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灵龟八法结合火针对失眠患者睡眠质量及炎症因子水平的影响 *

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摘要 目的:探讨灵龟八法结合火针对失眠患者睡眠质量及炎症因子水平的影响。**方法:**选取2017年5月~2019年3月期间空军杭州特勤疗养中心收治的失眠患者97例,根据数字表法将患者分为对照组(n=48,常规针刺治疗)和研究组(n=49,灵龟八法结合火针治疗),比较两组患者治疗4周后的临床疗效,比较两组治疗前、治疗4周后的中医症状积分、炎症因子水平,比较两组治疗前、治疗2周后、4周后的睡眠质量,记录两组治疗期间不良反应情况。**结果:**研究组治疗4周后的临床总有效率为93.88%(46/49),高于对照组的72.92%(35/48)($P<0.05$)。两组治疗4周后难以入睡、多梦易醒、头晕、心悸的症状积分均下降,且研究组低于对照组($P<0.05$)。两组治疗2周后、4周后匹兹堡睡眠质量指数(PSQI)评分均较治疗前降低($P<0.05$),研究组治疗4周后PSQI评分较治疗2周后降低($P<0.05$),研究组治疗4周后PSQI评分低于对照组($P<0.05$)。两组治疗4周后血清白介素-1 β (IL-1 β)、白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平均下降,且研究组低于对照组($P<0.05$)。治疗期间对照组不良反应发生率为12.50%(6/48),研究组不良反应发生率为16.33%(8/49),两组不良反应发生率对比无统计学差异($P>0.05$)。**结论:**灵龟八法结合火针治疗失眠患者,疗效显著,可改善患者临床症状,提高睡眠质量,并降低机体炎症因子水平,且安全性较好,具有一定的临床应用价值。

关键词:灵龟八法;火针;失眠;睡眠质量;炎症因子;疗效

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Effect of Lingui Bafa Combined with Fire Needling on Sleep Quality and Inflammatory Factor Levels in Insomnia Patients*

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ABSTRACT Objective: To explore the effect of Lingui Bafa combined with Fire Needling on sleep quality and inflammatory factor levels in insomnia patients. **Methods:** 97 insomnia patients who were admitted to Air Force Hangzhou Special Service Recuperation Center from May 2017 to March 2019 were selected, and they were divided into control group (n=48, routine acupuncture treatment) and study group (n=49, Lingui Bafa combined with fire needle treatment) according to the digital table method. The clinical effects of the two groups at 4 weeks after treatment were compared. The scores of TCM symptoms and levels of inflammatory factors before and 4 weeks after treatment were compared. The sleep quality of the two groups before treatment, 2 weeks after treatment and 4 weeks after treatment were compared, and adverse reactions during treatment were recorded in both groups. **Results:** After 4 weeks of treatment, the total clinical effective rate of the study group was 93.88% (46/49), which was higher than 72.92% (35/48) of the control group ($P<0.05$). The symptom scores of insomnia, wakefulness, dizziness and palpitation decreased in both groups, and those in the study group were lower than those in the control group after 4 weeks of treatment ($P<0.05$). After 2 weeks and 4 weeks of treatment, Pittsburgh Sleep Quality Index (PSQI) scores in both groups were lower than those before treatment ($P<0.05$), PSQI scores after 4 weeks of treatment in the study group were lower than after 2 weeks of treatment ($P<0.05$), after 4 weeks of treatment, PSQI scores in the study group were lower than those in the control group ($P<0.05$). The levels of serum interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in the two groups decreased after 4 weeks of treatment, and the levels in the study group were lower than those in the control group ($P<0.05$). The incidence of adverse reactions was 12.50% (6/48) in the control group and 16.33% (8/49) in the study group. There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Lingui Bafa combined with fire needle therapy for insomnia patients has remarkable curative effect. It can improve the clinical symptoms of patients,

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improve the quality of sleep, and reduce the level of inflammatory factors. It is safe and has certain clinical application value.

