



Immediate effect of acupuncture on the sleep pattern of patients with obstructive sleep apnoea

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ABSTRACT

Background Most patients with obstructive sleep apnoea (OSA) do not tolerate treatment with nasal continuous positive airway pressure, the 'gold standard' treatment for this condition. It was shown in a pilot study that acupuncture was more effective than placebo treatment (sham acupuncture) in producing significant changes in the respiratory events assessed by polysomnography (PSG).

Objectives To investigate the immediate effect of manual acupuncture (MA) and electroacupuncture (EA) on the sleep pattern of patients presenting with moderate OSA.

Methods 40 patients with an Apnoea–Hypopnoea Index (AHI) of 15–30/h were randomly allocated to MA treatment (n=10), EA 10 Hz treatment (n=10), EA 2 Hz treatment (n=10) and a no-treatment control group (n=10). The patients received MA or EA (2 or 10 Hz) just before the PSG study at 20:00.

Results The AHI ($p=0.005$; $p=0.005$), the Apnoea Index ($p=0.038$; $p=0.009$) and the respiratory events ($p=0.039$; $p=0.014$) decreased significantly in the MA and EA 10 Hz groups, respectively (AHI (21.9, 11.2), Apnoea Index (5.15, 0.7), respiratory events (120.5, 61.0) in the MA group before and after. AHI (20.6, 9.9), Apnoea Index (8.2, 0.3), respiratory events (117.0, 56.0) in the EA 10 Hz group before and after). The micro-arousals decreased only in the MA group (146.0 vs 88.5, $p=0.0002$). There were no significant changes in the EA 2 Hz group or in the control group.

Conclusion A single session of either MA or EA 10 Hz had an acute effect in reducing the AHI as well as the number of nocturnal respiratory events of patients presenting with moderate OSA.

INTRODUCTION

The pathogenesis of obstructive sleep apnoea (OSA) is complex but it is probably due to a combination of an anatomically small pharyngeal airway¹ in conjunction with a sleep-related decline in upper airway dilator muscle activity.² Control of upper airway muscle activity is complex. Factors that may affect upper airway muscle activity include direct input from the brainstem respiratory central pattern generator,³ chemoreceptive inputs,⁴

vagal input due to changes in lung volume⁵ and a tonic wakefulness drive that is present in the respiratory system.⁶ During wakefulness, patients with OSA have augmented activity of upper airway muscle such as the genioglossus muscle and tensor palatine.⁷ This increased activity is thought to represent a neuromuscular compensatory mechanism for an anatomically small and more collapsible pharyngeal airway. At sleep onset, this augmented upper airway dilator muscle activity is diminished or lost in association with pharyngeal collapse.⁸

We have recently demonstrated that acupuncture is more effective than placebo treatment (sham acupuncture)—providing significant changes in the respiratory events assessed by polysomnography, and improving the quality of life of patients with OSA.⁹ Manual acupuncture (MA) has been practised for thousands of years in China for the treatment of various diseases.¹⁰ Only in the past century has its potent alternative, electroacupuncture (EA), been used with increasing frequency in clinical and basic research,¹¹ and several studies suggest that the results of EA and MA differ.¹² EA causes the release of β -endorphin and adrenocorticotrophic hormone into plasma, whereas MA releases only β -endorphin.¹³ In addition to possible differences between EA and MA, a number of studies have suggested that EA at different frequencies causes different types of responses.^{13–14} Further evaluation showed that low-frequency (2 Hz) EA activated many more somatic afferents than high-frequency stimulation such as 10 and 20 Hz.¹⁵ These findings suggest that the central nervous system might have a frequency-specific response to peripheral electric stimulation.¹⁶

In our previous study the most prominent finding was the reduction in the Apnoea–Hypopnoea Index (AHI) after 10 sessions of MA. This result encouraged us to continue investigating the effects of acupuncture, which can be an affordable treatment for OSA. It is known that treatment with acupuncture requires time and several sessions are recommended for adequate results. However, we decided to test the immediate effect of only one session of acupuncture owing to the

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instant relief related the patients and also to compare the two techniques (EA and MA) in an acute model.

