doi: 10.13241/j.cnki.pmb.2020.05.019

# 针灸联合多奈哌齐和美金刚对重度老年痴呆患者行为能力和认知功能的影响 *

赵 萍 曹会芳 杨新利 卜 宁 舒粉宁

(西安交通大学第二附属医院神经内科 陕西 西安 710004)

**摘要 目的:**研究针灸联合多奈哌齐和美金刚对重度老年痴呆患者行为能力和认知功能的影响。**方法:**选择 2015 年 1 月～2018 年 12 月在我院精神科进行诊治的 50 例重度老年痴呆患者,采用随机数字表法将其平均分为两组,每组 25 例。对照组患者口服多奈哌齐以及美金刚治疗,初始给药剂量均为每天口服 5 mg,逐渐将给药剂量升高至每天口服 20 mg,每次 1 片,每天 2 次。观察组患者采取针灸联合多奈哌齐和美金刚治疗,每天针灸治疗 1 次,每治疗 6 d 后休息 1 d。两组患者均连续治疗 4 周。记录和比较两组患者治疗前后的日常生活能力与认知功能的变化情况。**结果:**观察组患者治疗 4w 后的治疗有效率为 92.00%(23/25),明显高于对照组[68.00%(17/25)]($P$<0.05);两组治疗 4 w 后的 MMSE 和 BI 评分均显著高于治疗前($P$<0.05),且观察组以上指标均显著高于对照组(P<0.05)。**结论:**针灸联合多奈哌齐和美金刚对重度老年痴呆患者的治疗效果明显优于单纯使用多奈哌齐和美金刚治疗,其可更有效改善患者的行为能力和认知功能。

**关键词:**多奈哌齐;美金刚;针灸;重度老年痴呆;行为能力;认知功能

**中图分类号:**R741;R749.16 **文献标识码:**A **文章编号:**1673-6273(2020)05-889-04

# Effect of Acupuncture and Moxibustion Combined with Donepezil and Memantine on the Behavior and Cognitive Function of Patients with Severe Alzheimer's Disease*

*ZHAO Ping, CAO Hui-fang, YANG Xin-li, BU Ning, SHU Fen-ning*

*(Neurology Department, The Second AffiliatedHospital of Xi 'an Jiaotong University, Xi'an, Shaanxi, 710004, China)*

**ABSTRACT Objective:** To investigate the effect of acupuncture and moxibustion combined with donepezil and memantine on the behavior and cognitive function of patients with severe Alzheimer's Disease. **Methods:** Fifty patients with severe Alzheimer's Disease who were diagnosed and treated in the department of psychiatry of our hospital from January 2015 to December 2018 were selected and divided into two groups with an average of 25 cases in each group using the random number table method. Patients in the control group were treated with donepezil and memantine orally. Patients in the observation group were treated with acupuncture and moxibustion combined with donepezil and memantine once a day, with a rest of 1 day after 6 days of treatment. Both groups were treated for 4 weeks. The changes of daily living ability and cognitive function before and after treatment were recorded and compared between the two groups. **Results:** The effective rate of the observation group was 92.00%(23/25) after 4w treatment, which was significantly higher than that of the control group [68.00%(17/25)]($P$<0.05). MMSE and BI scores after 4 w of treatment in both groups were significantly higher than those before treatment ($P$<0.05), and the above indexes in the observation group were significantly higher than those in the control group ($P$<0.05). **Conclusion:** Acupuncture combined with donepezil and memantine was more effective in the treatment of patients with severe Alzheimer's Disease than donepezil and memantine, which can more effectively improve the patients' behavior ability and cognitive function.