Key words: Linggui Bafa; Fire Needling; Insomnia; Sleep quality; Inflammatory factors; Curative effect

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前言

失眠是临床常见的睡眠障碍性疾病,主要是因为患者自身入睡困难或睡眠维持困难,而引起睡眠时间不足^[1,2]。随着现代人生活节奏的加快、高强度的工作以及生存竞争的压力的影响,不少人均饱受失眠的困扰^[3-5]。长期的失眠因无法满足人体的正常生理需求,可使其日常生活受到不同程度的影响。传统的西医治疗多以心理治疗、行为疗法以及药物治疗为主,虽可获得一定疗效,但药物长期使用增加不良反应发生风险,同时存在停药后复发的现象^[6]。而心理治疗、行为疗法虽无不良反应大等弊端,但其依旧存在疗效不稳定的情况。中医认为失眠属于“不寐”范畴,多数患者因劳倦思虑过度,引起气血虚亏,心神失养,最终阴阳失调,引起不寐^[7],故中医治疗失眠注重调整人体的气血阴阳。针灸是中医学的重要组成部分,其适应证广、疗效明显、操作方便,可在改善患者睡眠质量的同时提高日间的功能状态^[8]。本研究对空军杭州特勤疗养中心收治的49例失眠患者给予灵龟八法结合火针治疗,取得了较好的疗效,将结果报道如下。

1 资料与方法

1.1 临床资料

选取2017年5月~2019年3月期间空军杭州特勤疗养中心接收的失眠患者97例。纳入标准:(1)西医诊断标准参考《精神障碍诊断和统计手册》^[9]:临床表现为无法入睡、多梦、睡眠浅等,3次/周,且睡眠障碍>30d;(2)中医诊断标准参考《中医内科病证诊断疗效标准》^[10]:难以入寐、头晕、多梦易醒、心悸、四肢倦怠、舌质淡红、苔白、脉细弱,辨证分型为心脾两虚型;(3)患者及其家属知情本次研究且已签署同意书;(4)入组前未使用过其他药物者;(5)匹兹堡睡眠质量指数(PSQI)^[11]评分>8分。排除标准:(1)针刺不良反应不能耐受者;(2)继发于躯体疾病、精神障碍等疾病引起失眠的患者;(3)合并心肝肾等脏器功能不全者;(4)依从性差。已获我院伦理学委员会批准进行。根据乱数表法将患者分为研究组(49例)、对照组(48例),其中对照组男31例,女17例,年龄25~43岁,平均(35.19±3.27)岁;病程3~19月,平均(11.62±2.84)月;体质量指数22.3~26.8 kg/m²,平均(24.16±0.75)kg/m²。研究组男33例,女16例,年龄26~45岁,平均(35.26±3.38)岁;病程2~18月,平均(11.53±3.18)月;体质量指数22.6~26.9 kg/m²,平均(24.57±0.83)kg/m²。两组临床资料对比无差异($P>0.05$),资料均衡可比。

1.2 方法

对照组予以常规针刺治疗,穴位:脾俞、四神聪、心俞、照海、三阴交、申脉。进针方法:提插捻转补法。留针30 min,每15 min行针1次,1次/d,5次/周,共治疗4周。研究组给予灵龟八法结合火针治疗,火针治疗:患者取俯卧位,取心俞、脾俞两穴,穴位处进行常规消毒,进针方法:快速进针,将火针针

身的前中段烧红后进针,2次/周,共治疗4周。灵龟八法治疗:依据患者就诊时间,记录治疗当天的天干地支,随后逐日按时取穴,环周盘寻找当天所开的八脉交会穴以及对应的时辰,即后溪、足临泣、申脉、内关、外关、列缺、照海、公孙。进针方法:提插捻转补法。除列缺其余穴位均直刺10~20 mm,列缺则向肘部方向平刺10 mm,得气后再行辨证取穴治疗。辨证取穴穴位:四神聪、百会、风市、太冲、合谷、三阴交及神门。选用不锈钢毫针(规格:0.3 mm×30 mm),直刺神门、合谷、三阴交、风市、太冲,平刺四神聪、百会,进针方法:提插捻转补法,留针30 min,每15 min行针1次。1次/d,5次/周,连续治疗4周。火针购自苏州针灸用品有限公司,规格0.40 mm×35 mm。

