Electroacupuncture treatment of arrhythmias in myocardial ischemia

John C. Longhurst

Susan SamueI Center for Integrative Medicine, Departments of Medicine, Physiology and Biophysics and Bioengineering, University of California, Irvine, California

INTegrATIVE MEDICINE, sometimes also called complementary and alternative medicine (or CAM), has been classified by the National Center for Complementary and Alternative Medicine into five domains, including 1) alternative systems of medical practice, like traditional Chinese medicine; 2) mind-body interventions, e.g., meditation; 3) biologically based therapies, such as dietary supplements; 4) manipulative and body-based methods, including for example chiropractic treatment; and 5) energy therapies encompassing biofield- and bioelectromagnetic-based applications. The Western medical and scientific communities have looked skeptically at most areas of integrative medical therapy because there has been an absence of prospective, adequately powered, randomized, and controlled clinical trials and because the mechanisms of action of these therapies have not been well defined. In this day of reductionist biology, allopathic physicians and scientists demand to know how these potential therapies work to fully understand how they might best be applied in disease treatment.

Over the last two decades there has been increased appreciation for the role of some integrative medical therapies in health care because we are beginning to understand the biological mechanisms that underlie their action. Acupuncture is one such therapy. Acupuncture is a 2,000-plus-year-old practice that began in China, initially to reduce pain but more recently to treat a variety of clinical problems ranging from symptomatic control of nausea and vomiting, depression and drug addiction, to hypertension and arrhythmias, among other conditions (12). The World Health Organization lists approximately 40 diseases for which there is some evidence of efficacy with acupuncture (18a). According to traditional Chinese medicine theory, successful treatment involves using needles that are manipulated or stimulated with a mild electrical current [manual and electroacupuncture (EA), respectively] at acupoints located along body-surface meridians or channels to restore energy balance.

Work that began in China two decades ago and continued in North America has identified a neural basis for the effect of acupuncture on the cardiovascular system. We now know that acupuncture stimulation at select acupoints activates group III and IV afferent pathways that provide input to a number of regions in the hypothalamus, midbrain, and brain stem that are concerned with cardiovascular regulation. Recent studies published in the Journal of Applied Physiology and the American Journal of Physiology and in other Western journals have demonstrated both short- and long-loop pathways that are activated by low-frequency (2–6 Hz), low-intensity (2–4 mA) electrical stimulation of acupuncture needles (11, 18, 22). The short-loop pathway immediately increases neural discharge activity in hindbrain medullary pressor areas such as the rostral ventrolateral medulla (RVLM), a region concerned with the regulation of sympathetic premotor activity. Conversely, prolonged electrical acupoint stimulation leads to an activation of long-loop pathways in the arcuate nucleus of the ventral hypothalamus and the ventrolateral periaqueductal gray in the midbrain. These two regions provide either direct or indirect inhibitory input that reduces reflex-induced activation of RVLM sympathetic premotor neurons and ultimately sympathetic outflow. We are now beginning to understand the neurotransmitter mechanisms that underlie sympathetic regulation of blood pressure. The initial excitation is mediated by glutamate acting through both N-methyl-D-aspartate (NMDA) and non-NMDA receptors (21). The long-loop-mediated inhibition of sympathetic activity by EA is related to opioid μ- and δ-opioid receptor activation (suggesting endorphin, endomorphin, and enkephalin involvement), as well as to nociceptin (5, 10). Acupuncture at selective acupoints overlying deep somatic nerves, rather than superficial or cutaneous nerves, appears to lower blood pressure when it is elevated but not when it is within the normal range (8). Hence, most studies evaluate the influence of acupuncture during sustained or reflex-related hypertension. Furthermore, the effectiveness of acupuncture is greatest at certain cardiovascular acupoints, like the ones along the pericardial meridian, overlying the median nerve of the forearm [pericardial meridian (P) 5 and 6, called Jiashii and Neiguan] or those along the stomach meridian overlying the deep peroneal nerve in the leg (ST 36, called Zusanli). This ability of some acupoints to strongly influence the cardiovascular system is called point specificity and is a property related to greater input from afferents in nerves underlying these acupoints to cardiovascular regulatory regions in the brain like the RVLM (17, 22). One interesting aspect of EA is the prolonged nature of its effects. Thirty minutes of EA can evoke inhibition of RVLM premotor sympathetic activity that lasts for over an hour after stimulation and can lower blood pressure in spontaneously hypertensive rats for more than 10–12 h (16, 19). These observations are consistent with preliminary clinical trials, which demonstrate that application of acupuncture once or twice a week over a 2-mo period lowers the blood pressure of patients with mild to moderate hypertension by 15–25 mmHg (unpublished observations).