**Key words:** Donepezil; Memantine; Acupuncture; Severe Alzheimer's Disease; Behavior Ability; Cognitive Function

**Chinese Library Classification(CLC): R741; R749.16 Document code: A**

**Article ID: 1673-6273(2020)05-889-04**

## 前言

老年痴呆症导致患者的认知功能降低，对其语言表达、记忆、逻辑判断能力等造成影响,患者出现脾气暴躁、精神抑郁以及紧张感等异常的行为表现,重度老年痴呆症患者由于生活自理能力严重降低而需要给予特殊照料[1-3]。老年痴呆症的发病机制仍尚并未完全阐明,目前主要有以下几个假说:中枢胆碱能损伤、β 淀粉样蛋白级联学说、Tau 蛋白学说和兴奋性氨基酸毒性学说[4-7]。目前临床上对于重度老年痴呆症仍然未发现确切有效的治疗方法，西医主要以营养神经与雌激素替代法进行治

* 基金项目:陕西省卫生计生委科研基金项目(2016A003)

作者简介:赵萍(1972-),女,本科,主管技师,研究方向:针灸康复,电话:18092038672,E-mail:zhaoping1805@163.com

(收稿日期:2019-06-30 接受日期:2019-07-23)

疗,需长期服药,患者的治疗依从性普遍较差,使得治疗效果较差[8,9]。多奈哌齐是临床上治疗老年痴呆的主要药物之一,能可逆的抑制乙酰胆碱酯酶对乙酰胆碱的水解,提高神经传递突触间乙酰胆碱的含量,达到改善认知的作用。兴奋神经递质功能障碍能导致兴奋毒性与老年痴呆的发病有密切的关系,该神经毒性主要由 NMDA 型谷氨酸受体介导, 美金刚是一种非竞争性 NMDA 受体阻断剂,具有良好的临床疗效,多奈哌齐与美金刚联合用药治疗老年痴呆的报道较多,能显著的改善患者的认知能力和行为能力。已有研究表明,中医从整体出发采取辨证论治,在治疗此病方面具有一定的优势[10],针灸能与其他治疗方法并行使用,已成为治疗重度老年痴呆的热点问题。本研究主要探讨了针灸联合多奈哌齐和美金刚对重度老年痴呆患者行为能力和认知功能的影响,以期为重度老年痴呆患者的治疗提供更多的参考依据。

## 1 资料与方法

### 1.1 一般资料

选择 2015 年 1 月～2018 年 12 月我院收治的 50 例重度老年痴呆患者, 均符合重度老年痴呆的标准, 入选年龄≥ 65 岁,均知情同意,排除患有严重的肝、心、肾等疾病者;抑郁症、精神分裂症、头部外伤、严重的视力和听力障碍、中枢神经系统感染以及慢性酒精中毒等继发性痴呆症患者。将所有患者随机分为两组。观察组 25 例,男 14 例,女 11 例;年龄 65～81 岁,平均 (70.43 ± 6.25) 岁;病程 1～9 年,平均 ( 3.79 ± 0.63) 年。对照组 25 例,男 15 例,女 10 例;年龄 65～82 岁,平均 (69.52 ± 6.13) 岁;病程 1～9 年,平均 ( 3.85 ± 0.72) 年。两组重度老年痴呆患者的基线资料比较差异均无统计学意义($P$>0.05),具有可比性。

### 1.2 治疗方法

对照组:口服多奈哌齐(批号:国药准字 H20030472,生产厂家:江苏豪森药业公司)治疗,初始给药剂量为每天口服 5 mg,并且于睡前服用;给药 1w 后,如果老年痴呆患者未出现不良反应,则把给药剂量加倍至每天口服 10 mg,每天 2 次;在服药的第 3 w 把给药剂量升高至每天口服 15 mg,早晨服用 1 片药物,下午则服用半片;在服药的第 4 w 把给药剂量维持为每天口服 20 mg,每次 1 片,每天 2 次。并且采用美金刚(进口药品注册证号:H20120268,生产厂家:丹麦灵北药厂)治疗,初始给药剂量为每天口服 5 mg,并且于清晨服用,给药剂量的调整方法与多奈哌齐相同。