1.3 观察指标

(1)于治疗前、治疗4周后参考《中医病证诊断疗效标准》^[10],选取其中的4个主要症状:多梦易醒、难以入寐、心悸、头晕,根据病情严重程度由轻到重评分0~3分,分数越高,说明症状越严重。(2)记录两组不良反应。(3)于治疗前、治疗2周后、治疗4周后采用PSQI评分评价患者睡眠质量,其中PSQI评分共7项,包括睡眠障碍、睡眠时间、睡眠效率、催眠药物、入睡时间、日间功能及睡眠质量,每项0~3分,总分21分,分数越高表示睡眠质量越差。(4)记录两组治疗期间不良反应情况。(5)抽取患者6 mL治疗前、治疗4周后清晨空腹静脉血,离心半径12 cm,4200 r/min离心12 min,分离上清液,置于-40℃冰箱中待测。采用酶联免疫吸附试验检测白介素-6(IL-6)、白介素-1β(IL-1β)、肿瘤坏死因子-α(TNF-α),严格遵守试剂盒说明书(南京建成生物科技有限公司)进行操作。

1.4 疗效标准^[12]

睡眠时间恢复正常,或夜间睡眠时间>6 h,失眠等临床症状完全消失(痊愈);睡眠时间增加>3 h,失眠等临床症状显著改善(显效);睡眠时间增加≤3 h,失眠等临床症状较治疗前减轻(有效);无效:失眠症状未见改善甚至加重。总有效率=痊愈率+显效率+有效率。

1.5 统计学方法

采用SPSS26.0软件进行统计分析。计数资料以率的形式表示,采用卡方检验。计量资料以均值±标准差($\bar{x} \pm s$)的形式表示,采用LSD-t检验。检验标准 $\alpha=0.05$, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床疗效比较

研究组治疗后的临床总有效率为93.88%(46/49),高于对照组的72.92%(35/48)($P<0.05$);详见表1。

2.2 中医症状积分比较

两组治疗前难以入寐、多梦易醒、头晕、心悸的症状积分比较无差异($P>0.05$);两组治疗4周后上述症状积分均下降,且研究组低于对照组($P<0.05$);详见表2。

表 1 临床疗效比较例(%)

Table 1 Comparison of clinical effects [n(%)]

Groups	Recovery	Markedly effective	Effective	Invalid	Total effective rate
Control group(n=48)	9(18.75)	15(31.25)	11(22.92)	13(27.08)	35(72.92)
Study group(n=49)	13(26.53)	19(38.78)	14(28.57)	3(6.12)	46(93.88)
χ^2					7.734
P					0.005

表 2 中医症状积分比较($\bar{x} \pm s$, 分)Table 2 Comparisons of TCM Symptom Integral($\bar{x} \pm s$, scores)

Groups	Insomnia		Wakefulness		Dizziness		Palpitation	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group(n=48)	2.39 $\pm$ 0.23	1.54 $\pm$ 0.42*	2.08 $\pm$ 0.26	1.44 $\pm$ 0.19*	2.43 $\pm$ 0.19	1.65 $\pm$ 0.24*	2.23 $\pm$ 0.25	1.65 $\pm$ 0.23*
Study group(n=49)	2.41 $\pm$ 0.28	1.03 $\pm$ 0.37*	2.04 $\pm$ 0.22	0.98 $\pm$ 0.23*	2.45 $\pm$ 0.24	1.07 $\pm$ 0.19*	2.29 $\pm$ 0.27	1.13 $\pm$ 0.19*
t	0.395	12.586	0.821	24.786	0.397	14.638	1.158	16.736
P	0.713	0.000	0.416	0.000	0.667	0.000	0.249	0.000

Note: Compared with before treatment, * $P < 0.05$.

2.3 PSQI 评分比较

两组治疗前 PSQI 评分比较无差异($P > 0.05$); 两组治疗 2 周后、治疗 4 周后 PSQI 评分均较治疗前降低($P < 0.05$), 研究组

治疗 4 周后 PSQI 评分较治疗 2 周后降低($P < 0.05$); 研究组治疗 4 周后 PSQI 评分低于对照组($P < 0.05$); 详见表 3。

表 3 PSQI 评分比较($\bar{x} \pm s$, 分)Table 3 Comparison of PSQI scores ($\bar{x} \pm s$, scores)

Groups	Before treatment	2 weeks after treatment	4 weeks after treatment
Control group(n=48)	15.94 $\pm$ 1.90	10.15 $\pm$ 1.01*	10.03 $\pm$ 1.13*
Study group(n=49)	15.88 $\pm$ 1.34	9.74 $\pm$ 1.25*	6.12 $\pm$ 1.04**
t	0.180	1.775	17.738
P	0.858	0.079	0.000

Note: Compared with before treatment, * $P < 0.05$; Compared with 2 weeks after treatment, ** $P < 0.05$.

