

Traditional Chinese Medicine in Emergency Treatment Mechanism and Application

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Abstract: Traditional Chinese medicine has usually been recognized to be efficacious to treat chronic diseases from the western point-of-view. However, there is a long history in China of applying traditional Chinese medicine in many acute and urgent medical conditions. In this review, selected methods documented in traditional Chinese medicine including blowing air to ear, nose insufflating therapy, acupuncture and moxibustion were presented as the common practices to promote consciousness recovery from coma. We aimed to explore the mechanism of these four methods with current scientific evidence, further discuss the potential of traditional Chinese medicine to be applied in emergency medicine and provide a path forward to more rigorously validate these procedures. The development of the integrated traditional Chinese medicine and western medicines provides a new therapeutic direction for the new first-aid treatment.

Keywords: traditional Chinese medicine, first-aid, ear blowing, nose insufflating therapy, acupuncture, moxibustion

Introduction

Coma is a state characterized by a period of deep and prolonged unconsciousness. There are a variety of factors that may cause coma such as brain injury, brain tumor, the accumulation of drug or alcohol toxins, or even diabetes or an infection. The chances of recovery from coma vary greatly depending on different causes. The longer the coma period is, the more likely that people transit into a persistent vegetative state. Therefore, as a medical emergency, coma needs immediate actions to maintain respiration and circulation which are essential in preserving life and brain function.

Traditional Chinese medicine (TCM) has been widely developed against emergency conditions or acute illness for thousands of years,¹⁻⁴ though it is commonly believed in western communities that TCM may only have its efficacy in treating chronic diseases. The first Chinese clinical medicine handbook, *Zhouhou Bei Jifang (Elbow Reserve Emergency)*, was written in Eastern Jin dynasty by Ge Hong (A.D. 283-343). It documented the applications of herbal medicines, acupuncture and moxibustion to treat a variety of acute diseases.⁵ Moreover, artificial respiration was described in Tang dynasty (A.D. 653) by *Sun Simiao*, who was titled as King of Medicine in China, in one of his famous books *Beiji Qian Jin Yao Fang (Essential Formulas for Emergencies [Worth] a Thousand Pieces of Gold)*.⁶ There are many techniques in TCM that may possess considerable value in clinical practice against medical emergencies.

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Here, we selected four common TCM methods (Blowing air into the ear; Nose Insufflating Therapy; Acupuncture; and Moxibustion) targeting coma which may enhance the range of emergency treatments currently employed in modern emergency medical practice. We elucidate the specific techniques used for each method and detail the mechanism of action which is at the core of each technique. Finally, we provide a suggested path forward to develop the evidentiary data necessary to support the inclusion of these techniques in standard medical practice worldwide.

Practice and Mechanism

Blowing Air into the Ear

Early in Eastern Jin Dynasty, it has been proposed by Ge, Hong in *Elbow Reserve Emergency* that the continuous ear blowing of the air by the reed tube in each ear alternatively could rescue the person who suffered from the suicide-induced sudden death.⁵

It was originally documented in Huangdi Neijing [The Yellow Emperor's Classic of Internal Medicine], the first monograph of TCM, that an unconscious patient was saved by blowing air into the ear using the reed tube.^{5,7}

The blowing air travels through the external ear canal, vibrating the ear drum to elicit the nerve impulse from the cochlea. The Arnold's reflex on the relationship between the auricle and vagal regulation was first described by Germany anatomist Friedrich Arnold in 1832. He found that physical stimulation of the external ear canal could elicit a cough resembling to other cough reflexes induced by the vagal nerve. The Arnold's reflex regards the auricular branches of the vagus nerve, which is the only peripheral branch of the vagus nerve and mainly functions in most areas of the ear canal as its afferent nerve.⁸ It has been revealed that vagus nerve stimulation through the nucleus of the solitary tract not only modulates the ascending reticular activating system,^{9,10} but also enhances an essential pathway for arousal by inducing the release of norepinephrine in the thalamus.¹¹ Considering that the response induced by auricular branches of the vagus nerve is similar to that of the vagus nerve, delivery of the auricular branches of the vagus nerve fibers into the nucleus of the solitary tract upon ear stimulation could modulate both the autonomic nervous system and the central nervous system.⁷