观察组联合采取针灸治疗,选择水沟、内关、风池、完骨、天柱、百会、四神聪、神门、三阴穴、肾俞、太冲、丰隆等穴位,使用一次性不锈钢针灸针 (北京汉医医疗器械有限责任公司生产,规格为 0.25 mm× 50 mm)。指导患者取半卧位,于针刺得气后,留针半小时,每 10 min 行针一次。每天针灸治疗 1 次,每治疗 6 d 后休息 1 d。两组均治疗 4 w。

### 1.3 观察指标

分别于治疗前 1 d 以及治疗 4 w 末,采用 MMSE 量表测评重度老年痴呆患者的认知功能改变状况,该量表主要包含以下五个方面:回忆力、语言能力、注意力、定向能力以及记忆能力等,总计为 30 分,总分越低则提示患者的认知功能越差。按照治疗后的 MMSE 评分值判断疗效,标准:① 显效:采取 4 w 的治疗后,重度老年痴呆患者的 MMSE 评分值接近于满分;② 有效:采取 4 w 的治疗后,重度老年痴呆患者的 MMSE 评分值与治疗前相比升高幅度达到 15 %～40 %;③ 无效:采取 4 w 的治疗后, 重度老年痴呆患者的 MMSE 量表评分值未出现任何的升高。

采取日常生活能力评定量表(BI 量表)评价生活能力,该量表主要包括以下十个方面:上下楼梯、控制小便、转移床椅、控制大便、穿衣服、日常修饰、平地行走、进食以及进出卫生间等。总计为 100 分,评分值越低则提示其日常生活的能力越差。

### 1.4 统计学分析

数据采用 SPSS 17.00 进行统计学分析,计量资料的组间对比用 t 检验,组间率的比较用 $x^2$ 检验,以 P<0.05 表明差异有统计学意义。

## 2 结果

### 2.1 两组临床疗效的对比

治疗后, 观察组重度老年痴呆患者显效 12 例, 有效 10 例,无效 2 例,有效率为 92%,明显高于对照组(68%,$P$<0.05),见表 1。

表 1 两组临床疗效对比[例(%)]

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

| Groups | n | Effective | Valid | Invalid | The total effect rate |
|---|---|---|---|---|---|
| Control group | 25 | 10 (40.00) | 7 (28.00) | 8 (32.00) | 68.00 |
| Observation group | 25 | 12 (48.00) | 10 (40.00) | 2 (8.00) | 92.00* |

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

### 2.2 两组治疗前后认知功能 MMSE 评分对比

两组治疗 4 w 后的 MMSE 评分均较治疗前明显升高($P$<0.05),且观察组明显高于对照组($P$<0.05),见表 2。

### 2.3 两组日常生活能力 BI 评分对比

两组治疗 4 w 后的 BI 评分均较治疗前明显升高($P$<0.05),且观察组明显高于对照组($P$<0.05),见表 3。

## 3 讨论

目前, 已知的引发老年痴呆症的危险因素包括冠心病、糖尿病、高血压以及动脉硬化等[11,12],临床上以记忆功能障碍、失语、执行功能障碍、视空间技能受损、失认、人格行为改变和失用等为特征[13-15]。由于病因未明,临床上治疗重度老年痴呆仍无特别有效的方法[16]。治疗重度老年痴呆症的关键在于加速脑血液循环,促进神经系统重新建立有效的代偿功能,进而有效恢复神经系统的功能以及大脑的智力功能[17-21]。目前,临床上主要

表 2 两组治疗前后的认知功能 MMSE 评分的对比($\bar{x}\pm s$)

Table 2 Comparison of the MMSE scores of cognitive function between the two groups before and after treatment ($\bar{x}\pm s$)

| Groups | n | Before treatment | After treatment |
|---|---|---|---|
| Control group | 25 | 8.43 ± 2.17 | 19.15 ± 3.38# |
| Observation group | 25 | 8.31 ± 2.74 | 25.26 ± 3.54*# |