2.4 炎症因子指标比较

两组治疗前 IL-1 β 、IL-6、TNF- α 比较无差异($P > 0.05$); 两

组治疗 4 周后 IL-1 β 、IL-6、TNF- α 均下降, 且研究组低于对照组($P < 0.05$); 详见表 4。

表 4 炎症因子指标比较($\bar{x} \pm s$)Table 4 Comparison of inflammatory factor indicators($\bar{x} \pm s$)

Groups	IL-1 β (ng/mL)		IL-6(pg/mL)		TNF- α (pg/mL)	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group(n=48)	0.48 $\pm$ 0.09	0.32 $\pm$ 0.08*	128.76 $\pm$ 13.31	91.97 $\pm$ 10.12*	1.91 $\pm$ 0.27	1.36 $\pm$ 0.19*
Study group(n=49)	0.51 $\pm$ 0.06	0.21 $\pm$ 0.06*	127.38 $\pm$ 12.27	64.99 $\pm$ 9.14*	1.95 $\pm$ 0.31	0.84 $\pm$ 0.11*
t	1.935	7.672	0.531	13.785	0.677	16.537
P	0.056	0.000	0.597	0.000	0.500	0.000

Note: Compared with before treatment, * $P < 0.05$.

2.5 不良反应发生率比较

治疗期间, 对照组出现滞针、晕针各 2 例, 皮下血肿 2 例, 不良反应发生率为 12.50%(6/48); 研究组出现 1 例滞针、3 例

晕针、4 例皮下血肿, 不良反应发生率为 16.33%(8/49); 两组不良反应发生率对比无差异($\chi^2 = 0.287$, $P = 0.592$)。

3 讨论

失眠发病因素复杂,与性别、年龄、职业、体质、精神心理、环境等多方面影响因素有关^[13]。也有不少确诊患者会对睡眠形成恐惧心理,出现严重的心理负担,引起恶性循环^[14]。长期的失眠引起患者睡眠不足,进行社会活动时注意力不集中、记忆力下降,同时还可引起身体免疫力下降,给患者的社会功能造成一定影响,严重者甚至可诱发不同程度的社会意外^[15]。传统的西医疗法虽能提高患者的客观睡眠质量,但存在副作用大、耐受性差、依从性差等诸多不足,且停药后极易复发^[16]。随着祖国传统医学的发展,越来越多患者倾向于选择中医治疗。历代医学家将其归属于中医“不寐”范畴,并认为其病因病机为阴阳失调^[17]。故中医治疗失眠主张调和其气血阴阳,宜补其不足、泻其有余、调其虚实,最终使阴阳平衡^[18]。针刺为中医治疗疾病之经典手段,通过提神聚气,整体调整脏腑经络气血,从而恢复至疾病前状态^[19]。火针作为针刺和温灸的结合体,具有通经活络、逐风散寒之效^[20]。灵龟八法运用古代哲学的九宫八卦学说,取十二经脉与奇经八脉相通的8个穴位,按照日时干支的推演数字变化,作出按时取穴的一种针刺法^[21]。