MATERIAL AND METHODS

Trial design and participants

Between January 2007 and August 2008, we screened individuals for inclusion in this research. Eligible patients had a significant symptomatic OSA confirmed by a full polysomnographic (PSG) study with an AHI >15/h and <30/h (moderate OSA), were aged 30–70 years and were all acupuncture naïve. Patients with a high alcohol intake (>80 g/day), morbid obesity, significant lung disease, neurological disease, intellectual deficit, problems in the skeletal facial framework, central apnoea, insomnia, who had already undergone oropharyngeal operations, who had been treated with continuous positive airway pressure or oral devices and were taking any hypnotic drugs were excluded.

A total of 40 patients were eligible for the study and were submitted to a new PSG at the start of the study. They were randomly allocated by a blinded independent researcher to the following four groups: MA group, EA 10 Hz group, EA 2 Hz group and control group (n=10 each group). After randomisation, study procedures remained blind except for the researcher who applied MA/EA. All patients signed an informed consent form after receiving details of the possible risks of acupuncture such as infection, fainting, haematoma and life-threatening risks if the needle was inappropriately handled. The ethical committee of the Universidade Federal de São Paulo approved the study protocol (number 0503/06). The study was conducted according to a strict protocol.

Needle type: MA and EA

We used single-use, sterile, cooper-handle, prepacked needles with guide tubes, 40×0.25 mm (Dongbang Acupuncture; Boryeong City, South Korea). Before insertion of the needles all the points were sterilised with ethanol. The location and depth of insertions were as described in traditional texts.¹⁷ The points used were as follows: LU6, LU7, LI4, LI20, GV20, CV23, ST36, ST40, SP6, KI6. An extra point is located between the hyoid bone and the menton symphysis (*Shanglianquan*).

For EA the electrodes were placed in the points of the neck (deep enough to reach the genioglossus muscle—CV23 and *Shanglianquan*) (figure 1) and also along the body in LI4 and ST36. The electrodes were connected to LI4 and ST36 at both sides. The EA stimulation, consisting of 0.45 ms² wave pulses at 2 or 10 Hz, was delivered by a constant current EA machine (Plexus AP 585 electrostimulator; Accurate Pulse/Biotherapy, Lautz, Brazil) to produce a moderate muscle twitch. The intensity of stimulation was typically 0.6–0.8 mA.

The choice of acupoints was based on their specific characteristics, as already described.⁹ In the MA group the needles were inserted and manually stimulated until the *deqi* sensation of heaviness and numbness was elicited.¹⁸ All acupuncture procedures were done by an experienced doctor, specialist in acupuncture, according to traditional Chinese medicine acupuncture methods.¹⁸ Body needles were left in

situ for 30 min in the ventral part of the body. Immediately after the acupuncture or electroacupuncture stimulation the subjects were prepared for the PSG recordings.

PSG procedures

Every subject went to bed, in the laboratory, at their usual bedtime, and had a minimum of 7 h of PSG recordings. The following sleep variables were collected and stored using amplifiers and preamplifiers (Meditron) and a computerised 32-channel sleep system (Sonolab; Meditron, São Paulo, Brazil). A total of four electroencephalograph leads, two electro-oculogram channels, two electromyogram channels (chin and both legs) and one electrocardiogram channel were recorded. Respiration was monitored as follows: (1) nasal cannula with flow measured using a pressure transducer; (2) mouth thermocouple to monitor mouth flow; (3) two channels for chest and abdominal efforts with calibrated inductive respiratory plethysmography; and pulse oximetry was obtained using a Nellcor oximeter.

Sleep recordings were scored according to the criteria of Rechtschaffen and Kales¹⁹ and respiratory events were considered according to the criteria published by the American Academy of Sleep Medicine in 1999.²⁰ Two blinded experienced doctors assessed all the results.

Statistical analysis

Baseline characteristics of the patients were recorded as the median and compared between groups by the Kruskal–Wallis test. The results among groups were compared before and after the procedures by the Kruskal–Wallis test. The differences between the groups before and after the procedures were compared using a Mann–Whitney test.²¹ The level of statistical significance was set at 0.05. All data were computer-analysed using Statview software.

RESULTS

Forty patients who entered the study, were randomly assigned to the MA group, EA 10 Hz group, EA 2 Hz group or control group (n=10 each group). Baseline characteristics of the three groups were similar (table 1).