Nose Insufflating Therapy

It has been documented in TCM that sudden deaths in patients who suffer from suffocation can be treated by

nasal blowing of medicine, aiming to improve Qi flow in the lung. The medicine was made of pieces of *Gleditsiae Sinensis Fructus*, the size of an almond, with Asarum. After being ground into the fine powder, the medicine was blown into the patient's nose using the reed tube continuously until the sneeze occurred indicating the sign of life.¹²

It is stated in Huangdi Neijing that the lungs open to the nose, meaning that the nose is the starting-point of the respiratory system, while the lungs control the breath through the nose. Therefore, the nasal delivery of medicines is potent to treat the respiratory arrest. The medicines used in TCM for the first-aid treatment of coma are commonly mobile and piercing such as Zao Jiao [*Fructus Gleditsiae*], Xi Xin [*Herba Asari Cum Radice*], Bing Pian [*Borneol*], She Xiang [*Moschus*], Sheng Ban Xia [*Rhizoma Pinelliae Tematae*] et al. Through the direct nose-to-brain delivery route,¹³ these medicines insufflated into the nasal cavity will reach the cerebrum, where the cerebral cortex will be activated to stimulate senses (eg vision from occipital lobe) as well as the viscera function regulated via prefrontal cortex to regain the patients' consciousness.

The blood-brain barrier presents a significant challenge for many neurological disorders primarily due to the limitation of uptake of the therapeutics. The endothelial cells connected by tight junctions in blood-brain barrier restrict the paracellular permeability of these agents.¹⁴ To overcome the blood-brain barrier, intranasal administration is a promising alternative pathway to intravenous or intracerebral drug delivery routes with advantages of being non-invasive and achieving high drug bioavailability in brain.¹³ As the only pathway to connect the brain with the outside environment,¹⁵ direct intranasal administration delivers the drug along both the olfactory or trigeminal nerves to their origins in the cerebrum and pons of the brainstem, respectively.^{16,17} More specifically, the drug is initially absorbed through the mucus layer in nasal cavity and then transported via either extracellular diffusion or intracellular endocytosis into the olfactory sensory neurons. Upon trafficking along the axon, the agent will be released in the synapse via exocytosis and then dispersed throughout the brain following certain neuronal pathways.¹⁶

Acupuncture

It has been stated in TCM that the immediate application of the triangle pyramid needle to puncture the Twelve Hand Jing Points can help remove the noxious blood

from patients who suffer from coma and/or excessive phlegm production induced by the emergent wind stroke. It is well known that the Twelve Hand Jing Point is the golden recipe to rescue all kinds of emergencies such as sudden deaths, coma and cholera. With regard to the wind stroke-induced unconsciousness, the acupoints that are commonly applied are Renzhong (GV 26), Zhongchong (PC 9), Hegu (LI 4).¹⁸

Acupuncture has been widely applied in China for thousands of years to improve the recovery of consciousness post coma or traumatic brain injuries. The acupoints commonly applied in first aid emergency to show the therapeutic efficacy are Renzhong (GV 26), Yongquan (K-1), Shixuan (EX-UE 11), Hegu (LI 4), and Neiguan (PC 6) et al. Propagated sensation along the channels describes that the sensation stimulated from the acupoint radiates through the peripheral nervous system and finally reaches to the central nervous system via defined channels passing the pathological site.¹⁹ Propagated sensation along the channels is essential to measure whether the therapeutic efficacy of acupuncture is satisfactory.¹⁹⁻²¹