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

表 3 两组治疗前后的日常生活能力 BI 评分对比($\bar{x}\pm s$)

Table 3 Comparison of the BI scores of daily living ability between the two groups before and after treatment ($\bar{x}\pm s$)

| Groups | n | Before treatment | After treatment |
|---|---|---|---|
| Control group | 25 | 47.39 ± 8.57 | 59.29 ± 9.58# |
| Observation group | 25 | 47.65 ± 8.43 | 69.33 ± 10.42*# |

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

采取的药物包括谷氨酸受体拮抗剂(如美金刚)以及胆碱酯酶抑制剂(如多奈哌齐)两种,可在一定程度上缓解患者的痴呆症状,但仍无法有效地阻止病变的进一步发展[22-24]。

祖国传统医学认为老年痴呆属于"呆病、"神病"、"呆痴"和"健忘"范畴,其病机主要是由于机体血、精和气出现严重的亏损不足,使得痰、瘀、风、火诸邪内阻、髓海失充、脑失所养,清窍受蒙,脏腑失调,累及脑窍而致病[25-28]。随着祖国传统医学理论的不断发展,使用针灸治疗老年痴呆症患者取得了较为满意的应用效果。针灸一方面能有助于大脑侧支循环的重新建立,增加脑功能的代偿功能;另一方面还能通过刺激外周穴位临近的神经末梢,对于所属的脏腑和静脉进行强有效的激发,促进局部血液发生循环,从而加速脑功能代谢以及部分神经细胞功能代谢[29,30]。由于治疗老年痴呆的关键在于促进脑血液循环,恢复建立神经系统的代偿功能,针灸可以发挥较佳的疗效。

本研究结果显示观察组老年痴呆患者的治疗有效率明显高于对照组,提示针灸联合多奈哌齐+美金刚对重度老年痴呆患者的治疗效果明显优于单纯使用多奈哌齐+美金刚。分析其原因为针灸疗法具有开窍醒脑之功效,能有效疏通患者的脏器,调节内脏功能,所选择的水沟、内关、风池、完骨、天柱、百会、四神聪、神门、三阴穴、肾俞、太冲、丰隆等穴位与重度老年痴呆患者的思维活动以及精神意识等紧密相关。其中,针刺水沟穴具有醒脑开窍、回阳救逆、敛阴固脱之功;针刺内关穴引起的额、颞叶变化,与"心包"功能有关;针刺百会穴具有通络止痛之功效;针刺四神聪具有治疗头痛、眩晕、失眠、健忘、癫痫等神志病证;针刺神门穴具有改善心悸、帮助入眠、缓解胸胁痛、掌中热、便秘、食欲不振之功效;针刺丰隆穴具有沉降胃浊之功效;针刺太冲穴具有燥湿生风之功效。针灸可以通过刺激穴位周围的神经末梢,使其所属的脏腑和经脉得到有效的激发,加速局部的血液循环以及代谢,可以共同促进脑功能以及神经细胞功能的改善。本研究结果表明针灸治疗 4 w 后患者 MMSE 评分以及 BI 评分均明显升高,提示针灸可以通过使神经元的兴奋性增加,加快脑功能的代谢速度,使重度老年痴呆患者的行为能力和认知功能得到改善,其效果明显优于单独使用西医多奈哌齐+美金刚治疗。在我们今后的临床研究中,我们会进一步加强对针刺部位以及针刺手法等的研究,以期使针刺疗法更为准确有效。

综上所述,针灸联合多奈哌齐和美金刚对重度老年痴呆患者的治疗效果明显优于单纯使用多奈哌齐和美金刚治疗,其可更有效改善患者的行为能力和认知功能。

## 参 考 文 献(References)


[1] Iwasaki Y, Deguchi A, Mori K, et al. An autopsy case of a centenarian with the pathology of senile dementia of the neurofibrillary tangle type[J]. Psychogeriatrics, 2017, 17(2): 126-129