PSG parameters

Table 2 shows the PSG parameters before and after procedures for each group. It also shows the statistical differ-

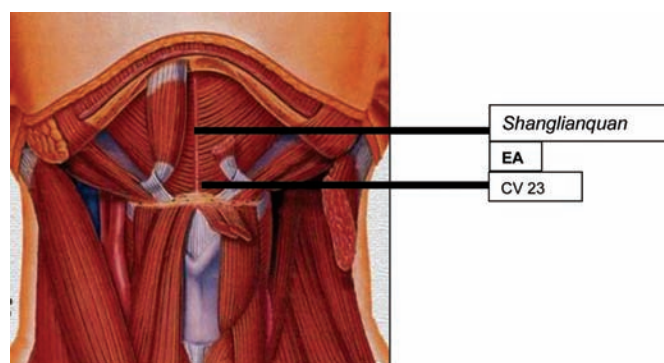


Figure 1 Local acupoints.

Table 1 Baseline characteristics of patients

	Manual Acp	EA 2 Hz	EA 10 Hz	Control	p
Age (years)	57.7 (44.0–68.0)	52.9 (33.0–69.0)	54.8 (35.0–71.0)	54.3 (35.0–69.0)	0.96
Apnoea–Hypopnoea Index	20.9 (16.9–27.8)	20.3 (17.0–26.3)	21.0 (17.3–28.5)	22.2 (15.0–34.5)	0.99
Apnoea Index	5.0 (0.0–16.8)	6.2 (2.0–15.0)	5.8 (0.5–10.4)	6.5 (0.0–23.0)	0.83
Hypopnoea Index	15.9 (6.3–21.9)	14.1 (4.0–23.5)	15.1 (8.9–23.7)	15.6 (9.0–27.6)	0.83

Data are median (5th–95th centiles). Comparison between the four groups by Kruskal–Wallis test.

Acp, acupuncture; EA, electroacupuncture.

Table 2 Polysomnographic data before and after procedures

	MA		EA 10 Hz		EA 2 Hz		Control	
	1st PSG	2nd PSG	1st PSG	2nd PSG	1st PSG	2nd PSG	1st PSG	2nd PSG
Sleep onset	10.6 (7.5)	8.75 (9.6)	12.4 (8.8)	9.0 (10.0)	8.95 (13.0)	7.45 (7.7)	7.7 (11.57)	6.5 (12.0)
REM onset	123 (34.5)	90.5 (103.5)	66.7 (97.0)	86.0 (51.0)	93.25 (109.5)	126.5 (87.0)	103.7 (51.5)	121.7 (57.5)
SI ef (%)	82.7 (11.2)	85.5 (10.6)	85.7 (9.6)	86.0 (16.8)	86.8 (6.6)	88.1 (4.5)	82.8 (16.1)	89.4 (12.3)
REM stage (%)	11.4 (14.9)	17.1 (6.4)	17.3 (6.4)	13.8 (7.0)	16.1 (9.2)	15.3 (7.7)	18.0 (3.1)	14.3 (4.3)
AHI	21.9 (8.3)	11.2 (5.5)*†	20.6 (5.6)	9.95 (5.1)†¶	21.0 (4.0)	23.8 (17.2)	18.9 (2.0)	21.5 (7.7)
Apnoea Index	5.15 (11.9)	0.7 (1.6)*†	8.2 (10.3)	0.3 (1.5)‡	5.1 (5.0)	1.4 (9.0)	3.2 (6.8)	5.9 (9.7)
Hypopnoea Index	13.9 (9.3)	8.45 (4.4)*	11.3 (7.0)	9.3 (5.5)†¶	15.5 (6.0)	17.0 (12.0)	15.8 (7.1)	15.0 (5.7)
Res Ev	120.5 (42.0)	61.0 (41.0)	117.0 (42.0)	56.0 (39.0)	130.0 (29.0)	135.0 (103.0)	125.5 (31.0)	129.0 (55.0)
Microarousal	146.0 (39.0)	88.5 (51.0)	108.0 (77.0)	73.5 (27.0)	153.5 (32.0)	129.0 (64.0)	94.5 (86.0)	111.0 (43.0)
M SaO ₂ (%)	93.9 (1.8)	94.4 (2.0)	94.9 (1.4)	95.3 (2.0)	94.5 (2.0)	94.6 (3.0)	95.0 (3.1)	94.2 (2.0)

Data are median (interquartile range).

Significant differences between groups ($p < 0.05$, Mann–Whitney): *MA versus control group; †MA versus EA 2 Hz; ‡EA 10 Hz versus control group; ¶EA 10 Hz versus EA 2 Hz.