本次研究结果证实,研究组治疗后的临床总有效率、中医症状积分、PSQI评分改善情况均优于对照组,可见失眠患者经灵龟八法结合火针治疗后,临床症状可得到显著改善,治疗效果获得有效提升。分析其原因,由于背部的背俞穴是人体五脏气血共同输注的部位,故五脏俞具有调节气血、情志的作用,加之失眠的主要病位在于心,针刺心俞穴位可安心宁神;脾胃是人体气血生化的源头部位,针刺脾俞可养血安神。火针针刺上述两穴,可发挥类似灸的作用,调整机体脏腑经络,使全身气机通畅,阴阳平和^[22-24]。由于经脉的气血流注以及八脉交会穴均呈现时间节律性,灵龟八法利用这一规律,对其他经络起着调节、统率和联络的作用,最终发挥平衡阴阳、调和脏腑之效,改善临床症状^[25,26]。另两组不良反应率对比未见明显差异,可见其联合治疗安全性较好。既往研究证实^[27],睡眠与免疫系统之间存在着双向联系,而炎症因子则在这种双向作用中发挥重要作用。IL-1 β 、IL-6、TNF- α 均是临床常见的炎症介质,具有广泛的生物学作用,不仅参与着机体免疫系统进程,同时还对机体中枢神经具有一定的调节作用^[28]。本研究两组患者血清炎症因子水平均有所改善,且灵龟八法结合火针治疗者改善效果更佳。这可能是因为火针针刺病位后可刺激局部邪气所犯之处,有效调节机体微循环,加之灵龟八法根据患者就诊的时间取八脉交会穴进行穴位补泻,调和阴阳气血,进而改善临床症状,提高机体免疫,抑制炎症因子的激活^[29,30]。

综上所述,灵龟八法结合火针治疗失眠患者,可改善患者临床症状,提高睡眠质量,并降低机体炎症因子水平,且安全性较好。

参考文献(References)

- [1] Reilly ED, Robinson SA, Petrakis BA, et al. Mobile App Use for?Insomnia Self-Management: Pilot Findings on Sleep Outcomes in Veterans[J]. Interact J Med Res, 2019, 8(3): e12408
- [2] Huebra L, Coelho FM, Filho FMR, et al. Sleep Disorders in Hereditary Ataxias[J]. Curr Neurol Neurosci Rep, 2019, 19(8): 59

- [3] Ghafarzadeh J, Sadeghniai-Haghighi K, Sadeghpour O, et al. Investigating the Prevalence of Sleep Disorder and the Impact of Sweet Almond on the Quality of Sleep in Students of Tehran, Iran [J]. Iran J Public Health, 2019, 48(6): 1149-1154
- [4] Rhon DI, Snodgrass SJ, Cleland JA, et al. Comorbid Insomnia and Sleep Apnea are Associated with Greater Downstream Health Care Utilization and Chronic Opioid Use after Arthroscopic Hip Surgery[J]. Pain Physician, 2019, 22(4): E351-E360
- [5] Chunhua X, Jiacy D, Xue L, et al. Impaired emotional memory and decision-making following primary insomnia [J]. Medicine (Baltimore), 2019, 98(29): e16512
- [6] He Y, Sun N, Wang Z, et al. Effect of repetitive transcranial magnetic stimulation (rTMS) for insomnia: a protocol for a systematic review [J]. BMJ Open, 2019, 9(7): e029206
- [7] 林宥廷, 李玉梅, 杨毅玲, 等. 失眠与中医体质关系的研究 [J]. 北京中医药大学学报, 2013, 36(7): 450-452
- [8] 裴清华, 李侠, 许静, 等. 308例原发性失眠患者的中医体质分布与睡眠质量的相关性研究 [J]. 北京中医药大学学报, 2018, 41(10): 859-862
- [9] 李功迎, 宋思佳, 曹龙飞. 精神障碍诊断与统计手册第5版解读[J]. 中华诊断学电子杂志, 2014, 2(4): 310-312
- [10] 国家中医药管理局. 中医内科病证诊断疗效标准 (十三)[J]. 湖北中医杂志, 2003, 25(7): 封三
- [11] 路桃影, 李艳, 夏萍, 等. 匹兹堡睡眠质量指数的信度及效度分析 [J]. 重庆医学, 2014, 43(3): 260-263
- [12] 郑筱萸. 中药新药临床研究指导原则(试行)[M]. 北京: 中国医药科技出版社, 2002: 48
- [13] 林炳岐, 李峰, 马捷, 等. 基于GABA能系统通路探讨失眠的机制 [J]. 现代生物医学进展, 2018, 18(3): 565-568
- [14] Riemann D. Sleep, insomnia and neurological and mental disorders [J]. J Sleep Res, 2019, 28(4): e12892
- [15] Pan C, Wang X, Deng Y, et al. Efficacy of mindfulness-based intervention ('mindfulness-based joyful sleep') in young and middle-aged individuals with insomnia using a biomarker of inflammatory responses: a prospective protocol of a randomised controlled trial in China[J]. BMJ Open, 2019, 9(7): e027061
- [16] DelRosso LM, Jackson CV, Ferri R. A 15-Year-Old Girl with Sleep-Onset Insomnia and Poor Sleep Quality[J]. Chest, 2019, 156(1): e23-e26
- [17] 赵丽娜, 贾跃进. 失眠与中医体质的相关性研究[J]. 中西医结合心脑血管病杂志, 2015, 13(12): 1448-1450
- [18] 王楦, 连心逸, 张晓阳, 等. 中医门诊初诊患者失眠认知状况调查与分析[J]. 中国临床医生杂志, 2016, 44(5): 107-109
- [19] 谭涛, 严洁. 严洁教授针刺治疗失眠经验[J]. 湖南中医药大学学报, 2015, 35(7): 25-26
- [20] 孙旭, 胡徽星, 李晓梅, 等. 火针心脾论治对顽固性失眠治疗作用的多中心随机对照研究[J]. 针灸临床杂志, 2017, 33(8): 31-34
- [21] 洪秋阳, 杨惠民, 王世广, 等. 灵龟八法结合火针针刺对心脾两虚型失眠患者觉醒状态的影响[J]. 针灸临床杂志, 2017, 33(8): 26-31
- [22] 石珍, 刘煊康. 灵龟八法结合火针针刺对心脾两虚型失眠的治疗效果[J]. 临床医学研究与实践, 2018, 3(34): 129-130
- [23] 冉茜, 姜兴鹏. 细火针治疗失眠临床观察 [J]. 河南中医, 2017, 37(7): 1288-1289

