤神经元的修复[25,26]。Inokuchi JI 等[27]认为由于突发性耳聋患者内耳神经末梢、听神经功能存在着明显损伤，给予神经节苷脂可能有助于进一步的改善病情，促进听力恢复。

研究表明炎症反应、血管内皮功能的紊乱等在突发性耳聋的发病过程中发挥了重要作用。HMGB1 是机体重要的炎症介质和致炎细胞因子，在肿瘤坏死因子 (Tumor necrosis factor，TNF)-α 、白细胞介素(Interleukin，IL)等刺激下，单核巨噬细胞可大量释放 HMGB1，HMGB1 的也可刺激单核巨噬细胞分泌大量炎性介质[16,17]。ENA-78 属 C-X-C 亚族趋化因子，主要来源自活化的巨噬细胞，具有趋化、激活中性粒细胞的作用，同样也是重要的血管增生因子[18]。Yoon SH 等[19]报道显示突发性耳聋患者在各类炎症因素以及缺氧、缺血的刺激下可诱导机体组织类产生大量的 HMGB1、ENA-78，从而促进白细胞粘附内皮细胞，加速血管上皮破坏程度，进一步加重损伤程度。也有研究显示突发性耳聋患者血清 HMGB1、ENA-78 的表达和纯音听阈值之间具有较高的相关性，并认为血清 HMGB1、ENA-78 在作为炎症标记物的同时，也可作为突发性耳聋患者疗效观察的指标[20]。

本研究显示联合神经节苷脂钠的患者纯音听阈测试结果、凝血功能等改变也优于对照组，临床疗效总有效率高达 93.75%，通过分析是由于在积极缓解内耳局部免疫炎症反应及血管内皮功能后，可改善耳部微循环障碍，同时神经节苷脂还有维持神经细胞膜 Na^+-K^+-ATP 酶的活性的作用，有助于保证细胞膜的稳定，并预防细胞水肿，从而令内耳神经损伤得以缓解[30]，加上高压氧在改善内耳循环的同时，也有助于减少血小板聚集、降低血液粘稠度等，两组方式通过不同的作用机制，进一步促进临床疗效的提高，修复患者听力。此外，联合神经节苷脂钠治疗的患者血清 HMGB1、ENA-78 水平明显降低，可能是由于神经节苷脂钠具有扩张血管、改善缺氧缺血等作用机制，有助于缓解再灌注损伤，从而减轻内耳局部免疫炎症反应，减少白细胞向内皮细胞的粘附[28]，Yoshikawa M 等[29]报道也指出神经节苷脂钠对耳蜗毛细胞结构的完整性、功能具有明显调节作用，有助于修复血管炎症损伤；且高压氧对内耳水肿、缺氧缺血损害也具有改善效果，因此联合治疗的患者血清 HMGB1、ENA-78 的降低程度更明显。患者治疗期间无明显的不良反应，提示该方案用于突发性耳聋患者具有较好的安全性。

针对突发性耳聋，临床上提倡早发现、早治疗，治疗效果和患病时间之间也有着密切联系。对于同样的治疗方式在不同听力损伤程度、不同类型的患者中是否有差异，以及对于双耳聋的患者是否也可获得较好的效果等，均值得进一步思考和研究。

综上所述，神经节苷脂钠联合高压氧治疗突发性耳聋患者的效果显著优于单用高压氧治疗，其可有效促进听力恢复，且不增加药物不良反应，其机制可能与降低血清 HMGB1、ENA-78 水平有关。

参 考 文 献(References)

[1] Xie Y, Orabi NA, Zwolan TA, et al. Outcomes of unilateral idiopathic sudden sensorineural hearing loss: Two decades of experience [J]. Laryngoscope Investig Otolaryngol, 2019, 4(6): 693-702

[2] Kim MA, Kim SH, Ryu N, et al. Gene therapy for hereditary hearing loss by SLC26A4 mutations in mice reveals distinct functional roles of pendrin in normal hearing [J]. Theranostics, 2019, 9 (24): 7184-7199

[3] Taha A, Shlamkovitch N, Abu-Eta R, et al. High Dose of Intratympanic Steroids for Sudden Sensorineural Hearing Loss Salvage [J]. Otol Neurotol, 2019, 40(9): 1134-1138

[4] Conte G, Di Berardino F, Zanetti D, et al. Early Magnetic Resonance Imaging for Patients With Idiopathic Sudden Sensorineural Hearing Loss in an Emergency Setting [J]. Otol Neurotol, 2019, 40 (9): 1139-1147

[5] Krajcovicova Z, Melus V, Zigo R, et al. Hyperbaric oxygen therapy in treatment of sudden sensorineural hearing loss: finding for the maximal therapeutic benefit of different applied pressures [J]. Undersea Hyperb Med, 2019, 46(5): 665-672