AHI, Apnoea–Hypopnoea Index; EA, electroacupuncture; MA, manual acupuncture; M SaO₂, mean SaO₂; PSG, polysomnography; REM, rapid eye movement; Res Ev, respiratory events; SI ef, sleep efficiency.

ences between the groups before and after treatment. The MA and the EA 10 Hz groups showed a marked significant improvement, in respiratory parameters. However, the control group and the EA 2 Hz group had no significant differences.

Comparison of the results between the groups after treatment showed that the MA group and the EA 10 Hz group significantly differed from both the EA 2 Hz and control groups in all the respiratory parameters, specifically in the primary outcome the AHI (figure 2). Those differences were supported by significant changes in other outcomes. The EA 10 Hz group differed from the control group and EA 2 Hz in the respiratory events ($p=0.006$; $p=0.025$, respectively). The MA was significant different only from the control group ($p=0.015$). Nevertheless, in the Hypopnoea Index the MA differed from the control group and EA 2 Hz ($p=0.010$; $p=0.034$, respectively) and the EA 10 Hz group only differed from the control group ($p=0.019$). No adverse events occurred during the trial.

DISCUSSION

The results of our study demonstrate that median frequency EA 10 Hz and MA exerts better immediate effects than low frequency EA 2 Hz in reducing the AHI as well as the number of nocturnal respiratory events of patients presenting with moderate OSA. In a previous study our group showed that MA was effective in providing significant changes in polysomnographic evaluations as well as in the quality of life of patients with OSA after 10 weekly

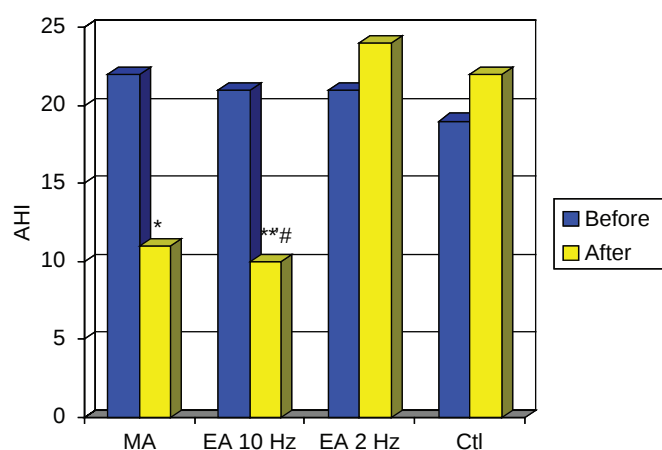


Figure 2 Comparison of the AHI at baseline (before) and after procedures among the four groups. *Manual acupuncture versus the control group ($p=0.034$); **electroacupuncture 10 Hz versus the control group ($p=0.010$); #electroacupuncture 10 Hz versus electroacupuncture 2 Hz ($p=0.049$). AHI, Apnoea–Hypopnoea Index; Ctl, control; EA, electroacupuncture; MA, manual acupuncture. $p < 0.05$, Mann–Whitney t test.

sessions of acupuncture.⁹ The speculative hypothesis for this improvement was the involvement of serotonergic pathways^{22 23} in the responses mediated by acupuncture as well as its anti-inflammatory effect.²⁴

Electrical acupoint stimulation has been widely used as a substitute for classical acupuncture. Nevertheless, the

studies dealing with electroacupuncture mainly consider its analgesic effect.²⁵ It has been shown that acupuncture analgesia can be induced by either low-frequency stimulation such as 2 Hz or high-frequency stimulation such as 100 Hz.²⁶ In our study pain was not the focus, but rather a lack of motor competence due to an inflammatory condition or to a central mechanism underlying reduction of activity of the airway dilator muscles.³ We observed that a low and medium frequency (2 and 10 Hz) showed divergent results in promoting acute relief of the apnoea symptoms. This led us to speculate about the differences that exist between other different frequencies and not only frequencies such as 2 and 100 Hz. Perhaps between two near frequencies, such as 2 and 10 Hz, or 15 and 20 Hz, particular properties exist that exert specific effects.