- 41(2): 125-136
- [14] Radić B, Petrović R, Golubić A, et al. EEG Analysis and Spect Imaging in Alzheimer's Disease, Vascular Dementia and Mild Cognitive Impairment[J]. *Psychiatr Danub*, 2019, 31(1): 111-115
- [15] Wu Y, Zhou Q, Zhang T, et al. Discovery of Potent, Selective, and Orally Bioavailable Inhibitors against Phosphodiesterase-9, a Novel Target for the Treatment of Vascular Dementia [J]. *J Med Chem*, 2019, 62(8): 4218-4224
- [16] Atti AR, Valente S, Iodice A, et al. Metabolic Syndrome, Mild Cognitive Impairment, and Dementia: A Meta-Analysis of Longitudinal Studies[J]. *Am J Geriatr Psychiatry*, 2019, 27(6): 625-637
- [17] Shang Y, Wang L, Li Y, et al. Vinpocetine Improves Scopolamine Induced Learning and Memory Dysfunction in C57 BL/6J Mice[J]. *Biol Pharm Bull*, 2016, 39(9): 1412141-8
- [18] Perng CH, Chang YC, Tzang RF. The treatment of cognitive dysfunction in dementia: a multiple treatments meta-analysis[J]. *Psychopharmacology (Berl)*, 2018, 235(5): 1571-1580
- [19] Solovyeva EY, Karneev AN, Chekanov AV, et al. Complex application 2-ethyl-6-methyl-3-hydroxypyridine-succinate and vinpocetine in cerebrovascular disorder [J]. *Zh Nevrol Psikhiatr Im S S Korsakova*, 2017, 117(5): 103-108
- [20] Gupta S, Singh P, Sharma BM, et al. Neuroprotective Effects of Agomelatine and Vinpocetine Against Chronic Cerebral Hypoperfusion Induced Vascular Dementia[J]. *Curr Neurovasc Res*, 2015, 12(3): 240-252
- [21] Mei Z, Zheng P, Tan X, et al. Huperzine A alleviates neuroinflammation, oxidative stress and improves cognitive function after repetitive traumatic brain injury[J]. *Metab Brain Dis*, 2017, 32(6): 1861-1869
- [22] Gul A, Bakht J, Mehmood F. Huperzine-A response to cognitive impairment and task switching deficits in patients with Alzheimer's disease[J]. *J Chin Med Assoc*, 2019, 82(1): 40-43
- [23] Xu M, Heidmarsson S, Thorsteinsdottir M, et al. Intraspecific Variation of Huperzine A and B in Icelandic Huperzia selago Complex[J]. *Planta Med*, 2019, 85(2): 160-168
- [24] Damar U, Gersner R, Johnstone JT, et al. Alterations in the Timing of Huperzine A Cerebral Pharmacodynamics in the Acute Traumatic Brain Injury Setting[J]. *J Neurotrauma*, 2018, 35(2): 393-397
- [25] Zhu HF, Yan PW, Wang LJ, et al. Protective properties of Huperzine A through activation Nrf2/ARE-mediated transcriptional response in X-rays radiation-induced NIH3T3 cells[J]. *J Cell Biochem*, 2018, 119(10): 8359-8367
- [26] Rydzewski J, Jakubowski R, Nowak W, et al. Kinetics of Huperzine A Dissociation from Acetylcholinesterase via Multiple Unbinding Pathways[J]. *J Chem Theory Comput*, 2018, 14(6): 2843-2851
- [27] Tabira T, Kawamura N. A Study of a Supplement Containing Huperzine A and Curcumin in Dementia Patients and Individuals with Mild Cognitive Impairment[J]. *J Alzheimers Dis*, 2018, 63(1): 75-78
- [28] He JT, Li H, Yang L, et al. Involvement of Endothelin-1, H2S and Nrf2 in Beneficial Effects of Remote Ischemic Preconditioning in Global Cerebral Ischemia-Induced Vascular Dementia in Mice [J]. *Cell Mol Neurobiol*, 2019, 39(5): 671-686
- [29] Ashok BS, Ajith TA, Sivanesan S. Hypoxia-inducible factors as neuroprotective agent in Alzheimer's disease [J]. *Clin Exp Pharmacol Physiol*, 2017, 44(3): 327-334
- [30] Salminen A, Kauppinen A, Kaarniranta K. Hypoxia/ischemia activate processing of Amyloid Precursor Protein: impact of vascular dysfunction in the pathogenesis of Alzheimer's disease [J]. *J Neurochem*, 2017, 140(4): 536-549
- [31] Iyalomhe O, Swierczek S, Enwerem N, et al. The Role of Hypoxia-Inducible Factor 1 in Mild Cognitive Impairment[J]. *Cell Mol Neurobiol*, 2017, 37(6): 969-977
- [32] Ishimaru K, Nakajima T, Namiki Y, et al. Influences of Pinpoint Plantar Long-Wavelength Infrared Light Irradiation (Stress-Free Therapy) on Chorioretinal Hemodynamics, Atherosclerosis Factors, and Vascular Endothelial Growth Factor [J]. *Integr Med Res*, 2018, 7(1): 103-107
- [33] Wallin A, Román GC, Esiri M, et al. Update on Vascular Cognitive Impairment Associated with Subcortical Small-Vessel Disease [J]. *J Alzheimers Dis*, 2018, 62(3): 1417-1441