It has been reported that acupuncture at Renzhong (GV 26) and Yongquan (K-1) inhibit the neurons in the brain of untreated rats. However, the nervous system was activated while stimulating the same acupoints in shocked rats.²² The inhibitory effects on propagated sensation along the channels in normal condition will be unleashed from whom with cerebral infarction, which significantly increases the excitability of the nerve cells to restore the cerebral functions.^{23,24} Moreover, acupuncture therapy also improves the patients' homeostasis by increasing the blood flow and oxygen supply in the traumatized brain area to promote the collateral circulation of the brain, the clearance of cerebral edema, and the proliferation of the astrocytes to repair the injury.²⁵⁻²⁷ Therefore, acupuncture is also advantageous in preventing the progression of secondary diseases involved in brain, lung and gastrointestinal tract due to neuroendocrine-related homeostasis disorders.

Studies demonstrated that acupuncture maintains the integrity of blood-brain barrier to protect the brain.²⁸ Application of transcutaneous electric acupoint stimulation in elder patients who have silent lacunar infarction can decrease the occurrence of postoperative delirium, which may be due to the reduction of blood-brain barrier permeability induced neuroinflammation alleviation.²⁹

Acupuncture also demonstrates its efficacy to treat many cardiovascular diseases by modulating the

autonomic nervous system to maintain homeostasis and restore energy balance.³⁰ The neurological-based mechanism has been revealed that stimulation of certain acupoints attenuates the sympathoexcitatory cardiovascular reflex responses.³¹ More specifically, upon the activation of Group III and IV muscle afferent neurons, the neural sensory input is propagated along to various brain regions such as hypothalamus, midbrain, and brain stem which are involved in the reduction of sympathetic pre-motor outflow and excitatory cardiovascular reflex responses to maintain homeostasis in cardiovascular system.³¹⁻³⁴

Moxibustion

Documentation of practices in TCM has revealed that the application of the moxibustion or the integration of moxibustion and acupuncture at the acupoints Baihui (DU-20), Qihai (BL-24), Shenque (RN-8), and Guanyuan (BL-26) can effectively treat Syncope (*Jue Zheng*) which is characterized as Qi deficiency.³⁵

According to TCM, the abdomen between the kidneys is considered where the source of life exists. The Ren Meridian, one of the eight extraordinary meridians known as the conception vessel, is a channel of pivotal importance to regulate the life-force energy (Qi) within the body. Moxibustion on particular points Qihai (BL-24), Shenque (RN-8), and Guanyuan (BL-26) along the Ren Meridian when people lose consciousness can stimulate the Yang Qi to maintain the fundamental energy level of the life.

The interaction between the gut microbiota and the brain has gained more interest and has become one of the hotspots in the field of neuroscience ever since the National Institute of Mental Health (NIMH) in the United States initially launched a research project with this focus in 2013.³⁶⁻³⁸ The gut-brain axis or brain-gut axis is a bidirectional communication network linking the central nervous system and the gastrointestinal tract along which lies in the enteric nervous system (the second brain) and the immune system.^{39,40} By taking advantage of the bidirectional manner, the influence between the gastrointestinal tract and the brain can be interchangeable. The information flowing from the brain to the gut relies on the vagal pathways that innervate the enteric nervous system to coordinate various functionalities of the gastrointestinal tract such as the nutrient absorption,^{41,42} the mucosal immune response modulation,^{43,44} et al. Vice versa, numerous factors including cytokines, neuropeptides and gut lipopolysaccharides released from the intestine, via spinal and vagus nerves, are involved in the regulation of central