In the early 1990s, several small studies suggested that acupuncture might reduce angina in patients with ischemic heart disease, especially the subgroup of responsive patients that demonstrate vasodilation during EA (1–3, 15). These clinical observations have been confirmed experimentally in cats instrumented to develop demand-induced ischemia (9). These studies have shown that acupuncture reduces myocardial ischemia by reducing oxygen demand, mainly through its effect in lowering reflex elevations in blood pressure, for example, during visceral organ stimulation.
Other studies employing electrical stimulation of the parafoveal region of the hypothalamus or the midbrain dorsal periaqueductal gray to induce the defense reaction and ventricular arrhythmias have shown that EA at acupuncture points located over deep somatic nerves, like the median nerve (P6) or deep peroneal nerve (ST 36), reduces the sympathoexcitatory response and the frequency of ventricular extrasystoles (6, 7). The article by Lujan and colleagues (13) published in this volume of the American Journal of Physiology, Heart and Circulatory Physiology extends these earlier observations. These investigators have shown in an elegant model of myocardial ischemia in conscious rats that EA improves the incidence of ischemia-reperfusion-induced ventricular tachycardia-ventricular fibrillation in association with reduced myocardial oxygen demand as estimated by the rate-pressure product. Ischemia was induced for 3 min followed by reperfusion, which in the untreated state typically caused ventricular tachycardia with hypotension, which evolved into ventricular fibrillation, if animals were not resuscitated. Thirty minutes of low-current, low-frequency EA at P 5–6 over the median nerve, but not control EA at the large intestine meridian (LI 6–7, called Pianli and Wenliu) over the superficial radial and cutaneous nerve branches in the forearm, reduced heart rate and blood pressure (the latter insignificantly) and decreased the incidence of ventricular tachycardia-ventricular fibrillation during reperfusion. The authors speculate that acupuncture reduced sympathetic outflow and possibly intracellular calcium, although it was not possible to measure calcium. The former conclusion seems warranted since the double product was reduced. The role of calcium as part of the EA response is less certain. One might also speculate that a lower myocardial oxygen demand might reduce the supply-demand imbalance and thereby reduce the extent of ischemia during vascular occlusion. It is interesting that heart rate but not blood pressure was significantly reduced, although there was an insignificant trend toward a decrease in blood pressure. This may be a function of stimulation in conscious rats, causing an alerting or excitatory response, or a type II statistical error related to the relatively small number of subjects (n = 14) studied in the active intervention group. The final issue to consider is the control group. Like all clinical interventions, acupuncture is associated with a placebo effect that can occur in up to 30% or more of the patients. Placebo responses could occur through handling the animals, while conditioning them to accept the acupuncture stimulation. In this study, the investigators initially used a control group that included handling and laboratory conditioning. However, previous reviews have suggested that acupuncture stimulation along a meridian at an inactive acupoint, termed the strong control, is more pertinent since it takes into account the additional electrical stimulation, including mild muscle contraction that occurs during low-intensity, low-frequency EA (14). This type of control was included in the present study and significantly increases the validity of its conclusions. Parenthetically, it is also possible to simple insert a needle at the active acupoint without either manual manipulation or electrical stimulation as a very valid control (20). Controls that utilize stimulation outside a meridian are less adequate since there is less chance to stimulate a major neural pathway and to produce the paresthesia that usually accompanies successful acupuncture, especially in conscious subjects, including either patients or experimental animals.

The study of Lujan et al. (13) is well done and helps to advance our knowledge about the potential clinical utility of EA. It is a clinically relevant model, and the conscious nature of the preparation and the strong control intervention to compare with the active intervention represent distinct advantages over previous studies in this area. However, the study does not really identify the mechanism by which EA reduces the ischemia-reperfusion-based arrhythmias. While alterations in calcium handling may be important, reduced sympathetic outflow to reduce the degree of ischemia or even improved blood supply are additional mechanisms that may be operative. Future studies will need to evaluate the underlying mechanisms in experimental preparations, and, clinically, it will be important to see whether EA can reduce the incidence or severity of arrhythmias in patients with myocardial ischemia or with sympathoexcitatory states and underlying cardiac pathologies that predisposes them to having serious arrhythmias. The potential of treating patients once or twice a week with EA may, in the future, serve as an adjunct or even as a replacement for antiarrhythmics in patients who either do not want to take these drugs or who have serious side effects that limit their use.

GRANTS

Work cited in this review was supported by National Heart, Lung, and Blood Institute Grants HL-63313 and HL-72125.

REFERENCES