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- [24] 宋慧敏. 火针治疗心脾两虚型失眠的临床随机对照研究[D]. 上海中医药大学, 2016
- [25] 车桂香, 朴联友. 灵龟八法为主治疗单纯性肥胖病并发失眠临床研究[J]. *吉林中医药*, 2011, 31(5): 432-434
- [26] 姚俊红, 王美兰. 灵龟八法针法配合辨证取穴治疗心脾两虚型不寐疗效观察[J]. *上海针灸杂志*, 2016, 35(11): 1284-1286
- [27] Lee EE, Ancoli-Israel S, Eyler LT, et al. Sleep Disturbances and Inflammatory Biomarkers in Schizophrenia: Focus on Sex Differences [J]. *Am J Geriatr Psychiatry*, 2019, 27(1): 21-31
- [28] Brager AJ, Ehlen JC, Castanon-Cervantes O, et al. Sleep loss and the inflammatory response in mice under chronic environmental circadian disruption[J]. *PLoS One*, 2013, 8(5): e63752
- [29] 陈裕曦. 灵龟八法配合呼吸补泻法治疗原发性失眠的疗效观察[D]. 广州中医药大学, 2017
- [30] 李净草. 灵龟八法治疗肝郁化火型失眠患者的临床研究[D]. 广西中医学院, 2010