nervous system process such as behavior, sleep and stress responses.⁴⁵⁻⁴⁷

More recent studies focus on elaborating the role of gut microbiome along with the gut-brain axis. The pathway including the gut microbiota is named as the brain-gut-enteric microbiota axis.⁴⁸ The microbiome in the gastrointestinal tract is shown to impact the central nervous system via the enteric nervous system through regulating the glial cells in the intestines.⁴⁹⁻⁵¹ Along with the progress in understanding the brain-gut-microbiota axis, it has been recognized as the potential therapeutic target for many neuronal and/or intestinal disorders. Stress plays a critical role on the interplay among the gut, microbiome, and brain in the development of inflammatory bowel disease, suggesting that the stress management therapy has its clinical potential in inflammatory bowel disease treatment.⁵² Evidence from preclinical and clinical studies revealed the essential function of gut microbiota in Alzheimer's disease and other neurodegeneration disorders, leading to the development of food-based therapy to modify the composition of gut microbes for Alzheimer's disease patients.⁵³ The dysfunction of brain-gut axis after a stroke involves the release of the damage-associated molecular patterns and cytokines induced by the injury, the migration of gut inflammatory and immune cells to the brain due to the leaky gut.⁵⁴ Recent studies showed that traumatic brain injuries compromise the intestinal barrier integrity to aid in the extrinsic infections to spread systemically, leading to the infection secondary to original brain damage.^{51,55,56}

Moxibustion is recognized as an effective therapeutic approach for many gastrointestinal tract disorders due to its low cost, convenience and non-invasiveness. Studies on the analgesic mechanisms of moxibustion for the treatment of visceral pain in irritable bowel syndrome revealed that the visceral hypersensitivity, brain-gut axis neuron endocrine system, and the immune system are highly regulated by the moxibustion action on meridian points.⁵⁷⁻⁶⁰ Acupuncture at Zusanli (ST-36) has also been shown to modulate the neural activity in the cerebrum, cerebellum, and limbic system from a functional magnetic resonance imaging study.⁶¹

Clinical Applications

Blowing Air into the Ear

Sufficient sensory inputs are essential in restoring the brain functions through the activation of the ascending reticular activating system in unconscious patients who are at

higher risk of developing sensory deprivation.⁶² For those who suffer severely from sensory deprivation, the supply of auditory stimulus is of great importance.⁶³ Several studies have demonstrated that the application of auditory stimulation on coma patients could be effective in improving the behavioral responses,⁶⁴⁻⁶⁸ though may not be sufficient to restore the consciousness.⁶⁸ Recently, vagus nerve stimulation has been employed as a less-invasive electric stimulation approach in patients who have disorders of consciousness. Results revealed that patients transitioned from the vegetative state/unresponsive wakefulness syndrome into the minimally conscious state upon the vagus nerve stimulation treatment, indicating the clinical potential of vagus nerve stimulation in patients with disorders of consciousness.⁶⁹

As a non-invasive approach, the direct air blowing through the auditory meatus significantly strengthens the signals to activate the vagus nerve and stimulate the ascending reticular activating system more effectively as compared to the application of regular external sound stimuli. In addition, the mechanical device based on the ear blowing technique can be developed to precisely control the parameters to standardize the operation process which will greatly reduce the demand of medical personnel. Therefore, it has a great potential in clinical application due to its easy operation, non-invasiveness and a lower burden on medical personnel.

Nose Insufflating Therapy

The direct nose-to-brain drug delivery is a short pathway bypassing the circulatory system. It is of great clinical importance to treat coma patients who usually develop cardiopulmonary arrest leading to a nonfunctional circulatory system. A case study revealed that aerosol inhalation of borneol is effective to raise awareness in a coma patient.⁷⁰ Application of borneol as a permeation enhancer, which opens the tight junctions between epithelial cells, has also been shown to improve the drug uptake in the brain from the nose.⁷¹

To optimize the efficacy in targeting the olfactory region, several novel delivery devices have been developed. VianaseTM developed by Kurve Technology combines a nebulizer to pulverize the medication and a vortex chamber to generate the flow,⁷² promoting the drug deposition to the olfactory region to maximize its brain uptake.⁷³ The insufflation method using pressurized gas to emit the drug or the patient's own exhalation force has also been applied in various designs of delivery devices.^{74,75}

The operational procedure of traditional Chinese nasal insufflating therapy is quite similar to the novel delivery systems as mentioned above. The medication needs to be ground into the fine powder and parched to increase its viscosity. The drug smoke is generated and blown into the patient's nose via the reed tube. Along with the elucidation of the nose-to-brain pathway, the nose insufflating therapy using the mobile and piercing Chinese medicines may have a great potential to be applied in clinic to rescue the coma patients.