The significance of frequency-specific EA stimulation on analgesia and the human brain has been recognised in several studies. One observation is that the release of neurotransmitters may differ between the stimuli of high (100 Hz) and low (2 Hz) frequencies.²⁶ This finding is compatible with an aspect of traditional Chinese medicine theory strongly emphasised by Chinese doctors—namely, the importance of needle manipulation during insertion. While EA has the advantage of objective settings of stimulation parameters, it is certainly possible that EA and MA elicit different brain reactions.²⁷ Our study demonstrated clear evidence of a difference in the acute effect of low-frequency EA and MA. The reason why two similar frequencies elicit different results is not known. We speculate that EA 10 Hz promotes a greater muscle toning effect than EA 2 Hz. Or perhaps the EA 2 Hz low frequency inhibits the effect of acupuncture?

The relation between EA and the muscular system has been little studied. One study by Yang *et al* (written in Chinese) observed that EA significantly increased an athlete's performance, improving the biomechanical indexes, and thus enhancing the athlete's strength.²⁸ However, for cardiovascular diseases and also pain, both EA and MA have positive therapeutic effects. Zhou *et al*²⁹ observed that stimulation of low-frequency EA of superficial (ie, cutaneous) somatic nerves exerted either a prolonged or no attenuation of the reflex sympatho excitatory cardiovascular responses. On the other hand, the inhibitory influence of EA on the pressor reflexes was observed in the stimulation of acupoints overlying deep somatic nerves (ie, ST36 acupoint). The stimulation of the ST36 acupoint overlying the deep peroneal nerve reduces the visceral pressor reflex response, as well as stimulating LI4, an acupoint located in the hand. In our work we used both acupoints, ST36 and LI4, obtaining stimulation of the deep somatic nerves. These data may have direct clinical implications for the practice of EA. We speculate that local EA or MA as well as distant-point EA or MA may have promoted a cascade of reactions ameliorating the nocturnal apnoeas. In our previous work the PSG examination was carried out 2 weeks after the last treatment, and in this recent work we have shown that just one application produces a positive result.

The central mechanism underlying reduction of activity of airway dilator muscles with sleep is related to the projection of caudal raphe serotonergic neurons to upper airway motoneurons. Schwartz *et al*³⁰ showed that stimulation of the lingual muscles can increase or decrease airflow, depending on the specific muscles stimulated, without arousing patients from sleep. In this work, specifically, we used mainly a muscle whose action protrudes the tongue (genioglossus) for MA and EA stimulation (we should also consider the mylohyoid, but the main stimulation was in the genioglossus, because the needles were deeply inserted). The influence of this lingual muscle on airflow dynamics in the upper airway is well known and we speculate that the effect on this muscle was one of mechanisms underlying the improvement of symptoms. Measuring the electric activity of this muscle was not the reason for our trial, but a study of this aspect may help to elucidate the mechanisms of acupuncture.

Another point to be considered is that we used EA both locally and systemically in two acupoints. Thus, further investigations are currently underway to investigate (1) the improvement of those patients after 10 sessions of EA and MA; (2) the effect of these treatments 3 months after the last treatment session. As we know, acupuncture treatment must be repeated weekly and for sustained effects should be carried out over a long period of time in chronic diseases—for example, once a month after the main protocol, if necessary; (3) the involvement of 5-hydroxytryptamine and anti-inflammatory substances in this effect; (4) the difference between acupuncture treatment and the current 'gold standard' treatment for OSA—namely, continuous positive airway pressure.

Although we concluded that a single session of both MA and EA 10 Hz had an acute effect in reducing the AHI of patients presenting with moderate OSA, larger studies are needed to validate the possible clinical significance of these findings.

Summary points

- Sleep apnoea is associated with malfunction of musculature in the upper airway.
- Forty patients with sleep apnoea were randomised to four groups.
- In a single treatment session, both manual acupuncture and 10 Hz electroacupuncture were superior to control and to 2 Hz electroacupuncture.

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The sponsors of the study had no role in the study design, the planning of the data analysis or interpretation of the results. All investigators had free and unlimited access to raw data and statistical reports. The authors made final decisions on all aspects of the manuscript.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the Universidade Federal de São Paulo (UNIFESP), Brazil.

Provenance and peer review Not commissioned; externally peer reviewed.

Contributors AOF and GCMS were responsible for all acupuncture and electroacupuncture procedures. AOF, GCMS, LEM, SMT and ST contributed to the study conception, supervision, review of the analysed data and writing of the report. SMT contributed to the analyses of the PSG examinations.

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