[6] Li LP, Shiao AS, Li CT, et al. Steady-state auditory evoked fields reflect long-term effects of repetitive transcranial magnetic stimulation in tinnitus[J]. Clin Neurophysiol, 2019, 130(9): 1665-1672

[7] Göde S, Turhal G, Kaya İ, et al. Evaluation of Procalcitonin and hs-CRP Levels in Sudden Sensorineural Hearing Loss [J]. J Int Adv Otol, 2018, 14(1): 44-47

[8] Rajati M, Saghafi M, Rafatpanah H, et al. Immunology-Rheumatology Approach to Sudden Sensorineural Hearing Loss [J]. Curr Rheumatol Rev, 2018, 14(1): 70-73

[9] Editorial Committee of Chinese Journal of Otorhinolaryngology and head and neck surgery, otorhinolaryngology and head and neck surgery branch of Chinese Medical Association. Guidelines for diagnosis and treatment of sudden deafness[J]. Chin Jof Otorhinolaryngology Head and Neck Surgery, 2015, 50(6): 443-447

[10] Kurz A, Grubenbecher M, Rak K, et al. The impact of etiology and duration of deafness on speech perception outcomes in SSD patients [J]. Eur Arch Otorhinolaryngol, 2019, 276(12): 3317-3325

[11] Lammers MJW, Young E, Fenton D, et al. The prognostic value and pathophysiologic significance of three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) magnetic resonance imaging in idiopathic sudden sensorineural hearing loss: A systematic review and meta-analysis[J]. Clin Otolaryngol, 2019, 44(6): 1017-1025

[12] Jeong J, Lim H, Lee K, et al. High Risk of Sudden Sensorineural Hearing Loss in Several Autoimmune Diseases according to a Population-Based National Sample Cohort Study [J]. Audiol Neurootol, 2019, 24(5): 224-230

[13] Kim JY, Ko I, Cho BJ, et al. Association of Obstructive Sleep Apnea with the Risk of Ménière's Disease and Sudden Sensorineural Hearing Loss: A Study Using Data From the Korean National Health Insurance Service[J]. J Clin Sleep Med, 2019, 15(9): 1293-1301

[14] Heo HJ, Choi CH, Hong SH, et al. Is auditory brainstem response a prognostic factor in patients with sudden sensorineural hearing loss? [J]. Acta Otolaryngol, 2019, 139(11): 1008-1013

（下转第 3090 页）

[17] Sun W, Triche TJr, Malvar J, et al. A phase 1 study of azacitidine combined with chemotherapy in childhood leukemia: a report from TACL consortium[J]. Blood, 2018, 131(10): 1145-1148

[18] Li C, Yuam BJ, Zhang SQ. Changes of neutrophil CD64 index, C-reaction protein and white blood cell levels in patients with blood bacterial infection [J]. Chinese J Laboratory Diagnosis, 2015, 19(10): 1693-1696

[19] Liat AH, Kfir O, Roy N, et al. A host-protein signature is superior to other biomarkers for differentiating between bacterial and viral disease in patients with respiratory infection and fever without source: a prospective observational study [J]. Eur J Clin Microbiol Infect Dis, 2018, 37(7): 1361-1371

[20] Haruna N, Takao FJ, Suga S, et al. Species differences in circulation and inflammatory responses in children with common respiratory adenovirus infections[J]. J Med Virol, 2018, 90(5): 873-880

[21] Sadettin Er, Bülent Çomçalı, Ahmet Soykurt, et al. Diagnosis of Appendicitis in Patients with a Normal White Blood Cell Count: A Cross-Sectional Study[J]. Bull Emerg Trauma, 2018, 6(2): 128-132

[22] Nelson DA, Hughes JD, Engel CE, et al. Use of Dual-Force Aggregation as a Multiplexed, Rapid Point-of-Care Screening Method for White Blood Cell Counting from Whole Blood Samples[J]. J Applied Laboratory Med, 2019, 2(1): 92-97

[23] Ebihara, Yasuhiro, Kobayashi, et al. Diagnostic performance of procalcitonin, presepsin, and C-reactive protein in patients with hematological malignancies[J]. J Clin Laborat Analysis, 2017, 31(6): e22147

[24] Dai X, Li JP, Li WQ, et al. Changes of Neutrophil CD64 in Patients with Hematological Mali-gnancies Combined with Bacterial Infections[J]. Zhongguo Shi Yan Xue Ye Xue Za Zhi, 2017, 25(2): 577-581

[25] Wang KH, Zang WZ, Li YL, et al. Effect of CD4 (+) T cell surface CD1d molecules on progression of multiple sclerosis in mouse experimental autoimmune encephalomyelitis model [J]. Zhonghua Yi Xue Za Zhi, 2018, 98(23): 1873-1875

[26] Yang F, Feng C, Zhang XD, et al. The Diverse Biological Functions of Neutrophils, Beyond the Defense Against Infections[J]. Inflammation, 2016, 40(1): 311-323