Acupuncture

Acupuncture therapy, as a key element of TCM, has a long history in China to be applied to improve neurological impairment induced by stroke and hemiplegia.⁷⁶ The recent published comprehensive meta-analyses including 3511 patients from 49 trials evaluated the efficacy of acupuncture on disorders of consciousness recovery from traumatic brain injury. Significant higher efficiency in disorders of consciousness treatment following traumatic brain injury was found with the acupuncture group as compared to that with the control.⁷⁷

The World Health Organization has reported that acupuncture can be used to effectively treat 31 symptoms including cardiac pain, hypertension and arrhythmias.⁷⁸ Many studies revealed the therapeutic efficacy in hypertension, hypotension, arrhythmias, angina pectoris and myocardial infarction with the emphasis on acupoints Neiguan (PC 6) and Zusanli (E 36).^{79–82}

Nowadays, the application of acupuncture therapy also extends into the first-aid emergency treatment for cardiovascular diseases. Clinical trials to apply Yongquan (K-1) stimulation after basic and advanced cardiopulmonary resuscitation failure in 58 patients since 1987 achieved about 85% of the survival rate, indicating that Yongquan (K-1) resuscitation maneuver should be formally included in the cardiopulmonary resuscitation sequence protocol.^{83–86} In addition, a case report demonstrated that a 45-year-old woman with a previous history of two acute myocardial infarctions had a cardiac arrhythmia and neurocardiogenic syncope after 20 mins of walking. The acupuncture at Yintang (EX-HN 3) and Chengjiang (RN 24) stabilized her condition before the arrival of mobile ICU. It revealed that the combinatory application of Yintang (EX-HN 3) and Chengjiang (RN 24) had an immediate effect on the autonomic nervous system to regulate the homeostasis and energy balance in the body.³⁰

Moxibustion

With more advances developed in the gut-brain axis, appropriate modulation of the enteric nervous system and the gastrointestinal tract has gradually become a therapeutic target for enhancing the recovery from traumatic brain injury and stroke. Dramatic changes in gut microbiome composition have been reported following a traumatic brain injury which could further aggravate brain damage.⁸⁷ Fecal microbiota transplant, attempting to restore the normal gut microbes by taking the feces from a healthy donor has been successfully applied to treat irritable bowel syndrome and Crohn's disease.^{88,89} Probiotics have been shown to reduce the production of cytokines and intestinal permeability by regulating the gut-brain axis.^{90,91} Moxibustion and acupuncture on particular points stimulate the release of active substances involved in the gut-brain axis to regulate the central nervous system, the satisfactory clinical efficacy of which, as well as the mechanism of action, has been demonstrated in irritable bowel syndrome.⁵⁷ With regard to the advantages of being non-invasive, convenient, low-cost, and efficacious in modulating the gut-brain axis, moxibustion possesses a great clinical potential for promoting recovery from the brain injuries.

Path Forward

All four of these techniques have been successfully deployed for centuries. As described, the underlying mechanisms of action of all these methods are well founded and documented in the scientific literature. There is ample anecdotal evidence to support their continued use in coma related emergencies. Although a few techniques mentioned here have been adopted in modern first-aid methods, the recognition of using TCM techniques in the first-aid is still limited. Considering distinct mechanisms of action from different techniques, it is worth exploring various strategies by integrating multiple traditional techniques to enhance the efficacy and provide the alternative operations in first-aid. In addition, the key factor to limit the application of TCM techniques in emergency conditions is lacking the depth of published case studies or rigorous scientific investigations which provide sufficient independent, replicable data that support the effectiveness of these techniques. There have been several published studies reports that investigate and discuss the potential synergies between TCM and western medicine.