[2] Sun Y P, Cai Y, Ji-Hui L, et al. Practice and experience of clinical pharmacists in the multidisciplinary team of senile dementia department[J]. Chinese Journal of New Drugs, 2018, 27(2): 245-248

[3] Workgroup A A C H. Calcium Hypothesis of Alzheimer's disease and brain aging: A framework for integrating new evidence into a comprehensive theory of pathogenesis[J]. Alzheimers & Dementia the Journal of the Alzheimers Association, 2017, 13(2): 178-182.e17

[4] Espunycamacho I, Arranz A M, Fiers M, et al. Hallmarks of Alzheimer's Disease in stem-cell-derived human neurons transplanted into mouse brain[J]. Neuron, 2017, 93(5): 1066-1081

[5] Staff P M. Correction: Genetic assessment of age-associated Alzheimer disease risk: Development and validation of a polygenic hazard score [J]. Plos Medicine, 2017, 14(3): e1002289

[6] Luo J, Wärmländer S K, Gräslund A, et al. Cross-interactions between the Alzheimer Disease Amyloid-β Peptide and Other Amyloid Proteins: A Further Aspect of the Amyloid Cascade Hypothesis [J]. Journal of Biological Chemistry, 2017, 292(5): 2046

[7] Mattsson N, Andreasson U, Zetterberg H, et al. Association of plasma neurofilament light with neurodegeneration in patients with Alzheimer Disease[J]. Jama Neurology, 2017, 74(5): 557

[8] Yang T, Li S, Xu H, et al. Large Soluble Oligomers of amyloid β-protein from alzheimer brain are far less neuroactive than the smaller oligomers to which they dissociate [J]. Journal of Neuroscience the Official Journal of the Society for Neuroscience, 2017, 37(1): 152

[9] Ambadipudi S, Biernat J, Riedel D, et al. Liquid-liquid phase separation of the microtubule-binding repeats of the Alzheimer-related protein Tau[J]. Nature Communications, 2017, 8(1): 275

[10] Lu Y J, Cai X W, Zhang G F, et al. Long-term acupuncture treatment has a multitargeting regulation on multiple brain regions in rats with Alzheimer's disease: a positron emission tomography study[J]. Neural

Regeneration Research, 2017, 12(7): 1159-1165

[11] Kerr J S, Adriaanse B A, Greig N H, et al. Mitophagy and Alzheimer's Disease: Cellular and molecular mechanisms [J]. Trends in Neurosciences, 2017, 40(3): 151-166

[12] Hampel H, O'Bryant S E, Durrleman S, et al. A Precision Medicine Initiative for Alzheimer's disease: the road ahead to biomarker-guided integrative disease modeling[J]. Climacteric, 2017, 20(2): 107-118

[13] Song W, Hooli B, Mullin K, et al. Alzheimer's disease-associated TREM2 variants exhibit either decreased or increased ligand-dependent activation[J]. Alzheimers & Dementia, 2017, 13(4): 381-387

[14] Bussè C, Anselmi P, Pompanin S, et al. Specific verbal memory measures may distinguish Alzheimer's Disease from dementia with lewy bodies[J]. Journal of Alzheimers Disease Jad, 2017, 15(13): 1797-1810

[15] Riancho J, Vázquez-Higuera J L, Pozueta A, et al. MicroRNA Profile in Patients with Alzheimer's Disease: Analysis of miR-9-5p and miR-598 in Raw and Exosome Enriched Cerebrospinal Fluid Samples [J]. Journal of Alzheimers Disease Jad, 2017, 57(2): 483-491

[16] Ferrari R, Wang Y, Vandrovcova J, et al. Genetic architecture of sporadic frontotemporal dementia and overlap with Alzheimer's and Parkinson's diseases[J]. J Neurol Neurosurg Psychiatry, 2017, 88(2): 152-164