[27] Lv J, Xiong YL, Li WJ, et al. BLT1 Mediates Bleomycin-Induced Lung Fibrosis Independently of Neutrophils and $CD4^+$T Cells [J]. J Immunol, 2017, 198(4): 1673-1684

[28] Maria Vono, Ang Lin, Anna Norrby-Teglund, et al. Neutrophils acquire antigen presentation capacity to memory $CD4^+$T cells in vitro and ex vivo[J]. Blood, 2017, 129(14): 1991-2001

[29] Elias A Said, Mohammed A Al-Abri, Iman Al-Saidi, et al. Altered Blood Cytokines, CD4 T Cells, NK and Neutrophils in Patients with Obstructive Sleep Apnea[J]. Immunology Letters, 2017, 190: 272-278

[30] Cheng S, Pole JD, Sung L. Early deaths in pediatric acute leukemi-a: a population-based study [J]. Leuk Lymphoma, 2014, 55 (7): 1518-1522

（上接第 3184 页）

[15] Varga L, Jovankovicova A, Huckova M, et al. Hereditary bilateral sudden sensorineural hearing loss[J]. Bratisl Lek Listy, 2019, 120(9): 699-702

[16] Fusconi M, Attanasio G, Capitani F, et al. Is there a relation between sudden sensorineural hearing loss and white matter lesions? [J]. Eur Arch Otorhinolaryngol, 2019, 276(11): 3043-3049

[17] Menezes AS, Ribeiro D, Lima A, et al. SCORE risk scale as a prognostic factor after sudden sensorineural hearing loss [J]. Eur Arch Otorhinolaryngol, 2019, 276(10): 2739-2745

[18] Tian G, Zhang S, Yang J. Coexistence of IL-6 -572C/G and ICAM-1 K469E Polymorphisms among Patients with Sudden Sensorineural Hearing Loss[J]. Tohoku J Exp Med, 2018, 245(1): 7-12

[19] Yoon SH, Kim ME, Kim HY, et al. Inflammatory cytokines and mononuclear cells in sudden sensorineural hearing loss[J]. J Laryngol Otol, 2019, 133(2): 95-101

[20] Niu SL, Huang YM, Zhou YQ, et al. Determination of serum HMGB1 and ENA-78 in patients with idiopathic sudden sensorineural hearing loss and its clinical significance [J]. Chin J of clinicians (Electronic Edition), 2011, 5(4): 1059-1062

[21] Bazzi K, Grierson K, Fagan P. Corticosteroid use in sudden sensorineural hearing loss and the risk of osteonecrosis: a potential medicolegal pitfall[J]. ANZ J Surg, 2019, 89(12): 1540-1541

[22] Bhandari A, Jain S. Early Intratympanic Methylprednisolone in Sudden SNHL: A Frequency-wise Analysis[J]. Indian J Otolaryngol Head Neck Surg, 2019, 71(3): 390-395

[23] Chandrasekhar SS, Hollingsworth DB, Monjur TM, et al. Plain Language Summary: Sudden Hearing Loss [J]. Otolaryngol Head Neck Surg, 2019, 161(2): 211-217

[24] Chandrasekhar SS, Tsai Do BS, Schwartz SR, et al. Clinical Practice Guideline: Sudden Hearing Loss (Update) Executive Summary[J]. Otolaryngol Head Neck Surg, 2019, 161(2): 195-210

[25] Sahu ID, Craig AF, Dunagan MM, et al. Probing Structural Dynamics and Topology of the KCNE1 Membrane Protein in Lipid Bilayers via Site-Directed Spin Labeling and Electron Paramagnetic Resonance Spectroscopy[J]. Biochemistry, 2015, 54(41): 6402-6412

[26] Psillas G, Arnaoutoglou M, Gatsios T, et al. Autoimmune recurrent facial palsy and bilateral sudden sensorineural hearing loss following Ramsay Hunt-like syndrome [J]. Auris Nasus Larynx, 2012, 39(2): 229-232

[27] Inokuchi JI, Go S, Yoshikawa M, et al. Gangliosides and hearing[J]. Biochim Biophys Acta Gen Subj, 2017, 1861(10): 2485-2493

[28] Shen F. Treatment of sudden hearing loss by monosialotetrahexosylganlioside [J]. J of Otolaryngology and Ophthalmology of Shandong University, 2013, 27(1): 24-25+30

[29] Yoshikawa M, Go S, Suzuki S, et al. Ganglioside GM3 is essential for the structural integrity and function of cochlear hair cells[J]. Hum Mol Genet, 2015, 24(10): 2796-2807

[30] Li S, Tan J, Zhang H, et al. Effect of Catgut Implantation on Spatial Learning-memory Ability, Expression of Hippocampal Protein Kinase C Interacting Protein 1 and GluR 2 and Ca^{2+} Content in Rats with Chronic Ischemic Cognitive Impairment [J]. Zhen Ci Yan Jiu, 2018, 43(6): 347-352