Table 1 Summary of Mechanism and Clinical Application of Four TCM Techniques

TCM Technique	Mechanism of Action	Clinical Application
Blowing air into the ear	Vagus nerve stimulation ↓ Activation of autonomic nervous system and central nervous system	Auditory stimulation in coma patients ⁶⁴⁻⁶⁹
Nose insufflating therapy	Piercing drug absorbed in nasal mucus ↓ Nose-to-brain activation of central nervous system	Borneol inhalation in coma patients ⁷⁰
Acupuncture	Acupoint stimulation ↓ Propagated sensation along the channels ↓ Activation of central nervous system & Autonomic nervous system	Traumatic brain injury ⁷⁷ Cardiovascular disease ^{30,83-86}
Moxibustion	Meridian point stimulation ↓ Brain-gut axis neuron endocrine system ↓ Activation of CNS	Irritable bowel syndrome ⁵⁷

This has included work by the World Health Organization on SARS as well as other investigations on topics such as diabetes and precision medicine.⁹²⁻⁹⁴ However, for emergency medicine, the lack of this type of independent data means these techniques will not be accepted into the toolbox of modern medicine regardless of their efficacy. Traditional Chinese medical hospitals offer the ideal opportunity to institute such investigations.

Traditional Chinese medical hospitals are found throughout China. Even though these hospitals specialize in TCM, many of these hospitals provide emergency services based on modern medical practices. This configuration, modern medical techniques practiced within a TCM-based hospital, offers the ideal opportunity to develop emergency medical protocols that can rigorously evaluate the effectiveness of the TCM techniques previously described both in conjunction with and independent of modern medical procedures. The development of data in this manner, at multiple traditional Chinese medical hospitals throughout China, will lead to the ability to publish case study and investigation results, positive or negative, in international journals. As data accumulates, this will enable hospitals world-wide to develop clinical trials to further evaluate these TCM techniques. This level of replicable data based on rigorously designed investigations will enable the medical community to make well-informed decisions on the incorporation of specific TCM techniques into their array of responses to coma related emergencies.

Conclusions

Though cardiopulmonary resuscitation has been the gold standard protocol in first-aid for cardiac arrest for decades, acute brain injuries induced from cardiac arrest, stroke and traumatic brain injury are the leading causes for permanent neurological deficits and deaths.^{95,96} Thus, brain-directed therapy, also known as cardio cerebral resuscitation, has become the main focus in first-aid medicine to demonstrate improved survival and cerebral function in patients.⁹⁷⁻⁹⁹ Here we discussed the mechanism and the clinical potential of four therapeutic options from TCM in first-aid medicine (Table 1). Blowing air into the ear and nose insufflating therapy exert direct stimulation on the central nervous system to promote the recovery of brain function. Acupuncture at certain points is able to maintain homeostasis by regulating the autonomic nervous system and protect the brain by preserving the integrity of blood-brain barrier. Taking advantage of the gut-brain axis, moxibustion can activate the central nervous system via the stimulation of the secondary brain in the intestines. Moxibustion at certain points such as Guanyuan (BL-26) and Qihai (BL-24) have shown satisfactory therapeutic efficacy in clinics to facilitate the energy level and homeostasis maintenance. It is worth mentioning that these TCM techniques stated here have great potential to be applied as immediate palliative interventions to relieve the emergency symptoms and increase the survival and recovery rate in patients in an effective and non-invasive manner. In addition, the follow-up identification of the cause of diseases

through appropriate diagnosis as well as the corresponding treatment towards the cause should be conducted in time and are of great importance to cure the patients.

These clinical practices described are a few examples taken from TCM, which possess significant merit in the modern first-aid medicine and may be applied in assistance in an emergency. By pursuing a path forward that develops and implements rigorous and critical scientific investigations, these techniques can be validated and add an important tool into emergency medical protocols ultimately leading to enhanced survivability and recovery of afflicted patients.

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Disclosure

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