[17] Fu H, Rodriguez G A, Herman M, et al. Tau pathology induces excitatory neuron loss, grid cell dysfunction, and spatial memory deficits reminiscent of early Alzheimer's Disease[J]. Neuron, 2017, 93(3): 533-541.e5

[18] Carballocc Acheco M, Strodel B. Comparison of force fields for Alzheimer's A β42: A case study for intrinsically disordered proteins [J]. Protein Science A Publication of the Protein Society, 2017, 26(2): 174

[19] Amin F U, Hoshiar A K, Do T D, et al. Osmotin-loaded magnetic nanoparticles with electromagnetic guidance for the treatment of Alzheimer's disease[J]. Nanoscale, 2017, 9(30): 10619-10632

[20] Mokhtari Z, Baluchnejadmojarad T, Nikbakht F, et al. Riluzole ameliorates learning and memory deficits in Aβ25-35-induced rat model of Alzheimer's disease and is independent of cholinoceptor activation[J]. Biomedicine & Pharmacotherapy, 2017, 87(Complete): 135-144

[21] Lin A L, Jahrling J B, Zhang W, et al. Rapamycin rescues vascular, metabolic and learning deficits in apolipoprotein E4 transgenic mice with pre-symptomatic Alzheimer's disease [J]. Journal of Cerebral Blood Flow & Metabolism, 2017, 37(1): 217-226

[22] Shimada H, Kitamura S, Shinotoh H, et al. Association between Aβ and tau accumulations and their influence on clinical features in aging and Alzheimer's disease spectrum brains: A [11C]PBB3-PET study[J]. Alzheimers & Dementia Diagnosis Assessment & Disease Monitoring, 2017, 6(7): 11-20

[23] Herukka S K, Simonsen A H, Andreasen N, et al. Recommendations for cerebrospinal fluid Alzheimer's disease biomarkers in the diagnostic evaluation of mild cognitive impairment[J]. Alzheimers & Dementia the Journal of the Alzheimers Association, 2017, 13(3): 285

[24] Noguchishinohara M, Komatsu J, Samuraki M, et al. Cerebral Amyloid Angiopathy-Related Microbleeds and Cerebrospinal Fluid Biomarkers in Alzheimer's Disease[J]. Journal of Alzheimers Disease Jad, 2017, 55(3): 1-9

[25] Peng W, Zhou J, Xu M, et al. The effect of electroacupuncture combined with donepezil on cognitive function in Alzheimer's disease patients: study protocol for a randomized controlled trial [J]. Trials, 2017, 18(1): 301

[26] Ding N, Jiang J, Lu M, et al. Manual Acupuncture Suppresses the Expression of Proinflammatory Proteins Associated with the NLRP3 Inflammasome in the Hippocampus of SAMP8 Mice [J]. Evid Based Complement Alternat Med, 2017, 2017: 3435891

[27] Lai C Y, Wu M Y, Chiang J H, et al. Utilization of Western medicine and traditional Chinese medicine among patients with Alzheimer's disease in Taiwan: a nationwide population-based study[J]. European Journal of Neurology, 2017, 24(3): 257-264

[28] Sreenivasmurthy S G, Liu J Y, Song J X, et al. Neurogenic Traditional Chinese Medicine as a Promising Strategy for the Treatment of Alzheimer's Disease [J]. International Journal of Molecular Sciences, 2017, 18(2): 272

[29] Zhou S, Dong L, He Y, et al. Acupuncture plus herbal medicine for Alzheimer's Disease: A systematic review and meta-analysis [J]. American Journal of Chinese Medicine, 2017, 45(7): 1327-1344

[30] Zheng W, Su Z, Liu X, et al. Modulation of functional activity and connectivity by acupuncture in patients with Alzheimer disease as measured by resting-state fMRI[J]. Plos One, 2018, 13(5): e0196933